Disease Models & Mechanisms 6, 217-235 (2013) doi:10.1242/dmm.008243

A cell-based fascin bioassay identifies compounds with potential anti-metastasis or cognition-enhancing functions

Robert Kraft[1], Allon Kahn[1,*], José L. Medina-Franco[2], Mikayla L. Orlowski[1], Cayla Baynes[1], Fabian López-Vallejo[2], Kobus Barnard[3,4], Gerald M. Maggiora[5,6] and Linda L. Restifo[1,4,7,8,‡]

SUMMARY

The actin-bundling protein fascin is a key mediator of tumor invasion and metastasis and its activity drives filopodia formation, cell-shape changes and cell migration. Small-molecule inhibitors of fascin block tumor metastasis in animal models. Conversely, fascin deficiency might underlie the pathogenesis of some developmental brain disorders. To identify fascin-pathway modulators we devised a cell-based assay for fascin function and used it in a bidirectional drug screen. The screen utilized cultured fascin-deficient mutant *Drosophila* neurons, whose neurite arbors manifest the 'filagree' phenotype. Taking a repurposing approach, we screened a library of 1040 known compounds, many of them FDA-approved drugs, for filagree modifiers. Based on scaffold distribution, molecular-fingerprint similarities, and chemical-space distribution, this library has high structural diversity, supporting its utility as a screening tool. We identified 34 fascin-pathway blockers (with potential anti-metastasis activity) and 48 fascin-pathway enhancers (with potential cognitive-enhancer activity). The structural diversity of the active compounds suggests multiple molecular targets. Comparisons of active and inactive compounds provided preliminary structure-activity relationship information. The screen also revealed diverse neurotoxic effects of other drugs, notably the 'beads-on-a-string' defect, which is induced solely by statins. Statin-induced neurotoxicity is enhanced by fascin deficiency. In summary, we provide evidence that primary neuron culture using a genetic model organism can be valuable for early-stage drug discovery and developmental neurotoxicity testing. Furthermore, we propose that, given an appropriate assay for target-pathway function, bidirectional screening for brain-development disorders and invasive cancers represents an efficient, multipurpose strategy for drug discovery.

INTRODUCTION

A highly conserved actin-bundling protein, fascin has diverse roles in the developmental and physiological regulation of cellular morphology and function (Kureishy et al., 2002; Jayo and Parsons, 2010; Sedeh et al., 2010; Hashimoto et al., 2011). It is also implicated in human disease pathogenesis, under both loss-of-function and gain-of-function conditions, which motivated us to develop a fascin bioassay for drug discovery. Note that fascin is unrelated to either the fasciclins or neurofascin, which are members of the immunoglobulin cell-adhesion molecule superfamily. Fascin drives the formation of cell-membrane protrusions, including lamellipodia (Yamashiro et al., 1998), microspikes (Svitkina et al., 2003), filopodia (Vignjevic et al., 2006) and invadopodia (Li et al., 2010a), in part because F-actin bundles increase mechanical stiffness (Tseng et al., 2005; Vignjevic et al., 2006). In addition, fascin-mediated actin bundling and crosslinking, which are regulated by phosphorylation (Ono et al., 1997; Aratyn et al., 2007) and the extracellular matrix (ECM), enhance cell migration (Ono et al., 1997; Yamashiro et al., 1998; Anilkumar et al., 2003; Jawhari et al., 2003) and ECM degradation (Li et al., 2010a).

Mammals have three fascin-coding genes, of which *Fascin-2* and *Fascin-3* are expressed in narrow domains (Tubb et al., 2000; Tubb et al., 2002; Shin et al., 2010), whereas *Fascin-1* is broadly and dynamically expressed. Fascin-1 is abundant early in development, especially in the central nervous system (CNS) and migrating cells, and is then downregulated as cells mature (De Arcangelis et al., 2004; Zhang et al., 2008; Zanet et al., 2009; Tang et al., 2010). In this paper, 'fascin' refers to the product of the *Fascin-1* genes (*FSCN1* in humans, MIM#602689; *Fscn1* in mouse; and *singed* in *Drosophila*, FBgn0003447).

Fascin has a pivotal role in tumor invasion and metastasis (Machesky and Li, 2010), leading to the proposal that fascin-blocking drugs might prevent the spread of malignant cancers (Yoder et al., 2005; Hashimoto et al., 2011). Because most cancer-related deaths are due to metastases, there is an urgent need for development of anti-metastasis agents (Sporn, 1996; Sleeman and Steeg, 2010). For carcinomas from numerous organs, high fascin

[1]Department of Neuroscience, University of Arizona, Tucson, AZ 85721, USA
[2]Torrey Pines Institute for Molecular Studies, Port St Lucie, FL 34987, USA
[3]School of Information: Science, Technology and Arts and Department of Computer Science, University of Arizona, Tucson, AZ 85721, USA
[4]BIO5 Interdisciplinary Research Institute, University of Arizona, Tucson, AZ 85721, USA
[5]Translational Genomics Research Institute, Phoenix, AZ 85004, USA
[6]Department of Pharmacology and Toxicology, Arizona Health Sciences Center, Tucson, AZ 85724, USA
[7]Departments of Neurology and Cellular & Molecular Medicine, Arizona Health Sciences Center, Tucson, AZ 85724, USA
[8]Center for Insect Science, Arizona Research Laboratories, University of Arizona, Tucson, AZ 85721, USA
*Present address: College of Medicine, University of Arizona-Phoenix, 550 E. Van Buren Street, Phoenix, AZ 85004, USA
‡Author for correspondence (LLR@neurobio.arizona.edu)

Received 12 January 2012; Accepted 31 July 2012

TRANSLATIONAL IMPACT

Clinical issue

The findings reported here address two major clinical problems that do not initially seem related. First, invasive cancers, including most brain tumors, cause death due to invasion or migration, which are not inhibited by currently available cancer treatments. Second, developmental brain disorders are not treatable with drugs that enhance cognitive function. For both of these unmet medical needs, a major obstacle has been the lack of cellular bioassays for compound screening. The actin-bundling protein fascin links these two challenging clinical conditions: excess fascin promotes tumor invasion and metastasis, whereas insufficient fascin disrupts brain development. Thus, the fascin pathway represents a highly desirable drug target.

Results

The filagree phenotype of fascin-deficient mutant *Drosophila* neurons enabled the authors to develop a bidirectional in vitro cellular bioassay to screen for drugs that modify the fascin pathway. A library of 1040 known compounds (NINDS-II) was chosen on the basis of high molecular diversity, and was screened with the aim of identifying drugs that could be repurposed for new indications. Of these compounds, 81 were active as fascin-pathway modifiers. There was wide pharmacological and chemical-structure diversity in each set of active compounds (34 blockers and 48 enhancers), strongly suggesting that each set has multiple targets along the fascin pathway. Comparison of closely related compounds that differ in activity provided structure-activity relationship (SAR) hypotheses that can be tested in follow-up studies. Notably, all four of the statin compounds in the library caused a unique, reversible neurotoxic morphological effect characterized by intraneurite nodules containing aggregations of organelles ['beads-on-a-string' (BOS)]. Fascin deficiency enhances the sensitivity of neurons to BOS.

Implications and future directions

These findings introduce a conceptually simple cell-based fascin bioassay and apply it to identify many compounds and preliminary SAR information that can be pursued for drug development, either by repurposing or lead optimization. Fascin-pathway blockers could serve as anti-invasion and anti-metastasis agents for patients with malignant carcinomas or gliomas. Fascin-pathway enhancers could improve neurocognitive function and behavior in a subset of children with developmental brain disorders. The potential of fascin-pathway modifiers warrants testing in various mammalian models of fascin-sensitive human disease. In addition, bidirectional cell-based screening could be applied to other important biological pathways with dual functions in brain development and tumor invasion.

The authors propose that the statin-induced BOS they observed represents a cellular correlate of statin-associated cognitive side effects experienced by some patients on statins. Because cholesterol is an essential nutrient in *Drosophila*, this system provides a unique opportunity to study statin-mediated neurotoxicity separately from cholesterol biosynthesis. The authors' demonstration that genetic background impacts the sensitivity of neurons to statin-induced BOS suggests experiments to identify potential human genetic risk factors for statin-associated cognitive deficits. More generally, this primary neuron culture system in *Drosophila* holds great promise as a neurotoxicity screening platform with the ability to identify biologically relevant gene-by-environment interactions.

expression levels are associated with increased invasiveness and earlier patient death (Machesky and Li, 2010). Fascin is also involved in tissue infiltration by circulating tumor cells (Kim et al., 2009a). Similar associations have been reported for malignant glioblastomas (Peraud et al., 2003; Roma and Prayson, 2005; Gunal et al., 2008), which are prone to extensive dispersion within the CNS (Giese et al., 2003).

The causal role of fascin in tumor phenotypes is supported by laboratory studies in which blocking of fascin expression reduced the invasive and/or metastatic properties of colon carcinoma (Hashimoto et al., 2007), glioblastoma multiforme (Hwang et al., 2008), gastric carcinoma (Fu et al., 2009; Kim et al., 2010) and breast carcinoma (Chen et al., 2010; Al-Alwan et al., 2011). Moreover, migrastatin-family compounds, which are potent inhibitors of tumor invasion and metastasis in the laboratory (Shan et al., 2005), bind to fascin and inhibit its actin-bundling activity (Chen et al., 2010). Thus, the experimental and clinical data strongly suggest that a fascin bioassay would be of great value for discovery of drugs with anti-invasion and/or anti-metastasis activity.

Fascin is also required for normal brain development (Yamakita et al., 2009) (R.K. and L.L.R., unpublished data), plausibly by regulating neuronal differentiation (Deinhardt et al., 2011; Marín-Vicente et al., 2011). Fascin insufficiency or dysregulation might underlie disorders of brain development and plasticity, resulting in intellectual disability (Kraft et al., 2006). Fascin regulation is likely to be faulty in the brain-development disorders Rubinstein-Taybi syndrome (Roelfsema and Peters, 2007) and tuberous sclerosis (Ess, 2006), which are caused by mutations in *CREBBP* (MIM#600140) and *TSC1* (MIM#605284) or *TSC2* (MIM#191092), respectively. *FSCN1* is an upregulated transcriptional target of CREB binding protein (CREBBP) (Megiorni et al., 2005), whereas fascin protein is a target of the TSC1-TSC2 complex (Gan et al., 2008).

The connection between fascin and brain plasticity has also been revealed by unbiased proteomics screens. Reduced fascin levels were found in two mouse models of absence epilepsy (Ryu et al., 2007; Ryu et al., 2008) and after long-term memory induction (Li et al., 2010b). These data suggest that fascin levels are downregulated by neural activity, perhaps to permit synapse-structure changes. By contrast, fascin levels were elevated in a polytransgenic mouse model of Down syndrome (Shin et al., 2007). This could be a molecular feature of the brain-development disorder or early-onset neurodegeneration, or both. In a neuron-culture model of neuroprotection, rapid induction of ischemic tolerance was associated with ubiquitylation of fascin, which was subsequently degraded, as well as with transient retraction of dendritic spines. This is consistent with the idea that fascin removal allows dissolution of actin bundles, thereby accelerating synapse remodeling (Meller, 2009). Finally, in a canine model of aging, slowing of cognitive decline by environment and diet was associated with reduced levels of fascin carbonyl, a marker of oxidation (Opii et al., 2008). This suggests that preventing fascin oxidation contributes to better cognitive performance. These reports point to a role for fascin in regulating neuronal differentiation and synaptic plasticity, which are disrupted in brain-development disorders (Johnston, 2004) and vulnerable during aging (Burke and Barnes, 2006). Hence, pharmacological enhancers of fascin expression or function could be beneficial for diverse neurodevelopmental and cognitive or behavioral conditions.

Loss-of-function *Fascin-1* mutations are available in *Drosophila melanogaster* and *Mus musculus*. The targeted *Fscn1* disruption in the mouse causes structural brain abnormalities and high rates of neonatal death (Yamakita et al., 2009). *Drosophila* has a single fascin-coding gene (Bryan et al., 1993; Kureishy et al., 2002), named *singed* for the gnarled bristles of mutant flies (Bender, 1960; Cant et al., 1994; Tilney et al., 1995; Wulfkühle et al., 1998). Wild-type *singed* function is also essential for oogenesis (Cant et al., 1994), blood cell migration (Zanet et al., 2009) and some aspects of brain

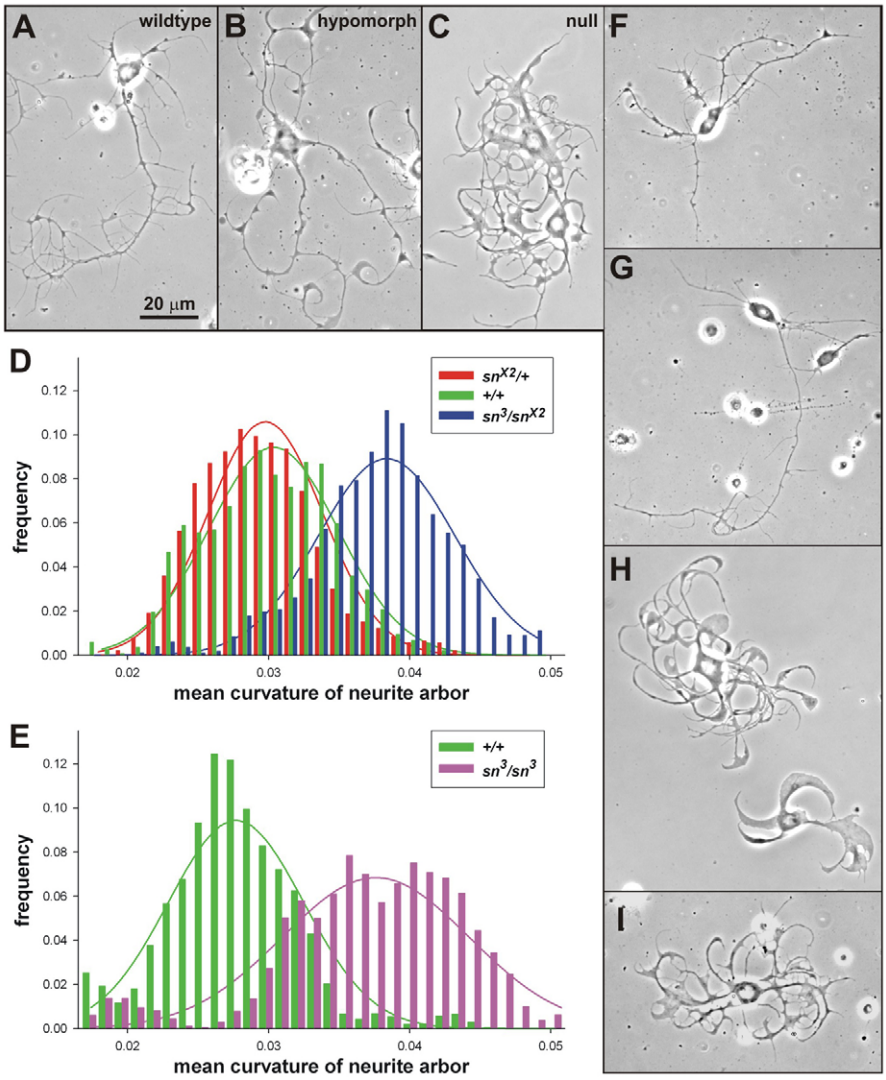


Fig. 1. Genetic and pharmacological modification of neurite curvature. (A-C,F-I) Phase-contrast images (60×) of neurons cultured for 3 d.i.v. from the CNS of wandering third instar larvae. Magnification is the same throughout. (A-C) Loss-of-function *singed* mutations increase neurite curvature and disrupt proximal-to-distal tapering. (A) Wild-type (sn^+/sn^+), *OreR-C* laboratory strain. (B) A partial loss-of-function (hypomorphic) mutation (sn^3/sn^3) causes a moderate filagree phenotype. (C) A null mutation (sn^{X2}/Y) causes a severe filagree phenotype. (D,E) Mean curvature distributions of neurite arbors of cultured neurons with differing genotypes, plotted with soft binning. Normal-distribution curves were fit to each population and scaled (*y*-axis) to the corresponding histograms. (D) Genetically marked γ-MB neurons. The increased curvature of sn^3/sn^{X2} (blue) neurons is easily seen. The similarity of $sn^{X2}/+$(red) and sn^+/sn^+ (green) curvature distributions demonstrates that filagree is recessive. (E) Random CNS neurons. The mean neurite curvature distribution of sn^3/sn^3 mutant neurons (magenta) is significantly increased over that of wild-type (sn^+/sn^+, *OreR-C*) neurons (green). (F-I) Exposure to drugs in vitro can modify the filagree phenotype of fascin-deficient sn^3/sn^3 neurons. (F,G) Two examples of filagree decreasers (fascin-pathway enhancers): estradiol propionate, 50 μM (E) and Anisindione, 50 μM (G). Neurite curvature, especially of terminal neurites, is reduced and the smooth proximal-to-distal tapering is restored. (H,I) Two examples of filagree increasers (fascin-pathway blockers): griseofulvin, 50 μM (H) and acetyltryptophan, 50 μM (I). Note the exaggerated neurite curvature and frequent expansions of neurite width.

development (R.K. and L.L.R., unpublished data), but not for viability (Bender, 1960). We discovered that *singed* mutations cause a neuronal morphogenesis defect, 'filagree', when developing mutant CNS neurons are cultured in vitro (Kraft et al., 2006). Filagree neurite arbors have exaggerated clockwise curvature and erratic variation in neurite caliber, but no reduction in length, branching or axon-dendrite ratio (Kraft et al., 2006). Filagree neurons have striking disruptions of their actin cytoskeleton which, like other *singed* phenotypes, can be explained by failure of actin bundling (Cant et al., 1994; Guild et al., 2003; Kraft et al., 2006; Zanet et al., 2009). Because decreasing fascin function causes increasing severity of the filagree phenotype, we reasoned that cultured neurons could provide a cellular bioassay for fascin function.

The use of a *Drosophila* cell-based fascin bioassay for drug discovery is justified by the phylogenetic conservation of fascin (Hashimoto et al., 2011) and of the pathways underlying cognition (Greenspan and Dierick, 2004; Inlow and Restifo, 2004; Bolduc and Tully, 2009), tumor invasion and metastasis (Miles et al., 2011). Here we present the results of a bidirectional screen for pharmacological modifiers of the filagree neuronal morphogenesis defect.

RESULTS

Drug screen design using the fascin bioassay

Filagree is a highly penetrant, quantifiable, pan-neuronal phenotype of fascin-deficient *singed*-mutant neurons cultured from the developing CNS of *Drosophila* mature larvae or young pupae (Fig. 1A-C) (Kraft et al., 2006). This developmental interval corresponds to high levels of *singed* transcript accumulation in wild-type CNS (Kaitlin L. Bergfield, R.K. and L.L.R., unpublished). The filagree phenotype is so distinctive and so consistent that trained observers can easily distinguish *singed*-mutant versus wild-type population cultures, typically containing 1500-2000 neurons each. In fact, both humans and a computational method for neurite-curvature quantification can classify individual photomicrographs of mutant or wild-type neurons with ≥90% accuracy (Kraft et al., 2006). To anticipate how much restoration of function would be required to rescue the fascin-deficient filagree phenotype, we asked whether filagree is recessive, like other *singed* phenotypes. We quantified the neurite-curvature distributions of wild-type and $sn^{X2}/+$ cultured larval CNS neurons, which have 100% and 50% of normal fascin function, respectively (Fig. 1D). The two distributions were statistically

indistinguishable, whereas neurons from sn^3/sn^{X2} (a near-null genotype) and $sn^{X2}/+$ were very different (Welch's *t*-test, $P<1\times10^{-18}$; Fig. 1D). Therefore, the results show that the *singed* neurite-curvature phenotype is recessive and that rescue of *singed*-mutant neurite-arbor morphology requires no more than 50% of wild-type fascin function.

A bidirectional drug-screen design requires that the baseline neuronal morphology be intermediate and distinct from both wild type (Fig. 1A) and *singed*-null (sn^{X2}/Y; Fig. 1C), allowing detection of both drug-induced worsening and drug-induced rescue of the filagree defect (Fig. 1B). The neurite-curvature distributions of the severe hypomorph, sn^3/sn^3 (Fig. 1B), and the wild-type (Fig. 1A) were significantly different (Welch's *t*-test, $P<1\times10^{-13}$; Fig. 1E), with greater overlap of distributions than between wild type and sn^3/sn^{X2} (Kraft et al., 2006). This is consistent with the relative function among the genotypes. Moreover, the sn^3 mutation leaves the fascin open reading frame intact, allowing small amounts of normal protein to be produced (Paterson and O'Hare, 1991; Cant et al., 1994). Thus, sn^3/sn^3 neurons have a desirable neuronal phenotype, and contain some wild-type fascin protein that can serve as a drug target.

The striking nature of the filagree defect makes it suitable for use in a modifier screen based on direct phenotype observation. Using an approach that parallels genetic-modifier screens commonly performed with model organisms, we conducted a chemical screen to identify small molecules that induce obvious changes in neuronal phenotype. Compounds were tested at 10 μM and 50 μM by adding them to the cultures at the time of plating the dissociated neurons, and evaluating their effects on the filagree phenotype after 3 days in vitro (d.i.v.). Thus, the neurons were exposed to the drug during the entire period of neurite-arbor morphogenesis. To facilitate the drug-screening process, we replaced quantitative analysis of immunostained images of randomly sampled neurons with holistic scoring by phase-contrast microscopy of populations of living cells, typically 1500-2000 neurons per ~50-mm^2 culture well.

Selection and diversity analysis of the NINDS-II compound collection

Inspired by striking examples of new uses for existing drugs, we took a 'repurposing' approach, also called 'repositioning' or 'indication switch' (Ashburn and Thor, 2004; Dueñas-González et al., 2008). For example, minoxidil was developed as an oral anti-hypertensive drug, but is now most popular as a topical treatment (e.g. Rogaine®) for hair loss (Zins, 1988). More dramatic is the repurposing of thalidomide, much-maligned for its teratogenic effects when taken during pregnancy (Ito and Handa, 2012), but now used to treat multiple myeloma, a bone marrow malignancy (Palumbo et al., 2008). Repurposing screens have the advantage of testing compounds whose pharmacology and side-effect profiles are partially understood.

Because fascin acts in diverse pathways (Jayo and Parsons, 2010; Hashimoto et al., 2011), modification of the filagree defect could occur through several potential drug targets, including but not limited to fascin itself. This called for a chemically diverse screening library. The new indications, including brain tumors and neurodevelopmental disorders, made good representation of neuroactive compounds highly desirable. A collaboration between the National Institute of Neurological Disorders and Stroke (NINDS) and the private sector (Heemskerk, 2005) produced a screening library of 1040 compounds (NINDS-II; supplementary material Table S1), comprised primarily of FDA-approved drugs for diverse indications, as well as natural products and laboratory reagents; many of these compounds are neuroactive. Screens of the NINDS-II library with various assays and protocols identified drugs with potential utility for Huntington's disease, spinomuscular atrophy, amyotrophic lateral sclerosis (ALS), stroke and familial dysautonomia (Aiken et al., 2004; Piccioni et al., 2004; Slaugenhaupt et al., 2004; Stavrovskaya et al., 2004; Rothstein et al., 2005; Vincent et al., 2005; Wang et al., 2005a; Wang et al., 2005b; Desai et al., 2006). The antibiotic ceftriaxone was protective in diverse neurodegeneration assays, leading to Phase III clinical trials for ALS (Traynor et al., 2006) (ClinicalTrials.gov identifier NCT00349622). This library does not contain any migrastatin-family compounds.

We evaluated the chemical diversity of the NINDS-II compounds (Fig. 2) based on: (i) the types and distribution of molecular scaffolds (Bemis and Murcko, 1996; Singh et al., 2009), (ii) measures of molecular similarity based on shared substructural features (Willett et al., 1998) and (iii) the chemical-space distribution of the compounds (Maggiora and Shanmugasundaram, 2011). The 1040 compounds of the collection are distributed over 617 scaffolds (Fig. 2B), of which 551 are cyclic systems. The highly populated scaffolds (Fig. 2C) are indoles, pyridines, quinolines and sterols, common among drug-like small molecules. Indicative of high diversity, 77% (424) of the cyclic scaffolds are singletons, i.e. populated by a single compound. From the perspective of the compounds, ~60% of them cover ~23% of the cyclic scaffolds. In other words, this relatively small collection allows sampling of a relatively large number of scaffolds. The molecular fingerprint, based on 166 structural features (Fig. 2D), of each compound was compared pair-wise with all others, and the Tanimoto coefficients were computed as measures of similarity (Maggiora and Shanmugasundaram, 2011). Overall molecular diversity is inversely proportional to the average Tanimoto similarity for all pair-wise comparisons. For the NINDS-II library, low similarity values (mean 0.295; median 0.284) reflect high diversity and compare favorably to those of the ~1500-compound DrugBank database (Wishart et al., 2008; Singh et al., 2009). The distribution of compounds in 'chemical space,' where the similarity of any pair is inversely related to the distance between them (Maggiora and Shanmugasundaram, 2011), was represented in a three-dimensional (3D) plot (Fig. 2E,F). The compounds are spread throughout the space, reflecting the high diversity of the collection. In summary, the high diversity of the modestly sized NINDS-II collection make it an efficient tool for conducting the first compound screen on the basis of the first fascin bioassay.

A bidirectional drug screen reveals diverse fascin-pathway enhancers and blockers

Of the 1040 compounds tested, 81 (7.8%) were active in the fascin bioassay at 10 and/or 50 μM concentrations, based on holistic scoring. We identified both drug-induced decreasers and increasers of the filagree phenotype (Figs 1, 3, 4; Table 1). Filagree decreasers (fascin-pathway enhancers; supplementary material Table S2) rescued the neurite-arbor shape defect of fascin-deficient mutant neurons, allowing them to extend neurites with normal trajectory and tapering (Fig. 1, compare F and G with A). Filagree increasers (fascin-pathway blockers; supplementary material Table S3)

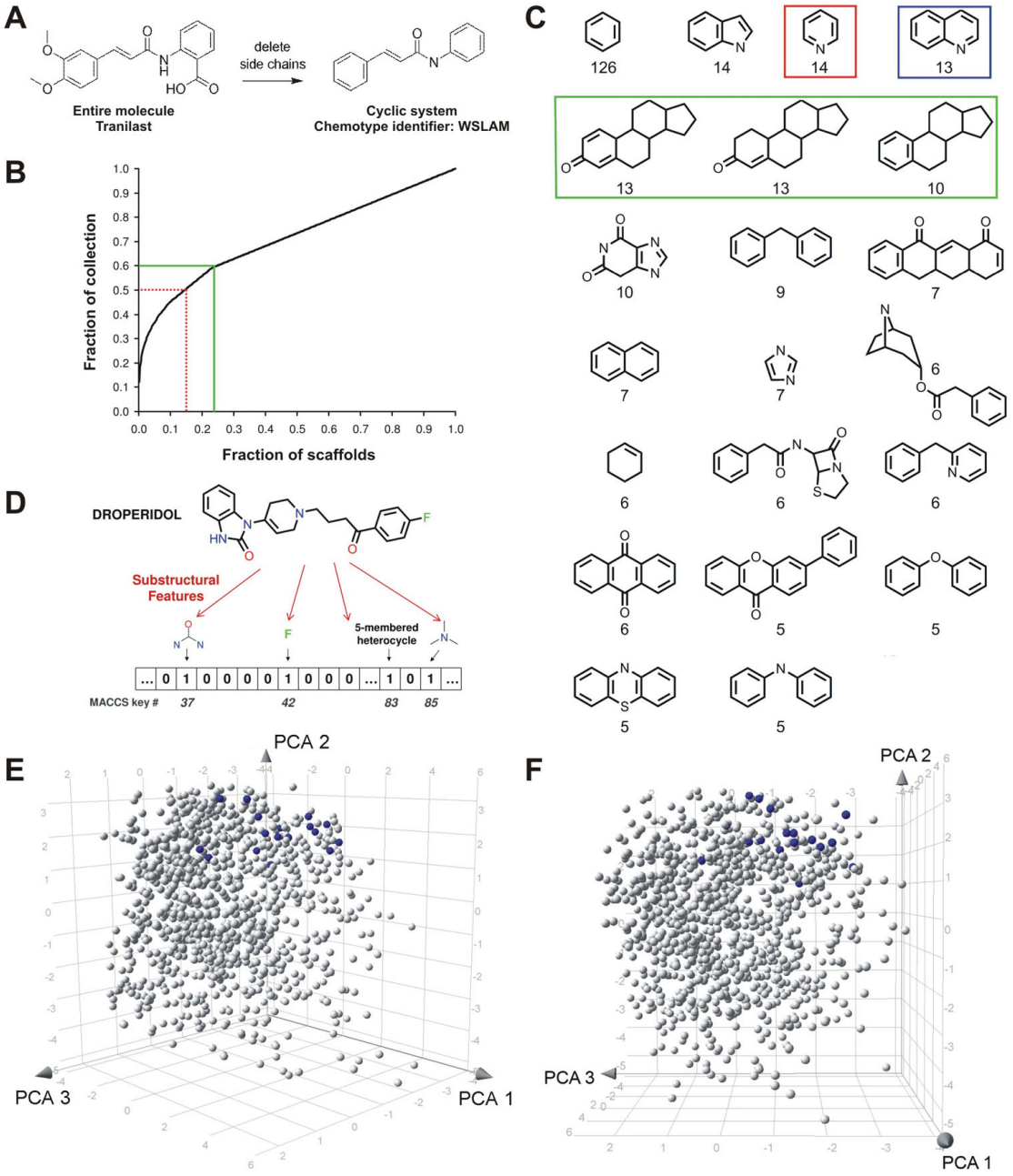
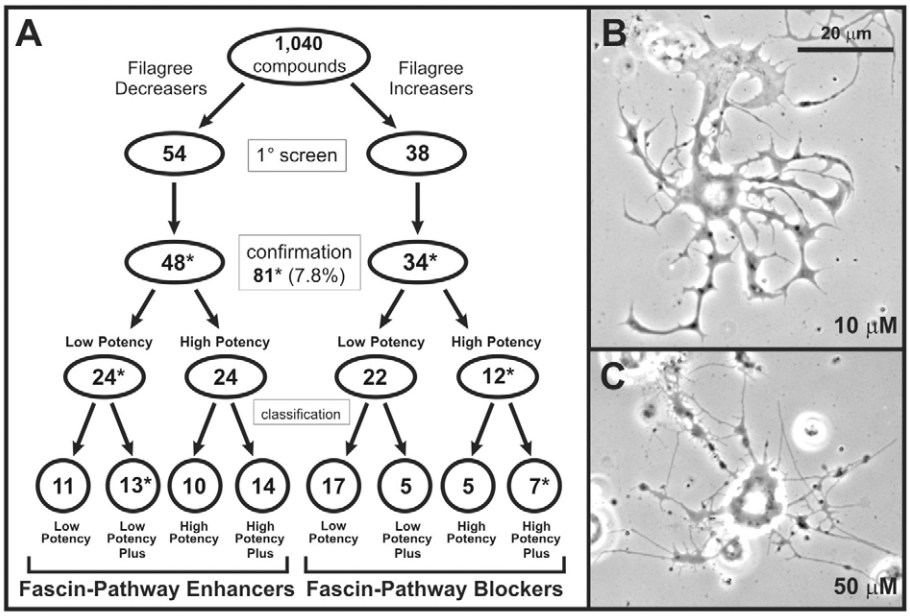


Fig. 2. Molecular diversity of the NINDS-II compound collection screened in this study. (A) Relationship between a molecule and its scaffold, using tranilast as an example. The scaffold or cyclic system is obtained after iteratively removing the side chains and is identified by a five-character chemotype identifier code. The WSLAM scaffold is a singleton, i.e. tranilast is the only compound in the collection with this scaffold. (B) Scaffold-recovery curve. The *x*-axis represents the scaffolds, organized left-to-right from the most common (benzene) to the singletons, plotted as a cumulative fraction of the total (552, with all 66 acyclic systems considered a single scaffold). The *y*-axis shows the cumulative fraction of the 1040 compounds occupied by a given fraction of the scaffolds: ~14% of the scaffolds contain 50% of the NINDS-II library (red lines), and 60% of the library is distributed over ~24% of the scaffolds (green lines). Beyond this point, each scaffold is a singleton and the relationship becomes linear. (C) Common scaffolds in the NINDS-II library. 2D representations of cyclic systems found with a frequency ≥5; the number is under each structure. Highlighted are the pyridines (red), the quinolines (blue), and the scaffolds containing a four-ring sterol (green; 36 compounds). (D) Representation of chemical fingerprint analysis based on MACCS keys, using the antipsychotic drug droperidol as an example. Each of 166 possible substructural features is coded using a bit score: present at least once (1) or absent (0). Four of droperidol's features (CN_2O, fluorine, five-membered heterocycle and C_3N) are shown with their positions in the MACCS keys bitstring. (E,F) 3D representations of the NINDS-II library in chemical space, obtained by principal component analysis (PCA) of the similarity matrix computed using MACCS keys and Tanimoto similarity. Each compound is shown as a sphere. The chemical space distribution of the compounds is extensive, with regional variation in population density. The 17 antipsychotic drugs (blue), are localized to a medium-sized sector of the space and interspersed among compounds with other activities. This is consistent with these drugs occupying 14 scaffolds and representing several different pharmacological mechanisms of action. (E) View centered on the vertical (PCA 2) axis. (F) The view obtained by rotation around the vertical axis. One antipsychotic drug is hidden behind another compound.



D

Therapeutic Class (# compounds)	Fascin-Pathway Enhancers (filagree decreasers)					Fascin-Pathway Blockers (filagree increasers)				
	High Potency			Low Potency		High Potency			Low Potency	
	Simple	+ Cyto-toxicity	+ Morph. effects	Simple	+ Morph. effects	Simple	+ Cyto-toxicity	+ Morph. effects	Simple	+ Morph. effects
Analgesic, Anti-inflammatory (8)	1			1	1	2		1	2	
Antibacterial (9)	2			1	3			1	2	
Antimicrobial (fungal, parasitic) (15)		4	1	1	4		1	1	3	
Antiviral (2)				1					1	
Cancer (13)	3	4		1	2			2		1
Cardiovascular or Cerebrovascular (11)		1	3	3		1			3	
CNS (11)	1	1		1	4	2			1	1
Endocrine: Diabetes (2)				1						1
Endocrine: other (4)	1			1					1	1
Pulmonary (3)	1			2						
Skin (5)		1		1	1				2	
Ulcers (3)	1	1							1	
Other[a] (8)				3	2	1		2		
None known (8)	1	2	1					1	2	1

Fig. 3. Summary of the fascin bioassay-based drug screen. (A) Compounds were screened by holistic scoring for their ability to modify the filagree phenotype, revealing two classes of activity, filagree decreasers (fascin-pathway enhancers) and filagree increasers (fascin-pathway blockers). One compound, cloxyquin, had dose-dependent activity (asterisk) and is counted in both groups. Confirmed active compounds were classified as 'high potency' (active at 10 and 50 μM) or 'low potency' (active at only 50 μM). Further classification distinguished between simple actives and those with cytotoxicity at the high dose or morphological effects (Plus). (B,C) Phase-contrast photomicrographs after 3 d.i.v. Cloxyquin increased the filagree phenotype at 10 μM (B), but decreased the filagree phenotype at 50 μM (C). (D) Therapeutic classes of filagree-modifying compounds, based on clinical and laboratory data. A compound may be in more than one therapeutic class. 'Other' includes compounds used for drug overdose, local anesthesia, gout, eye surgery, allergy, as homeopathic remedy or as insecticide. See supplementary material Tables S2 and S3 for information on chemical class, pharmacology and therapeutic use.

worsened the clockwise curvature and further disrupted neurite tapering, as seen in the fascin-null-mutant neurons (Fig. 1, compare H and I with C).

Compounds with activity at 10 μM were considered 'high potency' whereas those with activity only at 50 μM were considered 'low potency'. The 48 fascin-pathway enhancers were split equally between low- and high-potency compounds; the 34 fascin-pathway blockers included 22 low- and 12 high-potency compounds (Fig. 3A). Cloxyquin was the only compound with a bimodal effect, acting as a filagree increaser at 10 μM, but as a filagree decreaser at 50 μM (Fig. 3B,C). Within each potency class, we made a distinction between 'simple' actives (21 fascin-pathway enhancers, 22 fascin-pathway blockers) and those with other effects on the neurons beyond filagree modification (Fig. 3A,D; see below). The compounds of each activity group span a broad range of therapeutic indications (Fig. 3D; supplementary material Tables S2, S3).

When active compounds were re-tested for quantification of neurite curvature, we found that holistic scoring is relatively insensitive and very likely to underestimate true drug potencies. For example, the antifungal agent griseofulvin, initially identified as a low-potency fascin-pathway blocker (Fig. 1H), was active at both 10 μM (P=0.011) and 50 μM (P=0.0002), causing a dose-dependent increase in neurite curvature. Surprisingly, the mushroom body γ-neurons (γ-MB neurons) in the griseofulvin-treated cultures failed to show a significant change in neurite curvature at either 10 μM (P=0.13) or 50 μM (P=0.08). This also raises the question of whether any of the ten filagree-modifying compounds whose activity failed to replicate in confirmation tests

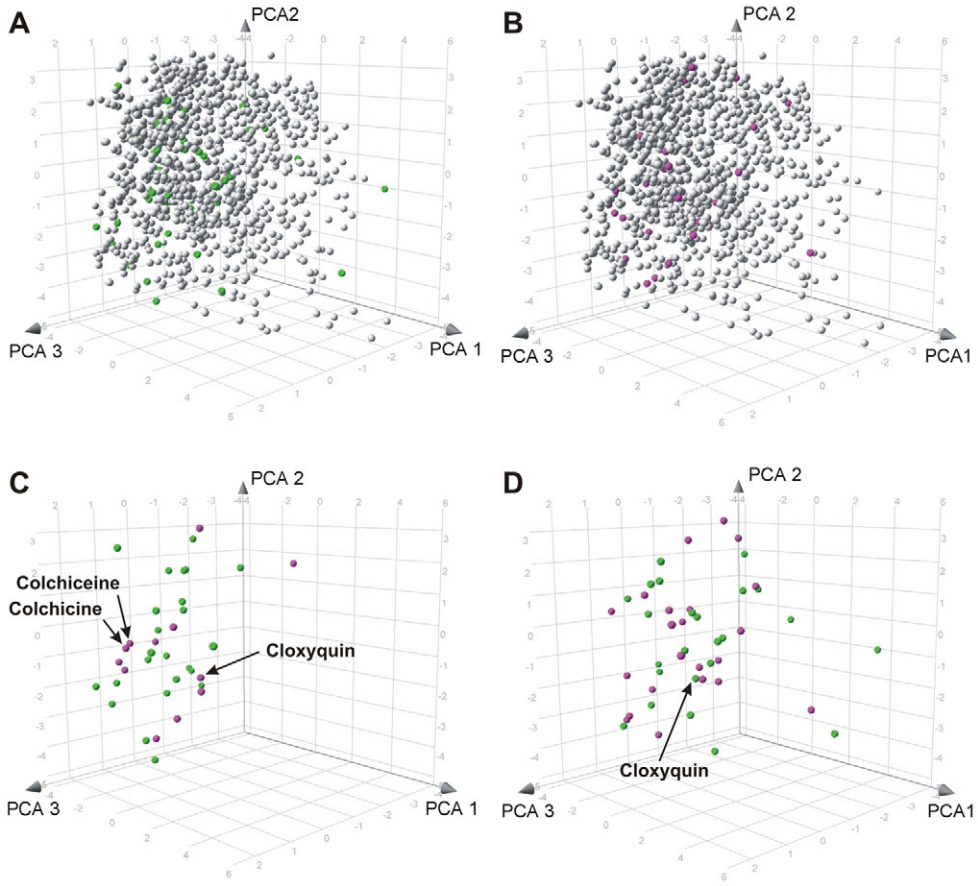


Fig. 4. Chemical space distribution of compounds active in the fascin bioassay. 3D views of the chemical space occupied by NINDS-II, centered on the vertical (PCA 2) axis and highlighting different subsets of fascin-pathway modifiers. (A,B) Each class of active compounds is distributed throughout a large fraction of the chemical space occupied by the whole collection. Each compound is represented as a sphere with (A) the 48 fascin-pathway enhancers in green and (B) the 34 fascin-pathway blockers in magenta against the gray background of the inactive compounds. (C,D) Fascin-pathway modifiers of the same potency class, plotted in contrasting colors without the whole collection. Within each class, there is some intermingling of compounds with opposite activities, and some clustering of compounds with the same activity. (C) High-potency fascin-pathway enhancers (green; 24) and blockers (magenta; 12). (D) Low-potency fascin-pathway enhancers (green; 24) and blockers (magenta; 22). See supplementary material Fig. S2 for chemical structures of all active compounds.

(Fig. 3A) might have been too close to the detection threshold by holistic scoring, but nonetheless have some activity. This highlights the differential drug sensitivity of classes of neurons in the fascin-deficient brain. It is therefore possible that we did not detect drugs whose effects were restricted to neuron subtypes.

The 3D chemical-space distribution of the 48 fascin-pathway enhancers (filagree decreasers) and 34 fascin-pathway blockers (filagree increasers) are shown plotted against the background of the compound collection (Fig. 4, A and B, respectively). Each set of active compounds is quite diverse, as indicated by its distribution throughout the chemical space of the collection without obvious localization to any particular neighborhood. A notable exception is the pair of high-potency fascin-pathway blockers, colchicine and colchiceine (Fig. 4C), which are closely related alkaloids that differ only by a methyl group (Tanimoto similarity 0.956). When the fascin-pathway enhancers and blockers were plotted together in chemical space, many instances of intermingling between the two were seen among both high- and low-potency active compounds (Fig. 4, C and D, respectively). The chemical structures of the high-potency simple actives are shown in Fig. 5, along with 2D chemical-space plots. The ten simple high-potency fascin-pathway enhancers (Fig. 5C) and the five simple high-potency fascin-pathway blockers (Fig. 5D) each belong to a different scaffold.

Consistent with this level of structural diversity, the active compounds represent diverse chemical classes and wide-ranging pharmacological mechanisms of action (supplementary material Tables S2, S3). For example, drugs that directly impact neurotransmitter systems were found among both fascin-pathway enhancers (acetylcholine, adiphenine HCl, mephenesin, metaraminol bitartrate, spaglumic acid) and fascin-pathway blockers (amantadine, baclofen, imipramine, spiperone). Several of the steroid hormones in the library were fascin-pathway enhancers (cyproterone, estradiol acetate, estradiol propionate, methylprednisolone). Among the fascin-pathway modifiers were two dozen antimicrobial agents, including antibacterial, antiviral, antifungal and anti-amoebic compounds.

Neither pharmacological nor chemical class reliably predict the direction of activity in the fascin bioassay. Of two sulfanilamide-type antibacterial agents, one (sulfamethoxazole) was a fascin-pathway blocker and the other (sulfamethazine) was a fascin-pathway enhancer. Four non-steroidal anti-inflammatory drugs that inhibit cyclooxygenase (COX) were fascin-pathway blockers (diflunisal, naproxen, salicin, suprofen), whereas other COX inhibitors, including diclofenac and ibuprofen, were inactive. The diversity of the active compounds suggests that multiple drug targets and mechanisms are operative, which is consistent with a screen based on a pathway that is regulated at multiple levels (Jayo and Parsons, 2010). These considerations led to further analysis of the chemical structures of active compounds and their inactive relatives.

Structure-activity relationships of fascin-pathway enhancers and blockers

Due to the complexity of any cell-based assay, the activity of a compound can be affected by its transport, metabolism, binding

Table 1. Compounds active in the fascin bioassay

Compound	Potency and activity category[1]
Fascin-pathway enhancers	
5-Nitro-2-(3-phenylpropyl-amino)-benzoic acid[2]	High, S
Acetylcholine	Low, M
Acetylcysteine	Low, S
Adiphenine HCl	Low, S
Amlodipine besylate	High, M
Anisindione	Low, S
Apigenin	Low, M
Atorvastatin calcium	High, M
Benzyl isothiocyanate	Low, M
Bithionol	Low, M
Caffeine	Low, M
Carbenoxolone sodium	High, S
Cefditorin pivoxil	Low, M
Ceftriaxone sodium	Low, S
Chloroacetoxyquinoline	High, C
Ciclopirox olamine	Low, M
Cloxyquin	Low, M
Cyclocreatine	High, S
Cyproterone	High, S
Deguelin(–)	High, C
Dyclonine HCl	Low, M
Dyphylline	High, S
Emetine dichloride	High, M
Estradiol acetate	Low, S
Estradiol propionate	High, S
Gedunin	High, C
Geneticin	Low, S
Hydroxytacrine maleate	Low, M
Juglone	High, C
Lasalocid sodium	High, C
Mechlorethamine	Low, S
Mephenesin	High, S
Metaraminol bitartrate	Low, S
N-Formylmethionyl-phenylalanine	High, C
Oxaprozin	Low, M
Oxcarbazepine	Low, M
Palmatine chloride	High, S
Pomiferin	High, C
Prednisolone	Low, S
Pyrvinium pamoate	High, C
Rosolic acid	High, M
Rosuvastatin	High, M
Spaglumic acid	Low, S
Sulfamethazine	High, S
Sulfasalazine	High, S
Tannic acid	High, C
Thiothixene	Low, M
Tolbutamide	Low, S

Table 1. Continued

Compound	Potency and activity category[1]
Fascin-pathway blockers	
4′-Demethylepipodophyllotoxin	High, M
Acetyltryptophan	Low, S
Amantadine HCl	Low, S
Aminolevulinic acid HCl	Low, S
Azadirachtin	High, M
Baclofen	Low, M
Broxyquinoline	High, C
Citrinin	Low, M
Cloxyquin	High, M
Colchiceine	High, M
Colchicine	High, M
Diflunisal	High, S
Econazole nitrate	Low, S
Griseofulvin	Low, S
Hydroflumethiazide	Low, S
Imipramine HCl	High, S
Iopanic acid	Low, M
Metoprolol tartrate	Low, S
Naproxen(+)	Low, S
Nateglinide	Low, M
Nifedipine	High, S
Oxybenzone	Low, S
Paclitaxel	Low, M
Picropodophyllotoxin	High, M
Propylthiouracil	Low, S
Salicin	Low, S
Sarafloxacin HCl	Low, S
S-Nitroso-*N*-acetylpenicillamine[3]	Low, S
Spiperone	High, S
Sulfamethoxazole	Low, S
Suprofen	High, S
Telenzepine HCl	Low, S
Triadimefon	Low, S
Vinburnine	Low, S

Compounds are listed alphabetically.
[1]S, simple (only neurite trajectory affected); C, cytotoxicity at 50 μM; M, morphological effects.
[2]NPPB.
[3]SNAP.

to the molecular target(s) or a combination thereof. Nonetheless, small subsets of structurally similar compounds in the NINDS-II collection allowed us to conduct a preliminary analysis of structure-activity relationships (SARs) (Fig. 6) based on the concept of activity landscapes. Analogous to geographical landscapes, the latitude and longitude correspond to the position of a molecule in a 2D chemical space, and the altitude corresponds to its activity in a given assay. Because structurally similar compounds tend to have similar biological activities (Johnson and Maggiora, 1990), regions of active molecules in an activity landscape tend to resemble rolling hills. In some cases, however, similar molecules have significantly

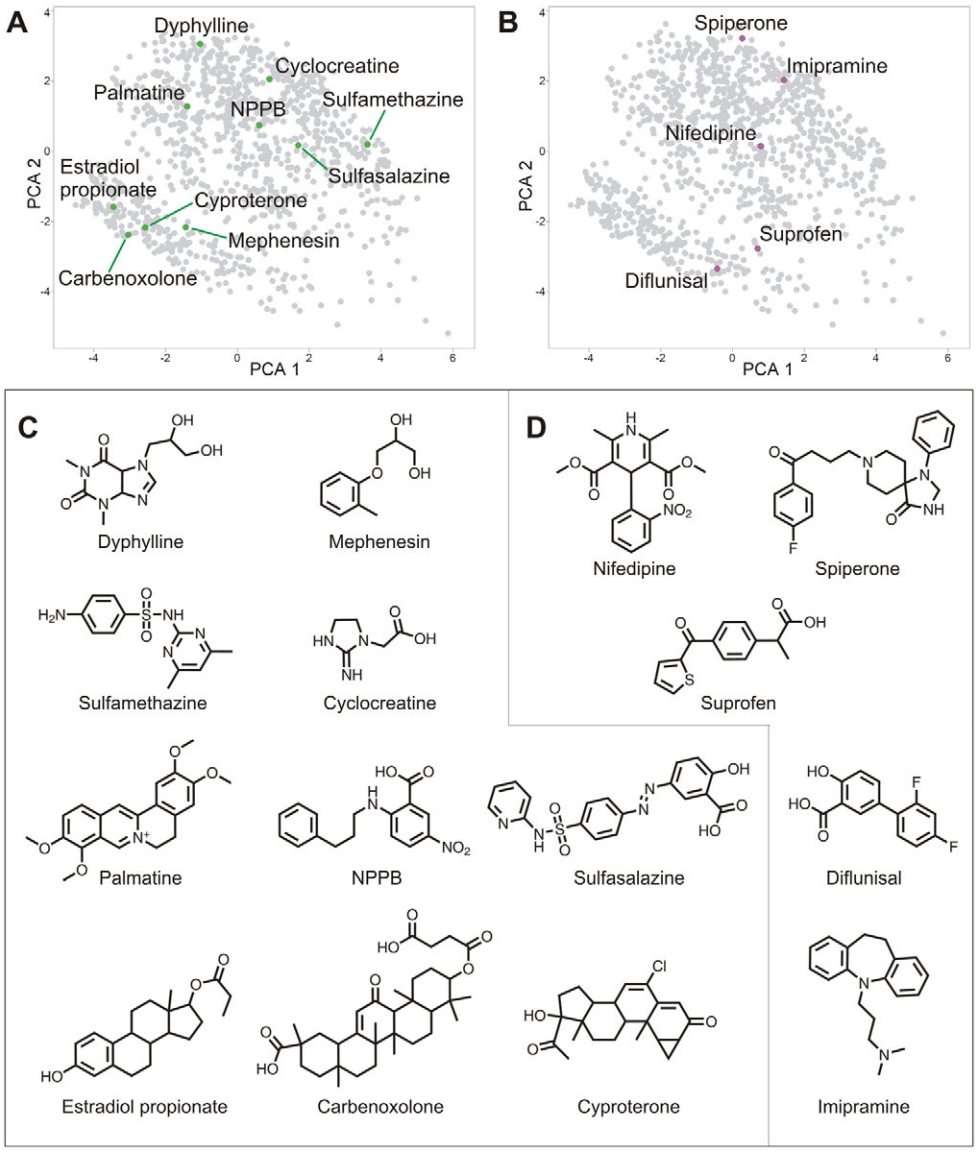


Fig. 5. Structures of high-potency simple fascin-pathway enhancers and blockers. (A,B) 2D chemical-space distributions of the high-potency simple filagree modifiers plotted against the background of the NINDS-II compound collection in gray. Each compound is represented as a circle; due to the projection, some compounds are hidden from view. (A) Ten fascin-pathway enhancers (green). (B) Five fascin-pathway blockers (magenta). (C,D) 2D chemical structures of the high-potency simple filagree modifiers. Within each class, there is considerable structural diversity. (C) Fascin-pathway enhancers. (D) Fascin-pathway blockers.

different activities, leading to cliff-like features. These activity cliffs contain significant information on SARs because they identify relatively small yet biologically relevant structural features associated with the dramatic changes in activity (Maggiora and Shanmugasundaram, 2011). We evaluated cases in which high-potency fascin-pathway enhancers (Fig. 6A-C) or blockers (Fig. 6D-F) were structurally very similar to low-potency or inactive compounds. By comparing the structures at the top of each cliff with those at its base, we could infer which structural features are necessary for activity. In some cases, the SAR hypotheses were also informed by the physical and/or chemical properties of the active and inactive compounds.

Comparing estradiol propionate with estradiol acetate (diminished activity) and two inactive estradiols (similarity to estradiol propionate ≥0.94), the key structural feature appears to be the substituent on the carboxy moiety (Fig. 6A, green ovals). Removing a methyl group lowers the activity, whereas lengthening the alkyl chain (estradiol valerate) or adding a terminal cyclopentane ring (estradiol cypionate) renders the compounds inactive. Because the steroid moiety remains unchanged, it can be inferred that the size of the carbon chain on the carboxy moiety is a crucial structural determinant of fascin-pathway enhancement.

For the high-potency fascin-pathway enhancer sulfamethazine, the focus is the pyrimidine ring, which is dimethylated in the active compound (Fig. 6B, green circles). Three inactive sulfonamides, sulfamerazine, sulfadiazine and sulfapyridine (with similarities to sulfamethazine of 0.98, 0.96 and 0.88, respectively), have reduced numbers of methyl substituents (Fig. 6B, asterisks). In sulfapyridine there is also a carbon atom replacing one of the nitrogens in the pyrimidine ring (Fig. 6B, green arrow). Because removing one or two methyl substituents renders the compound inactive, the importance of removing the ring nitrogen cannot be interpreted. Nevertheless, we can infer that dimethylation of the pyrimidine ring is important for activity. The high-potency fascin-pathway enhancer mephenesin was compared with the structurally related but inactive guaifenesin

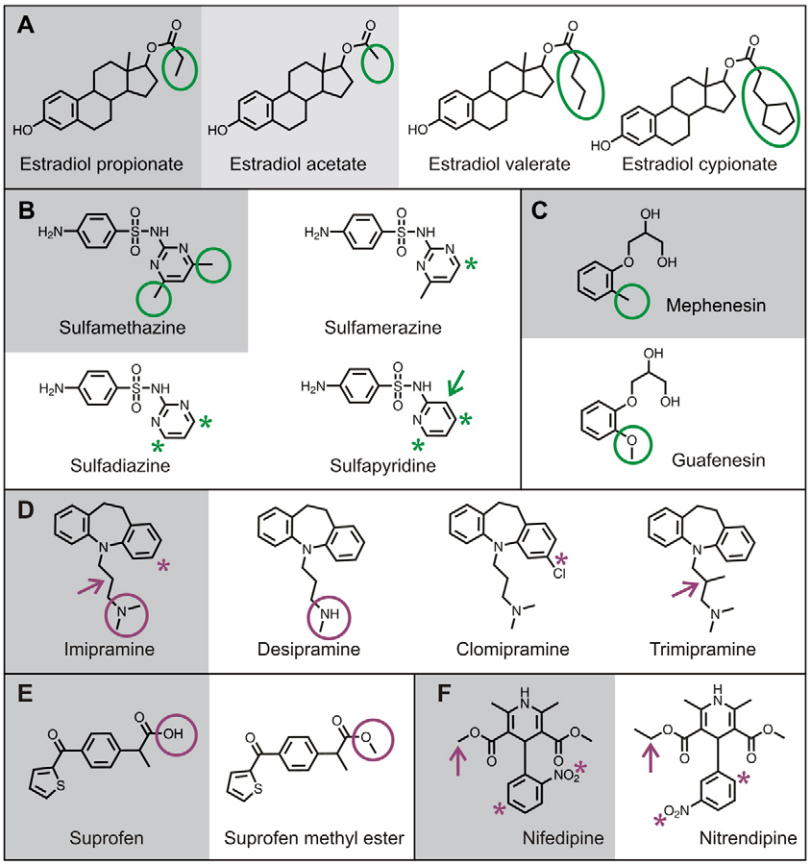


Fig. 6. SAR analysis based on activity cliffs. (A-F) High-potency fascin-pathway modifiers (gray background) compared with structurally similar low-potency (light gray background) or inactive (white background) compounds. The highlighted substructures can be inferred to influence activity in the fascin bioassay. (A-C) Fascin-pathway enhancers (green highlights). (A) Estradiol propionate: the size of the side chain (oval) on the carboxy group on the sterol D ring is associated with activity, suggesting that in estradiol acetate the side chain is too small, whereas in estradiol valerate and cypionate, it is too large. (B) Sulfamethazine: activity is associated with dimethylation (circles) of the pyrimidine ring. Removal (asterisk) of one (sulfamerazine) or both (sulfadiazine and sulfapyridine) methyl groups is associated with loss of activity. (C) Mephenesin: replacement of the methyl group with a methoxy group in guaifenesin (circles) is associated with lack of activity. (D-F) Fascin-pathway blockers (magenta highlights). (D) Imipramine: in three other tricyclic compounds, single changes are associated with lack of activity. Desipramine is lacking a methyl group of the alkyl nitrogen (circles); clomipramine has a chloride on one of the aromatic rings (asterisks); trimipramine has a methyl substitution in the middle of the alkyl chain (arrows). (E) Suprofen: replacement of a hydrogen with a methyl group (circles) creates suprofen methyl ester, which is inactive. (F) Nifedipine: two changes, the position of the nitro group on the aromatic ring (asterisks) and addition of a methyl group (arrows), are associated with lack of activity of nitrendipine.

(similarity 0.87), which differs only by the replacement of the methyl substituent in the phenyl ring by a methoxy group (Fig. 6C, green circles). Thus, it can be inferred that activity is sensitive to substitution at that position of the phenyl ring.

The high-potency fascin-pathway blocker imipramine differs by a single change from each of three inactive tricyclic compounds, with similarities to imipramine of 0.93, 0.91 and 0.88 (Fig. 6D). Desipramine, an imipramine metabolite produced in the mammalian liver, lacks a methyl group on the alkyl nitrogen (Fig. 6D, circles). On the basis of experimentally determined dissociation constants, desipramine is a considerably stronger base than imipramine (Shalaeva et al., 2008). Hence, it has a harder time losing a proton to cross the plasma membrane and enter the neuron. This suggests that access to an intracellular target could be a factor controlling activity of tricyclic compounds in the fascin bioassay. For clomipramine, the single substitution of a chlorine atom on one aromatic ring (Fig. 6D, asterisks) eliminates activity. Lastly, trimipramine differs only by the presence of a methyl substitution on the alkyl chain (Fig. 6D, arrows). From these observations, it can be inferred that three distinct features are essential for imipramine activity.

In Fig. 6E, the high-potency fascin-pathway blocker suprofen is compared with its inactive methyl ester (similarity 0.82). Replacement of a hydrogen atom by a methyl group might disrupt activity because the acid moiety in suprofen is undoubtedly ionized in solution. Thus, the active form of suprofen is most probably an anion, whereas the inactive ester is uncharged. The high-potency fascin-pathway blocker nifedipine has two structural differences from its inactive analog nitrendipine (similarity 0.90). First, nifedipine has a methyl ester whereas nitrendipine has an ethyl ester (Fig. 6F, arrows). Second, the nitro group (Fig. 6F, asterisks) is in the *ortho* position in nifedipine, but in the *meta* position in nitrendipine. This change might affect the 3D conformation of nifedipine or indicate that a specific orientation of the nitro group is required for activity.

Other drug effects on cultured neurons

Roughly half of the actives had effects beyond modifying the filagree phenotype (Fig. 3A,D; Table 1; supplementary material Tables S2, S3), which we classified as cytotoxicity or morphological effects. Cytotoxicity was defined as apparent cell death without a neurite arbor (Fig. 7A,B) or, rarely, degeneration of neurites after formation of an arbor (data not shown). A subset of high-potency fascin-pathway modifiers caused overt cytotoxicity at the 50-µM concentration. Some inactive compounds also caused cytotoxicity. Distinctive morphological effects, the most common of which was reduced neurite outgrowth (Fig. 7E,F,H-K), were caused by both active and inactive compounds. Less common, but more dramatic, were changes in neuronal cell-body size or shape (Fig. 7C,D) and bizarre alterations in neurite morphology (Fig. 7C-E,G-K).

Within the NINDS-II library, 22% of the compounds are experimental (i.e. research reagents) rather than marketed pharmaceuticals or drugs that have been tested in clinical trials (supplementary material Table S1, Status column). Experimental compounds were over-represented in the cytotoxic-at-high-dose (54%) and morphological-effects (31%) groups, and were under-

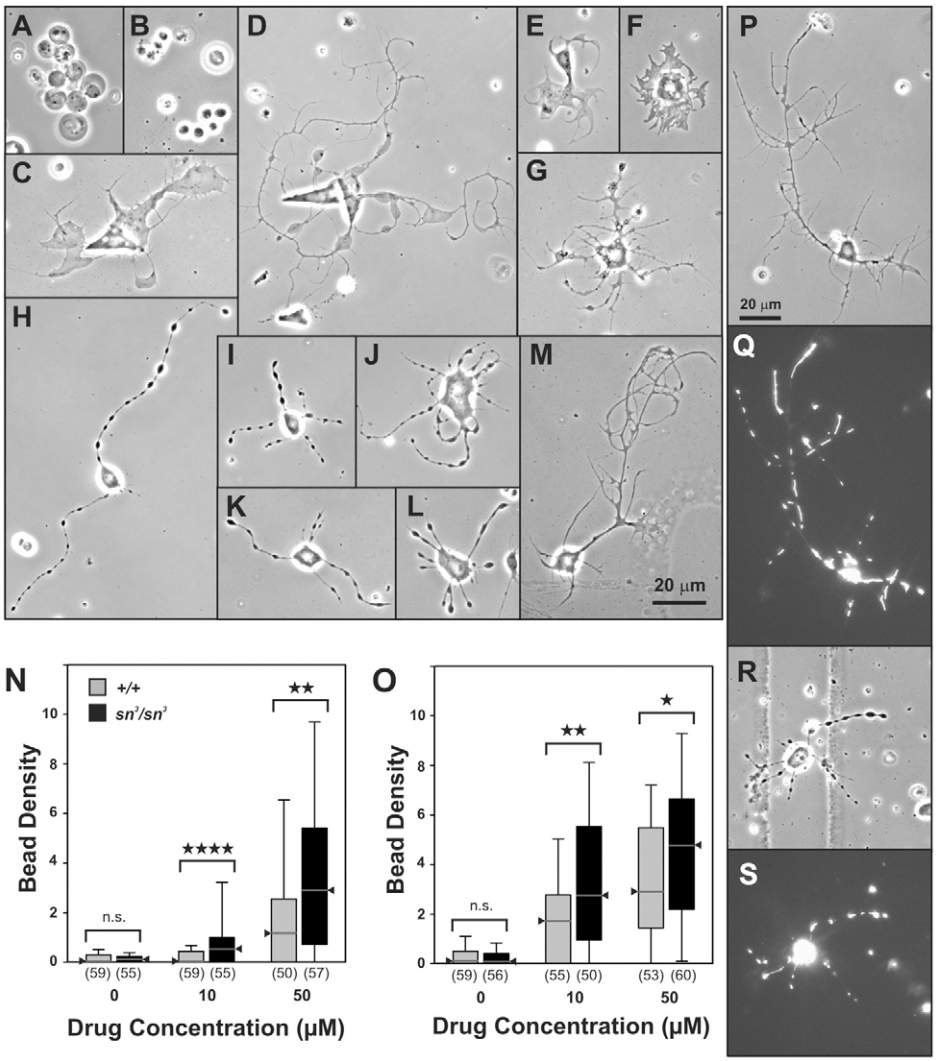


Fig. 7. Neurotoxic morphological defects revealed in primary neuron culture. (A-M) Phase-contrast images (60×) of CNS neurons from sn^3/sn^3 (A-K) or wild-type (*OreR-C*; L-M) wandering third instar larvae, cultured for 3 d.i.v. with the following drugs (scale bar in M for images A-M): (A) tannic acid, 50 μM; (B) 3-3′-diindolylmethane; (C) ginkgolic acid, 50 μM; (D) tegaserod maleate, 50 μM; (E) azadirachtin, 50 μM; (F) 4′-demethylepipodopyllotoxin, 10 μM; (G) usnic acid, 10 μM; (H) atorvastatin, 50 μM; (I) rosuvastatin, 50 μM; (J) lovastatin, 50 μM; (K) pravastatin, 50 μM; (L) atorvastatin, 50 μM; (M) no-drug control. (N-O) The statin-induced BOS defect is modulated by genetic background. Box-plot distributions of the bead density (beads per 100 μm) along neurites of wild-type (+/+; gray) or fascin-deficient mutant (sn^3/sn^3; black) larval neurons cultured for 3 d.i.v. with pravastatin (N) or rosuvastatin (O) at the indicated concentrations. The median is indicated by the triangle. The top and bottom of the box represent the 75th and 25th percentiles, respectively; the top and bottom 'whiskers' represent the 90th and 10th percentiles, respectively. The number of neurons analyzed is indicated in parentheses below each group. At both concentrations, the mutant neurons are more sensitive than the wild-type neurons to the BOS effect of the statins (Mann-Whitney Rank Sum test). n.s., not significant; **P*<0.05; ***P*<0.01; *****P*<0.0001. (P-S) BOS beads contain mitochondria (scale bar in P for images P-S). Wild-type larval neurons expressing a GFP-tagged mitochondrial protein cultured for 3 d.i.v. and imaged live by phase-contrast (P,R) or fluorescence microscopy (Q,S). (Grid lines on the dish floor are visible behind the neuron in R.) In the no-drug control cultures (P,Q) GFP-tagged mitochondria are distributed as clusters or linear aggregates scattered throughout the neurite arbor, with a range of sizes and densities. In the atorvastatin-treated cultures (R,S), the GFP-tagged mitochondria are localized almost exclusively to the beads.

represented among the simple fascin-pathway modifiers (16%). It is not surprising that compounds with well-established toxicity, such as the sodium pump inhibitor ouabain and the protein synthesis inhibitors cycloheximide and anisomycin, had overt cytotoxic effects on cultured neurons. Similarly, the ionophore lasalocid, a high-potency fascin-pathway enhancer with cytotoxicity at 50 μM, is a known neurotoxin (Safran et al., 1996). Hence, much of the neurotoxicity among the active compounds was caused by molecules that are not drugs in the strict sense of the repurposing strategy. In many cases, synthetic chemistry can be used to modify such parent compounds to produce analogues that retain the desired activity but have reduced toxicity (e.g. Harrap, 1985).

Statin-induced BOS defect is modified by genetic background

Beads-on-a-string (BOS) is a striking morphological defect that was induced solely by the four statins in the library: atorvastatin,

lovastatin, rosuvastatin and pravastatin (Fig. 7H-K). Wild-type neurons are also susceptible to the BOS defect when cultured with any of these four statins (Fig. 7L and data not shown). BOS has two components, ovoid intracellular nodules distributed along the length of the neurites and reduced neurite outgrowth (Fig. 7, compare L with M). These four statins differ in their potency of HMG-CoA reductase inhibition (White, 2002), and this paralleled their potency to induce BOS. Pravastatin and lovastatin induced BOS only at 50 μM, whereas rosuvastatin and atorvastatin did so at both 10 μM and 50 μM (Fig. 7N,O and data not shown). BOS was reversible when the culture media was replaced with drug-free media; the beads resolved and neurite outgrowth was markedly accelerated (data not shown). Using a transgenic GFP-tagged mitochondrial protein (Pilling et al., 2006), we found that the beads contained aggregations of mitochondria (Fig. 7P-S). The appearance of statin-induced beads is consistent with disrupted microtubule transport (Pilling et al., 2006), which would also contribute to reduced neurite outgrowth.

Because statin-induced myopathy is affected by genetic variants (Niemi, 2010), we tested the hypothesis that sensitivity of *Drosophila* neurons to statin-induced BOS is influenced by genotype. We compared the bead density of wild-type and fascin-deficient *singed*-mutant neurons in response to incubation with a low-potency (pravastatin) and a high-potency (rosuvastatin) statin. For both drugs at both 10 μM and 50 μM, fascin deficiency significantly enhanced the sensitivity of cultured neurons to statin-induced BOS (Fig. 7N,O).

DISCUSSION

The fascin pathway as a drug-discovery target

Motivated by the importance of fascin function in tumor invasion, as well as in brain development and plasticity, we designed and conducted a screen for pharmacological modifiers of the fascin pathway. By using primary cultured neurons in a cell-based assay, we avoided the disadvantages of immortalized cell lines and made use of the fact that dissociated mutant neurons can reveal cellular phenotypes with a magnitude far greater than that in the intact brain (Kraft et al., 2006; Liu et al., 2007; Chen and Herrup, 2008; Sawallisch et al., 2009). The filagree phenotype of fascin-deficient neurons, which is associated with a marked disruption of actin cytoskeleton organization (Kraft et al., 2006), causes a striking exaggeration of the intrinsic tendency of cultured neurites to turn clockwise (Tamada et al., 2010). This cell-based assay, with its easily observable morphological read-out, allowed us to cast a wide net, targeting the pathway without trying to predict a priori which molecule (fascin or one of its regulators or mediators) would be the best drug target for modulating fascin function. By choosing a well-characterized hypomorphic *singed* mutation, we were able to screen simultaneously for fascin-pathway blockers and enhancers in cells containing small amounts of wild-type fascin protein that could potentially serve as a drug target. Despite the limited sensitivity of holistic scoring, by screening a diverse collection we identified diverse high-potency compounds in both activity classes.

Fascin-pathway blockers identified in the *Drosophila* neuronal fascin bioassay are predicted to inhibit tumor invasion. Malignant glioblastoma represents a particularly challenging clinical problem because these cells migrate avidly along many routes beyond the boundaries of the main tumor mass. Chemotherapy with the new anti-proliferation drug temozolomide has increased patient survival, but only by months (Mangiola et al., 2010). It is likely that long-term survival will require a second drug to inhibit glioma dispersion (Giese et al., 2003; Salhia et al., 2006). Hence, we tested seven fascin-pathway blockers in a radial migration assay with two human glioblastoma multiforme cell lines, and found that three of the compounds caused dose-dependent inhibition of migration in both lines (L.L.R., W. S. McDonough, A.K. and M. E. Berens, unpublished results). This is encouraging preliminary cross-species evidence that a subset of compounds identified through the *Drosophila* fascin bioassay will have predictable effects on the phylogenetically conserved fascin pathway of mammalian cells. We note that, for both RET-dependent thyroid cancer (Das and Cagan, 2010) and fragile X syndrome (Bhogal and Jongens, 2010), *Drosophila* models have provided evidence of drug efficacy on the road to clinical trials (ClinicalTrials.gov database, NCT00514046 and NCT00965432, respectively).

The tricyclic antidepressant imipramine was a high-potency fascin-pathway blocker in our assay. An intriguing study of imipramine blue reported that this triphenylmethane derivative has anti-invasion properties against malignant glioma cells in vitro and in vivo (Munson et al., 2012). Although that study design was based on inhibition of NADPH oxidase by imipramine blue, glioma cells treated in vitro showed dramatic reorganization of their actin cytoskeleton, with a marked loss of actin bundle-based protrusions and extensions (Munson et al., 2012), consistent with the loss of fascin function (Vignjevic et al., 2006).

What can we infer about molecular mechanisms of action of the fascin-pathway modulators? Some possibilities can be proposed or ruled out based on the nature of the fascin bioassay. First, the molecular diversity of the fascin-pathway modulators argues strongly against a common target for either the enhancers or the blockers. Candidate targets, in addition to fascin per se, include CREB, CREBBP, Stat3, PKCα, Rab35, Rac and myosin X (Hashimoto et al., 2011).

Second, the 'known' pharmacology of the active compounds (supplementary material Tables S2, S3) might not be relevant, and this is implicit in the rationale of drug repurposing. For example, because the dissociated neuron cultures are low density by design, with limited cell-cell contact, the effects on neurite trajectory of neuroactive compounds like acetylcholine, adiphenine, baclofen and spiperone cannot be mediated through classical neurotransmission at functional synapses. Rather, their effects are better classified with the morphogenetic phenomena by which neurotransmitters influence brain development (Herlenius and Lagercrantz, 2001; Verney, 2003). Similarly, the antibiotic ceftriaxone, best known for blocking bacterial cell wall synthesis, has neuroprotective activity due to upregulation of glutamate transporter GT1 expression (Rothstein et al., 2005). However, this mechanism is unlikely to explain the activity of ceftriaxone in the fascin bioassay because GT1 is a glial protein, and our cell culture system is neuron-only.

Third, blockers that target the residual wild-type fascin in the *singed*-mutant neurons most probably do not have the same mechanism as the migrastatin family. This is because *Drosophila* and mammalian fascin differ at amino acid position 474, which is essential for migrastatin binding (Chen et al., 2010). That site is on the surface of fascin (Jansen et al., 2011), a location with potential

disadvantages for drug targeting. By contrast, high-resolution X-ray crystallographic studies identified internal pockets within the two actin-binding sites of fascin that, on the basis of glycerol and polyethylene glycol binding, could accommodate small-molecule blockers (Jansen et al., 2011).

Fourth, the fascin-pathway modulators with additional effects (Table 1) might represent distinct targets. For instance, 16 of the 18 fascin-pathway enhancers with other morphological effects caused reduced neurite outgrowth. Note that very small neurite arbors can manifest the filagree phenotype (Kraft et al., 2006). Therefore, our observations suggest that slowing neurite outgrowth compensates for fascin deficiency, allowing straighter neurite trajectory. Consistent with this, in vitro treatment of fascin-deficient neurons with a physiological hormone that boosts neurite outgrowth increases neurite curvature (Kraft et al., 2006). Although slowing the rate of neurite outgrowth might not be appropriate for therapeutic intervention, the observed relationship between neurite trajectory and outgrowth rate provides an important clue to fascin biology.

Repurposing and structure-activity relationships

Repurposing drug screens are done in the hope that the time to clinical efficacy trials will be considerably shorter than for a new molecular entity and, at least in theory, that retail prices will therefore be lower (Dueñas-González et al., 2008). Nonetheless, SAR investigation continues to be useful for probing the molecular requirements for activity. For example, the inferences from the activity cliffs (Fig. 6) represent SAR hypotheses that can be tested in the fascin bioassay using commercially available compounds that are similar to the original actives. Moreover, the actives can also be the starting point for structural modification for lead optimization, to enhance potency or to enhance blood-brain barrier penetration and CNS distribution (Denora et al., 2009).

Primary neuron culture for neurotoxicity screening in a genetic model organism

Insects lack the post-squalene sterol biosynthetic pathway and thus cannot synthesize cholesterol (Chapman, 1998). Hence, the BOS defect cannot be due to statin effects on cholesterol levels. HMG-CoA reductase inhibition also blocks the synthesis of isoprenoids that serve as membrane anchors for small GTPases such as Ras, Rho and Rac (Cordle et al., 2005; Wang et al., 2008). Isoprenyl membrane anchors are necessary for the activation of these signaling molecules, which serve essential roles in nervous system development and synaptic plasticity (Hall and Lalli, 2010; Samuel and Hynds, 2010; Ye and Carew, 2010). In mammals, statin neurotoxicity is manifest as reduced neurite outgrowth in vitro due to blockade of the isoprenoid pathway (Schulz et al., 2004) and, in the case of sympathetic neurons, specifically by inhibition of RhoA activation (Kim et al., 2009b). Thus, the BOS neurotoxic effect could involve the functional inhibition of small GTPases. We propose that BOS reflects disruption of microtubule-based transport, resulting in large aggregations of organelles, including mitochondria (Fig. 7P-S) and synaptic vesicles (data not shown). The synergistic effect of statin exposure and fascin deficiency highlights the importance of fascin for actin-myosin interactions (Ishikawa et al., 2003; Nagy et al., 2008; Tamada et al., 2010) that link actin and microtubule cytoskeletons (Cao et al., 2004).

BOS stands out from other neurotoxic effects (Fig. 7A-G) because of growing evidence that statins can cause significant, reversible neurocognitive or psychiatric side effects (King et al., 2003; Wagstaff et al., 2003; Golomb et al., 2004; Galatti et al., 2006; Tatley and Savage, 2007; Evans and Golomb, 2009). Recognition and reporting of these statin-caused adverse events, previously under-recognized and under-reported (Golomb et al., 2007), are likely to increase now that the FDA has added confusion and memory loss to statin warning labels (for more details, see http://www.fda.gov/Drugs/DrugSafety/ucm293101.htm). There is some urgency to address statin-induced cognitive side effects. In a randomized clinical trial, statin treatment disrupted learning in patients, who did not perceive that they had developed a cognitive deficit (Muldoon et al., 2004). In addition, there is a push from industry to approve statins for over-the-counter sales (Tinetti, 2008) and for use in children (de Ferranti and Ludwig, 2008). The latter is particularly worrisome because the developing brain might well be at higher risk for sides effect from statins.

There is presently no way to predict which patients will have statin-induced neurocognitive side effects. By contrast, statin-induced myopathy is associated with a single-nucleotide polymorphism in *SLCO1B1* (MIM#604843), which encodes a hepatic statin transporter (Niemi, 2010). Our demonstration that fascin modulates BOS (Fig. 7N-O) suggests that *Drosophila* genetics and neuron culture could be applied systematically to identify candidate genes whose human orthologs control sensitivity to statin-induced cognitive side effects. More generally, tens of thousands of environmental compounds await testing for developmental neurotoxicity (Landrigan, 2010). Primary culture of developing *Drosophila* neurons could provide a starting point for neurotoxicity screening. There are many potential benefits for screening with an invertebrate in vitro model system (Coecke et al., 2007), especially one so well-suited to examining gene-X-environment interactions.

Brain development and malignant tumors: two sides of the same genetic coin

Fascin is not unique in being essential for brain development, yet also having pathological consequences when overexpressed or overactive in tumor cells. For example, the proto-oncogene *MET* (MIM#64860) encodes a receptor tyrosine kinase whose activation drives tumor progression and drug resistance (Stella et al., 2010). On the other hand, *MET* controls neuronal differentiation and is a risk gene for both schizophrenia (Cannon, 2010) and autism, with the autism-associated variants disrupting *MET* or reducing *MET* expression (Judson et al., 2011). Similarly, the group I *PAK* (*p21-activated kinase*) genes, which regulate cytoskeletal dynamics, are drivers of tumor invasion (Molli et al., 2009). However, they play crucial roles in brain development and synaptic plasticity, with cognitive and behavioral deficits resulting from *PAK3* (MIM#300142) loss-of-function mutations (Kreis and Barnier, 2009).

Extrapolating further, one would predict that patients with developmental brain disorders due to loss-of-function mutations should be at lower risk for invasive cancers. A relevant case report describes a child with fragile X syndrome whose untreatable glioma had an indolent course for more than 8 years despite high-grade histopathology (Kalkunte et al., 2007). In fact, this biological

duality might explain why patients with schizophrenia, a highly heritable, late-onset brain-development disorder (Karlsgodt et al., 2008), have lower rates of cancer despite engaging in high-risk behaviors such as smoking and drinking (Cannon, 2010). Thus, two seemingly unconnected medical conditions are linked by genes with dual roles in brain development and tumor biology. We propose that the bidirectional screen presented here represents a powerful new approach for simultaneous drug discovery for brain-development disorders and cancer.

METHODS

Drosophila culture and genetics

Fly stocks were maintained at room temperature on corn meal-yeast-agar medium obtained from the University of Arizona fly food facility. Experimental cultures were reared at 25°C and 60-80% relative humidity on corn flour-yeast-agar medium as previously described (Kraft et al., 2006). *OreR-C* was the wild-type laboratory strain. The sources of *singed* mutant stocks, the *w(z)* strain of w^{1118} (in a *CantonS* background), and the γ-MB driver/reporter stock (*P[Gal4]201Y UAS-lacZ*) were as described previously (Kraft et al., 1998; Kraft et al., 2006). The neuron-specific driver line *elav-Gal4*^{C155} (Lin and Goodman, 1994) was provided by Mani Ramaswami (then at University of Arizona, Tucson, AZ). The GAL4-responsive mitochondria-targeted GFP transgenic line w^{1118}*; P(UAS-mitoGFP)* (Pilling et al., 2006) was provided by Konrad Zinsmaier (University of Arizona, Tucson, AZ). To identify mitochondria in living neurons, we generated *elav-GAL4*^{C155} */* w^{1118}*; P(UAS-mitoGFP) /* + progeny larvae.

γ-MB neurons with wild-type *fascin/singed* function were identified in vitro by crossing the γ-MB driver/reporter line to *w(z)* to generate *w sn*$^{+}$ */ w sn*$^{+}$*; P[Gal4]201Y UAS-lacZ /* +. To study the effect of *fascin/singed* mutation severity on the filagree phenotype of γ-MB neurons, we performed three crosses in parallel using the *201Y* driver to produce female larval progeny of the desired genotypes. Crossing *y w sn*^{3} */ Y; P[Gal4]201Y UAS-lacZ* males to *sn*^{3} */ sn*^{3} virgin females yielded *y w sn*^{3} */ sn*^{3}*; P[Gal4]201Y UAS-lacZ /* + daughters. *In(1) dl-49, sn*^{X2} */ Y males* were crossed either to *y w sn*^{3}*; P[Gal4]201Y UAS-lacZ* females to produce *y w sn*^{3} */ sn*^{X2}*; P[Gal4]201Y UAS-lacZ /* + daughters, or to *w; P[Gal4]201Y UAS-lacZ* females to produce *sn*^{X2}*/ +; P[Gal4]201Y UAS-lacZ /* + daughters.

Chemical informatics

Scaffold analysis

The analysis of the scaffold distribution described in this work is based upon specific molecular chemotypes (Medina-Franco et al., 2006) called cyclic systems, originally defined by Xu and Johnson (Xu and Johnson, 2002). This approach is consistent with general guidelines for defining molecular scaffolds (Langdon et al., 2010). A cyclic system consists of a set of rings and the chains of atoms that link them to one another. To obtain the scaffold, all substituent groups are removed from the rings and the linkers except endocyclic carbonyls and imines. Heteroatoms are retained and all hydrogen atoms attached to them are considered side chains and therefore removed. The Meqi program (version 2.41), originally developed by Xu and Johnson (Xu and Johnson, 2002), was obtained from Mark Johnson (Pannanugget Consulting, Kalamazoo, MI) and used to determine the specific cyclic system (described by a five-character alphanumeric chemotype identifier) present in each compound in the NINDS-II library. The Scaffold Recovery Curve was generated as previously described (Lipkus et al., 2008; Medina-Franco et al., 2009).

Molecular similarity and library diversity

Molecular similarity refers to the relation between pairs of molecules, whereas molecular diversity is based on pair-wise relations of a population of molecules (e.g. a compound collection). Molecular fingerprints of each compound were used to measure all pair-wise similarities (Willett et al., 1998; Maggiora and Shanmugasundaram, 2011). In general, this approach involves designating the presence or absence of specific structural features, which can be considered molecular fragments. This information is encoded in 'bit vectors', each of whose components are assigned a value of '1' if the fragment is present at least once in the molecule and '0' if it is not. Thus, multiple occurrences of specific fragments are not explicitly counted. The work presented here employed MACCS key fingerprints (Anderson, 1984), the current version of which represents 166 molecular fragments and related structural data. MACCS Structural Keys software, now available through Accelrys, Inc. (San Diego, CA), was used to determine the fingerprints of all compounds in the library. The molecular fingerprints were then used to evaluate the Tanimoto similarities using the program Molecular Operating Environment (MOE, v.2010), available from the Chemical Computing Group, Inc. (Montreal, Quebec, Canada; www.chemcomp.com). The Tanimoto coefficient between two molecules, A and B, is given by $T(A,B)=c/(a+b-c)$, where a is the number of fragments present in molecule A, b is the number of fragments present in molecule B and c is the number of fragments common to both A and B. Details of this procedure, which is widely used in chemical informatics applications, are available (Willett et al., 1998; Maggiora and Shanmugasundaram, 2011).

Principal component analysis of chemical-space distribution

Molecular similarity measures do not provide explicit information about the chemical space that molecules inhabit. To obtain a graphical representation of this space we created 3D plots using principal component analysis (PCA) (Jolliffe, 2002) based on the Tanimoto similarity matrix associated with the molecules in the NINDS-II collection. In the rectangular data matrix usually employed in PCA, the rows correspond to the objects under study and the columns to the descriptors, features or parameters used to describe the objects. By contrast, the similarity matrix for a set of n molecules is an $n \times n$ square symmetric array of Tanimoto similarity values where the rows and columns both correspond to the molecules under study. To obtain the principal components, the similarity matrix was treated as if it were a typical rectangular data matrix and the usual principal component procedure was applied. The columns were mean-centered, matrix multiplication was applied, and the product matrix was diagonalized yielding the eigenvectors and eigenvalues. The molecules (the objects in this study) were then plotted in the principal-component coordinate system using the first two or three eigenvectors or the principal components. Typically, the first three principal components represent most (65-75%) of the variance of the data. In this study, they represent ~67% of the variance, whereas the first two represent ~55% of the variance. The principal component data and plots were obtained using the Spotfire® dynamic data visualization program

(v.9.1.2) from TIBCO Software, Inc. (Somerville, MA; spotfire.tibco.com).

Primary neuronal cell culture preparation and evaluation

Primary neuronal cell cultures from the central nervous system (CNS) of wandering third instar larvae were prepared as previously described (Kraft et al., 1998; Kraft et al., 2006) with minor modifications. This method generates pure-neuron cultures within several days of incubation. Enzymatic treatment of the dissected tissue prior to dissociation was done with a commercial blend of purified collagenase I, collagenase II and the neutral protease dispase (Liberase Blendzyme 1, #1988409; Roche, Indianapolis, IN) at a concentration of 72 μg/ml in Rinaldini's saline. Schneider's Insect Medium (#11720; Invitrogen, San Diego, CA) was supplemented with 10% fetal bovine serum of US origin (#SH30071; lot #APC20860; Hyclone, Logan, UT) and 50 μg/ml bovine insulin (#I-6634; Sigma, St Louis, MO). For experiments analyzed by random-neuron sampling and quantification of morphometric parameters, the floor of the culture dish was made with a photoetched ('gridded') glass cover slip (#1916-91818; Bellco, Vineland, NJ). For cultures to be evaluated by holistic scoring (see below), a round German #1 glass cover slip (#1943-10012; Bellco) was used. In either case, the resulting 8-mm-diameter wells were coated with Conconavalin A (#C-2010; Sigma) and laminin (#354232; BD Biosciences, Franklin Lakes, NJ).

Unless otherwise specified, CNS of female larvae were explanted by microdissection and the entire CNS was dissociated, with the cells distributed into six culture dishes, followed by incubation at 25°C for 3 days (70-80 hours). After this time, each culture dish typically contained 1500-2000 neurons bearing scorable neurite arbors. The phenotypic severity of the filagree defect of fascin-deficient *singed*-mutant neurons is similar whether they are from late larval or early pupal CNS (Kraft et al., 2006). We chose the larval stage for the screen because the CNS dissection is far easier. Neuronal cultures prepared from individual CNS regions (optic lobes, brain, ventral ganglion) of sn^3/sn^3 larvae had indistinguishable filagree severity (data not shown).

Although neurite curvature can be quantified using image-analysis software (Kraft et al., 2006; Narro et al., 2007), the method requires immunostaining, random sampling, image acquisition and image processing. Alternatively, classification of neurite-curvature phenotypes can be performed much more quickly by holistic scoring of all neurons in a culture well (generally 1500-2000 neurons distributed over a ~50 mm^2 area). Classification of wild-type (+/+), intermediate-filagree (sn^3/sn^3), and severe-filagree (sn^{X2}/Y) cultures using phase-contrast microscopy of live neurons is 100% accurate when performed by trained observers. Training was done using non-drug-treated cultures of known genotype after 3 d.i.v. Training consisted of (i) a learning phase, with repeated observations by phase-contrast microscopy of live cultured neurons with known genotypes (+/+, sn^3/sn^3, sn^{X2}/Y), exhibiting wild-type, moderate filagree, or severe filagree phenotypes, respectively; and (ii) a testing phase, using coded dishes or images of individual microscopic fields. Training continued until dishes were assigned the correct genotype with 100% accuracy, and individual fields with ~90% accuracy (see Kraft et al., 2006).

To guide the selection of compound concentrations for screening, we tested the effect of the solvent dimethyl sulfoxide (DMSO, USP grade; #D-2438, Sigma) on neurite-arbor morphogenesis, selecting genetically marked γ-MB neurons (Kraft et al., 1998; Kraft et al., 2006) to minimize biological variation. There was no systematic concentration-dependent effect of DMSO on neurite curvature of fascin-deficient sn^3/sn^3 larval γ-neurons (supplementary material Fig. S1). However, at a concentration equivalent to a 100-μM drug treatment, DMSO significantly reduced neurite arbor size (data not shown). We therefore tested the compounds at 10 μM and 50 μM.

Screening the compound collection

The NINDS Custom Collection II (NINDS-II) library of 1040 biologically active compounds was purchased from Microsource Discovery Systems (Gaylordsville, CT). The collection was provided in 13 microplate-formatted storage racks, each with ten columns of eight polypropylene storage tubes sealed with a single non-separable CapStrip (#4415; Matrix Technology, Hudson, NH). Each compound was provided as a 10-mM solution in DMSO and uniquely identified by its rack number, row and column location. Each column of eight compounds was screened at the same time. The racks were stored at −80°C and each rack was removed only long enough to retrieve or replace a single column of compounds. Because the melting point for DMSO is 19°C, each column of tubes held together by a CapStrip was floated upright in a room-temperature water bath for 15 minutes to facilitate thawing the contents before use.

For each experiment, primary cultures were prepared from CNS of wild-type (*OreR-C*) and homozygous sn^3 mutant larvae as described above, with each dissociated CNS preparation distributed into six 8-mm-diameter culture wells. Two of the sn^3 mutant dishes served as no-drug controls for the baseline filagree phenotype. *OreR-C* cultures served as no-drug controls for wild-type neurite outgrowth and arbor morphology, and to verify that the culture medium and dish coating supported typical neuron survival and morphology. The cell suspension from each CNS was distributed equally into six culture dishes and the total volume in each dish was brought to 100 μl with culture medium. While the cells were allowed to settle and adhere for 2 hours at 25°C, eight compounds were each diluted in culture medium as needed for testing at final concentrations of 10 and 50 μM (final volume 1 ml). Liquid handling was facilitated by using an eight-channel electronic pipettor (Matrix) and barrier tips. Each dish of cells was supplemented with 900 μl of culture medium for final drug concentrations of 0, 10, 50 or 100 μM. The dishes were sealed with Parafilm-M® to minimize evaporation and then incubated with humidification at 25°C.

To minimize microbial contamination risk during the compound screening, we adopted a number of exceptional measures. A dissecting microscope and fiber-optic light source were moved into a dedicated tissue culture room that was decontaminated nightly with germicidal ultraviolet light. Dissections and dissociation were performed wearing sterile surgical gloves and a laboratory coat. The drug-containing racks were handled and the tubes thawed by a second person. The CapStrip was replaced after the column of drug vials was accessed.

After 3 d.i.v., the live cultured neurons were evaluated independently by two or three trained observers using phase-contrast microscopy on a Nikon Diaphot 300 inverted microscope using a 40× objective (numerical aperture, 0.7). Holistic scoring

was performed by systematic scanning of each entire dish to assess the overall effect of each drug treatment on the severity of the moderate filagree phenotype of the sn^3/sn^3 mutant neurons. A compound at a given dose was scored as decreasing the filagree phenotype (fascin-pathway enhancer) or increasing the filagree phenotype (fascin-pathway blocker) when a clear preponderance of neurons in the dish were observed to exhibit an unambiguous shift of the phenotype in the same direction. If no change was evident or there was more than the usual variability in the filagree phenotype, the score was recorded as 'no effect'. In addition to scoring the filagree phenotype, other effects on neuronal morphology were noted, again only when a significant majority of neurons in the culture displayed a consistent feature. An 'other effect' scoring scheme evolved over the course of the drug screening. A minimum of 3-5 minutes was required to examine each dish and additional time was necessary when an effect was noticed and its distribution throughout the dish was evaluated.

Scores for each compound at the low and high dose were recorded by each observer, after which the outcomes between observers were compared and discussed. In most cases, the scores were concordant. In cases of disagreement, the individuals would re-assess the cultures together and come to a consensus score. Drug-induced changes in filagree (increased or decreased severity) or in other aspects of neuronal morphology were documented by image acquisition of representative examples using a 60× oil-immersion objective (numerical aperture, 1.4) and a Hamamatsu ORCA285 digital camera with HCImage software (Hamamatsu Photonic Systems, Bridgewater, NJ).

Experiments were repeated for compounds causing filagree modification or other effects on neuron morphology so that the scores could be confirmed. In cases where the scores in the second test were not consistent with the original experiment, the compounds were repeated a third time and the majority score from the three experiments was taken as the definitive outcome. Compounds were also retested in instances when low neuron density or microbial contamination had compromised scoring. Once a coded compound was successfully evaluated, its name was revealed. A survey of published biomedical literature and publicly available databases was then conducted to collect pharmacology, toxicology and usage information.

Immunostaining and morphometric analysis of 2D neuron images

Statin compounds were re-tested on wild-type (*OreR-C*) neurons, on neurons expressing a mitochondria-targeted GFP and on *singed*-mutant neurons. Reciprocal drug wash-out experiments were performed on wild-type neurons in which the culture medium was replaced after 1 d.i.v. after a random sample of 25 neurons was imaged by phase-contrast microscopy. Those neurons were re-imaged live at 2 and 3 d.i.v. To quantify BOS severity, bead counting was based on phase-contrast images of live neurons. A 'bead' was defined as a phase-dark round or ovoid swelling within a neurite with a diameter greater than that of the flanking neurite on both sides. Because neurite expansions are often seen at branch points and neurite tips, potential beads at these locations were difficult to assess and therefore not counted.

Neurite length and curvature measurements were based on images of immunofluorescently labeled neurons. Fixation and immunostaining were performed after 3 d.i.v. as previously described (Kraft et al., 1998; Kraft et al., 2006). To visualize neuronal membranes with high resolution, the *Drosophila* Nervana 2 protein (Sun and Salvaterra, 1995) was labeled with a polyclonal goat anti-horseradish peroxidase antiserum (Sigma) at 1:500 and detected with an Alexa-Fluor®-488-conjugated donkey anti-goat antiserum (Invitrogen) at 1:500. To visualize β-galactosidase expression in genetically marked γ-MB neurons, a preabsorbed polyclonal rabbit anti-β-galactosidase antiserum (Cappel, West Chester, PA) was used at 1:5000 and detected with a Cy3-conjugated donkey anti-rabbit antiserum (Jackson ImmunoResearch, West Grove, PA) at 1:500. Labeled neurons were identified on the Nikon Diaphot 300 inverted microscope with the 60× oil-immersion objective using epifluorescence illumination. The Alexa Fluor 488 fluorescent signal was detected with filter cube Chroma #41001 (exciter 460-500 nm, dichroic 505 nm, band-pass emitter 510-560 nm) and the Cy3 signal with Nikon G-2A filter cube (exciter 510-560 nm, dichroic 580 nm, long-pass emitter 590 nm). Images were collected with the Hamamatsu ORCA285 digital camera and HCImage software.

Acquisition of images of γ-MB neurons and their generic neuron neighbors was performed as described (Kraft et al., 2006). The nearest-neighbor neurons constitute a random sample of the heterogeneous non-γ CNS neuron types in the culture. For quantitative study of neurons in non-genetically marked cultures, a rigorous method of random sampling was done by following the alphanumeric grid of the dish in a systematic manner, up and down a 'staircase', acquiring images of neurons along the 'steps' until at least 50 neurons were imaged.

Computer-assisted analysis of the fluorescent neuron images was performed using NeuronMetrics™ software, which converts each neurite arbor into a one-pixel-wide skeletal representation from which morphometric parameters, including length, are calculated (Narro et al., 2007). For each neuron, the number of beads per 100 μm (bead density) was calculated from the total bead count and total neurite length. The nonparametric Mann-Whitney rank sum test was used to compare the distributions of bead-density values between populations of the same genotype treated with different drug concentrations, and between populations with different genotypes treated with the same drug concentration. The statistical tests and graphical representation of the data were performed using SigmaStat and SigmaPlot (Systat Software, San Jose, CA). The neurite-arbor skeletons were also used for fully automated determination of mean neurite curvature for each neuron (Kraft et al., 2006). Distributions of neurite curvature were plotted as histograms with soft binning, to reduce the effect of discretization error, and a normal-distribution curve was plotted over the data. In soft binning, each value is considered the mean of a normal distribution, with the standard deviation being set to the bin size. We then distribute the value of that point to each of the bins in proportion to the value of the normal distribution at the bin centers. Comparisons of curvature distributions between groups were made using the Welch's *t*-test (Myers and Well, 1991), which accounts for different variances and sample sizes.

ACKNOWLEDGEMENTS

The authors thank Mindy Escobar, Benjamin Reddoch, Michelle O'Shea, David Andrew and Katie Olson for assistance in the early stages of the drug screen. We are also grateful to Anna Burns and Lynne Oland for expert oversight of the

Department of Neuroscience tissue culture facility, to Konrad Zinsmaier and Mani Ramaswami for *Drosophila* stocks, to Andrew Predoehl for help running the neurite-curvature software, to Nina Ossanna and Laurence Hurley for advice about drug discovery, and to Mark Johnson (Pannanugget Consulting) for providing the Meqi program.

COMPETING INTERESTS

G.M.M. was previously employed by Upjohn and Pharmacia.

AUTHOR CONTRIBUTIONS

L.L.R. conceived and developed the experimental concepts and directed the project; L.L.R. and R.K. designed experiments; R.K., A.K., M.L.O. and C.B. performed laboratory experiments; R.K., K.B., G.M.M., J.M.-F., F.L.-V., M.L.O., C.B. and L.L.R. contributed data analysis; and L.L.R., R.K., K.B., G.M.M., F.L.-V. and J.M.-F. prepared and edited the manuscript and figures.

FUNDING

The project was funded by awards to L.L.R. from the National Institutes of Health [grant number NS055774], to L.L.R. and G.M.M. from the Center for Insect Science (University of Arizona), and to J.L.M.-F. from the State of Florida and the Menopause & Women's Health Research Center (Port St Lucie, FL). C.B. was funded by NIGMS (Minority Access to Research Careers).

SUPPLEMENTARY MATERIAL

Supplementary material for this article is available at
http://dmm.biologists.org/lookup/suppl/doi:10.1242/dmm.008243/-/DC1

REFERENCES

Aiken, C. T., Tobin, A. J. and Schweitzer, E. S. (2004). A cell-based screen for drugs to treat Huntington's disease. *Neurobiol. Dis.* **16**, 546-555.

Al-Alwan, M., Olabi, S., Ghebeh, H., Barhoush, E., Tulbah, A., Al-Tweigeri, T., Ajarim, D. and Adra, C. (2011). Fascin is a key regulator of breast cancer invasion that acts via the modification of metastasis-associated molecules. *PLoS ONE* **6**, e27339.

Anderson, S. (1984). Graphical representation of molecules and substructure-search queries in MACCS^{TM}. *J. Mol. Graph.* **2**, 83-90.

Anilkumar, N., Parsons, M., Monk, R., Ng, T. and Adams, J. C. (2003). Interaction of fascin and protein kinase Cα: a novel intersection in cell adhesion and motility. *EMBO J.* **22**, 5390-5402.

Aratyn, Y. S., Schaus, T. E., Taylor, E. W. and Borisy, G. G. (2007). Intrinsic dynamic behavior of fascin in filopodia. *Mol. Biol. Cell* **18**, 3928-3940.

Ashburn, T. T. and Thor, K. B. (2004). Drug repositioning: identifying and developing new uses for existing drugs. *Nat. Rev. Drug Discov.* **3**, 673-683.

Bemis, G. W. and Murcko, M. A. (1996). The properties of known drugs. 1. Molecular frameworks. *J. Med. Chem.* **39**, 2887-2893.

Bender, H. A. (1960). Studies on the expression of various *singed* alleles in *Drosophila melanogaster*. *Genetics* **45**, 867-883.

Bhogal, B. and Jongens, T. A. (2010). Fragile X syndrome and model organisms: identifying potential routes of therapeutic intervention. *Dis. Model. Mech.* **3**, 693-700.

Bolduc, F. V. and Tully, T. (2009). Fruit flies and intellectual disability. *Fly (Austin)* **3**, 91-104.

Bryan, J., Edwards, R., Matsudaira, P., Otto, J. and Wulfkühle, J. (1993). Fascin, an echinoid actin-bundling protein, is a homolog of the *Drosophila* singed gene product. *Proc. Natl. Acad. Sci. USA* **90**, 9115-9119.

Burke, S. N. and Barnes, C. A. (2006). Neural plasticity in the ageing brain. *Nat. Rev. Neurosci.* **7**, 30-40.

Cannon, T. D. (2010). Candidate gene studies in the GWAS era: the MET proto-oncogene, neurocognition, and schizophrenia. *Am. J. Psychiatry* **167**, 369-372.

Cant, K., Knowles, B. A., Mooseker, M. S. and Cooley, L. (1994). *Drosophila* singed, a fascin homolog, is required for actin bundle formation during oogenesis and bristle extension. *J. Cell Biol.* **125**, 369-380.

Cao, T. T., Chang, W., Masters, S. E. and Mooseker, M. S. (2004). Myosin-Va binds to and mechanochemically couples microtubules to actin filaments. *Mol. Biol. Cell* **15**, 151-161.

Chapman, R. F. (1998). Nutrition. In *The Insects–Structure and Function*, pp. 69-93. Cambridge: Cambridge University Press.

Chen, J. and Herrup, K. (2008). Selective vulnerability of neurons in primary cultures and in neurodegenerative diseases. *Rev. Neurosci.* **19**, 317-326.

Chen, L., Yang, S., Jakoncic, J., Zhang, J. J. and Huang, X. Y. (2010). Migrastatin analogues target fascin to block tumour metastasis. *Nature* **464**, 1062-1066.

Coecke, S., Goldberg, A. M., Allen, S., Buzanska, L., Calamandrei, G., Crofton, K., Hareng, L., Hartung, T., Knaut, H., Honegger, P. et al. (2007). Workgroup report: incorporating *in vitro* alternative methods for developmental neurotoxicity into international hazard and risk assessment strategies. *Environ. Health Perspect.* **115**, 924-931.

Cordle, A., Koenigsknecht-Talboo, J., Wilkinson, B., Limpert, A. and Landreth, G. (2005). Mechanisms of statin-mediated inhibition of small G-protein function. *J. Biol. Chem.* **280**, 34202-34209.

Das, T. and Cagan, R. (2010). *Drosophila* as a novel therapeutic discovery tool for thyroid cancer. *Thyroid* **20**, 689-695.

De Arcangelis, A., Georges-Labouesse, E. and Adams, J. C. (2004). Expression of *fascin-1*, the gene encoding the actin-bundling protein fascin-1, during mouse embryogenesis. *Gene Expr. Patterns* **4**, 637-643.

de Ferranti, S. and Ludwig, D. S. (2008). Storm over statins – the controversy surrounding pharmacologic treatment of children. *N. Engl. J. Med.* **359**, 1309-1312.

Deinhardt, K., Kim, T., Spellman, D. S., Mains, R. E., Eipper, B. A., Neubert, T. A., Chao, M. V. and Hempstead, B. L. (2011). Neuronal growth cone retraction relies on proneurotrophin receptor signaling through Rac. *Sci. Signal.* **4**, ra82.

Denora, N., Trapani, A., Laquintana, V., Lopedota, A. and Trapani, G. (2009). Recent advances in medicinal chemistry and pharmaceutical technology – strategies for drug delivery to the brain. *Curr. Top. Med. Chem.* **9**, 182-196.

Desai, U. A., Pallos, J., Ma, A. A., Stockwell, B. R., Thompson, L. M., Marsh, J. L. and Diamond, M. I. (2006). Biologically active molecules that reduce polyglutamine aggregation and toxicity. *Hum. Mol. Genet.* **15**, 2114-2124.

Dueñas-González, A., García-López, P., Herrera, L. A., Medina-Franco, J. L., González-Fierro, A. and Candelaria, M. (2008). The prince and the pauper. A tale of anticancer targeted agents. *Mol. Cancer* **7**, 82.

Ess, K. C. (2006). The neurobiology of tuberous sclerosis complex. *Semin. Pediatr. Neurol.* **13**, 37-42.

Evans, M. A. and Golomb, B. A. (2009). Statin-associated adverse cognitive effects: survey results from 171 patients. *Pharmacotherapy* **29**, 800-811.

Fu, H., Wen, J. F., Hu, Z. L., Luo, G. Q. and Ren, H. Z. (2009). Knockdown of fascin1 expression suppresses the proliferation and metastasis of gastric cancer cells. *Pathology* **41**, 655-660.

Galatti, L., Polimeni, G., Salvo, F., Romani, M., Sessa, A. and Spina, E. (2006). Short-term memory loss associated with rosuvastatin. *Pharmacotherapy* **26**, 1190-1192.

Gan, B., Sahin, E., Jiang, S., Sanchez-Aguilera, A., Scott, K. L., Chin, L., Williams, D. A., Kwiatkowski, D. J. and DePinho, R. A. (2008). mTORC1-dependent and -independent regulation of stem cell renewal, differentiation, and mobilization. *Proc. Natl. Acad. Sci. USA* **105**, 19384-19389.

Giese, A., Bjerkvig, R., Berens, M. E. and Westphal, M. (2003). Cost of migration: invasion of malignant gliomas and implications for treatment. *J. Clin. Oncol.* **21**, 1624-1636.

Golomb, B. A., Kane, T. and Dimsdale, J. E. (2004). Severe irritability associated with statin cholesterol-lowering drugs. *QJM* **97**, 229-235.

Golomb, B. A., McGraw, J. J., Evans, M. A. and Dimsdale, J. E. (2007). Physician response to patient reports of adverse drug effects: implications for patient-targeted adverse effect surveillance. *Drug Saf.* **30**, 669-675.

Greenspan, R. J. and Dierick, H. A. (2004). 'Am not I a fly like thee?' From genes in fruit flies to behavior in humans. *Hum. Mol. Genet.* **13 Suppl. 2**, R267-R273.

Guild, G. M., Connelly, P. S., Ruggiero, L., Vranich, K. A. and Tilney, L. G. (2003). Long continuous actin bundles in *Drosophila* bristles are constructed by overlapping short filaments. *J. Cell Biol.* **162**, 1069-1077.

Gunal, A., Onguru, O., Safali, M. and Beyzadeoglu, M. (2008). Fascin expression in glial tumors and its prognostic significance in glioblastomas. *Neuropathology* **28**, 382-386.

Hall, A. and Lalli, G. (2010). Rho and Ras GTPases in axon growth, guidance, and branching. *Cold Spring Harb. Perspect. Biol.* **2**, 1-18.

Harrap, K. R. (1985). Preclinical studies identifying carboplatin as a viable cisplatin alternative. *Cancer Treat Rev.* **12 Suppl. A**, 21-33.

Hashimoto, Y., Parsons, M. and Adams, J. C. (2007). Dual actin-bundling and protein kinase C-binding activities of fascin regulate carcinoma cell migration downstream of Rac and contribute to metastasis. *Mol. Biol. Cell* **18**, 4591-4602.

Hashimoto, Y., Kim, D. J. and Adams, J. C. (2011). The roles of fascins in health and disease. *J. Pathol.* **224**, 289-300.

Heemskerk, J. (2005). Screening existing drugs for neurodegeneration: The National Institute of Neurologic Disorders and Stroke (NINDS) model. *Retina* **25**, S56-S57.

Herlenius, E. and Lagercrantz, H. (2001). Neurotransmitters and neuromodulators during early human development. *Early Hum. Dev.* **65**, 21-37.

Hwang, J. H., Smith, C. A., Salhia, B. and Rutka, J. T. (2008). The role of fascin in the migration and invasiveness of malignant glioma cells. *Neoplasia* **10**, 149-159.

Inlow, J. K. and Restifo, L. L. (2004). Molecular and comparative genetics of mental retardation. *Genetics* **166**, 835-881.

Ishikawa, R., Sakamoto, T., Ando, T., Higashi-Fujime, S. and Kohama, K. (2003). Polarized actin bundles formed by human fascin-1: their sliding and disassembly on myosin II and myosin V *in vitro*. *J. Neurochem.* **87**, 676-685.

Ito, T. and Handa, H. (2012). Deciphering the mystery of thalidomide teratogenicity. *Congenit. Anom. (Kyoto)* **52**, 1-7.

Jansen, S., Collins, A., Yang, C., Rebowski, G., Svitkina, T. and Dominguez, R. (2011). Mechanism of actin filament bundling by fascin. *J. Biol. Chem.* **286**, 30087-30096.

Jawhari, A. U., Buda, A., Jenkins, M., Shehzad, K., Sarraf, C., Noda, M., Farthing, M. J., Pignatelli, M. and Adams, J. C. (2003). Fascin, an actin-bundling protein, modulates colonic epithelial cell invasiveness and differentiation in vitro. *Am. J. Pathol.* **162**, 69-80.

Jayo, A. and Parsons, M. (2010). Fascin: a key regulator of cytoskeletal dynamics. *Int. J. Biochem. Cell Biol.* **42**, 1614-1617.

Johnson, M. A. and Maggiora, G. A. (eds) (1990). *Concepts and Applications of Molecular Similarity*, pp. 393. New York, NY: Wiley-Interscience.

Johnston, M. V. (2004). Clinical disorders of brain plasticity. *Brain Dev.* **26**, 73-80.

Jolliffe, I. T. (2002). *Principal Component Analysis*. New York, NY: Springer Series in Statistics.

Judson, M. C., Eagleson, K. L. and Levitt, P. (2011). A new synaptic player leading to autism risk: Met receptor tyrosine kinase. *J. Neurodev. Disord.* **3**, 282-292.

Kalkunte, R., Macarthur, D. and Morton, R. (2007). Glioblastoma in a boy with fragile X: an unusual case of neuroprotection. *Arch. Dis. Child.* **92**, 795-796.

Karlsgodt, K. H., Sun, D., Jimenez, A. M., Lutkenhoff, E. S., Willhite, R., van Erp, T. G. and Cannon, T. D. (2008). Developmental disruptions in neural connectivity in the pathophysiology of schizophrenia. *Dev. Psychopathol.* **20**, 1297-1327.

Kim, M. Y., Oskarsson, T., Acharyya, S., Nguyen, D. X., Zhang, X. H., Norton, L. and Massagué, J. (2009a). Tumor self-seeding by circulating cancer cells. *Cell* **139**, 1315-1326.

Kim, W. Y., Gonsiorek, E. A., Barnhart, C., Davare, M. A., Engebose, A. J., Lauridsen, H., Bruun, D., Lesiak, A., Wayman, G., Bucelli, R. et al. (2009b). Statins decrease dendritic arborization in rat sympathetic neurons by blocking RhoA activation. *J. Neurochem.* **108**, 1057-1071.

Kim, S. J., Choi, I. J., Cheong, T. C., Lee, S. J., Lotan, R., Park, S. H. and Chun, K. H. (2010). Galectin-3 increases gastric cancer cell motility by up-regulating fascin-1 expression. *Gastroenterology* **138**, 1035-1045, e1-e2.

King, D. S., Wilburn, A. J., Wofford, M. R., Harrell, T. K., Lindley, B. J. and Jones, D. W. (2003). Cognitive impairment associated with atorvastatin and simvastatin. *Pharmacotherapy* **23**, 1663-1667.

Kraft, R., Levine, R. B. and Restifo, L. L. (1998). The steroid hormone 20-hydroxyecdysone enhances neurite growth of *Drosophila* mushroom body neurons isolated during metamorphosis. *J. Neurosci.* **18**, 8886-8899.

Kraft, R., Escobar, M. M., Narro, M. L., Kurtis, J. L., Efrat, A., Barnard, K. and Restifo, L. L. (2006). Phenotypes of *Drosophila* brain neurons in primary culture reveal a role for fascin in neurite shape and trajectory. *J. Neurosci.* **26**, 8734-8747.

Kreis, P. and Barnier, J. V. (2009). PAK signalling in neuronal physiology. *Cell. Signal.* **21**, 384-393.

Kureishy, N., Sapountzi, V., Prag, S., Anilkumar, N. and Adams, J. C. (2002). Fascins, and their roles in cell structure and function. *Bioessays* **24**, 350-361.

Landrigan, P. J. (2010). What causes autism? Exploring the environmental contribution. *Curr. Opin. Pediatr.* **22**, 219-225.

Langdon, S. R., Ertl, P. and Brown, N. (2010). Bioisosteric replacement and scaffold hopping in lead generation and optimization. *Mol. Inf.* **29**, 366-385.

Li, A., Dawson, J. C., Forero-Vargas, M., Spence, H. J., Yu, X., König, I., Anderson, K. and Machesky, L. M. (2010a). The actin-bundling protein fascin stabilizes actin in invadopodia and potentiates protrusive invasion. *Curr. Biol.* **20**, 339-345.

Li, L., Mauric, V., Zheng, J. F., Kang, S. U., Patil, S., Höger, H. and Lubec, G. (2010b). Olfactory bulb proteins linked to olfactory memory in C57BL/6J mice. *Amino Acids* **39**, 871-886.

Lin, D. M. and Goodman, C. S. (1994). Ectopic and increased expression of Fasciclin II alters motoneuron growth cone guidance. *Neuron* **13**, 507-523.

Lipkus, A. H., Yuan, Q., Lucas, K. A., Funk, S. A., Bartelt, W. F., 3rd, Schenck, R. J. and Trippe, A. J. (2008). Structural diversity of organic chemistry. A scaffold analysis of the CAS Registry. *J. Org. Chem.* **73**, 4443-4451.

Liu, A. C., Welsh, D. K., Ko, C. H., Tran, H. G., Zhang, E. E., Priest, A. A., Buhr, E. D., Singer, O., Meeker, K., Verma, I. M. et al. (2007). Intercellular coupling confers robustness against mutations in the SCN circadian clock network. *Cell* **129**, 605-616.

Machesky, L. M. and Li, A. (2010). Fascin: Invasive filopodia promoting metastasis. *Commun. Integr. Biol.* **3**, 263-270.

Maggiora, G. M. and Shanmugasundaram, V. (2011). Molecular similarity measures. In *Chemoinformatics and Computational Chemical Biology* (ed. J. Bajorath), pp. 39-100. New York: Humana Press, Springer.

Mangiola, A., Anile, C., Pompucci, A., Capone, G., Rigante, L. and De Bonis, P. (2010). Glioblastoma therapy: going beyond Hercules Columns. *Expert Rev. Neurother.* **10**, 507-514.

Marín-Vicente, C., Guerrero-Valero, M., Nielsen, M. L., Savitski, M. M., Gómez-Fernández, J. C., Zubarev, R. A. and Corbalán-García, S. (2011). ATP enhances neuronal differentiation of PC12 cells by activating PKCα interactions with cytoskeletal proteins. *J. Proteome Res.* **10**, 529-540.

Medina-Franco, J. L., Petit, J. and Maggiora, G. M. (2006). Hierarchical strategy for identifying active chemotype classes in compound databases. *Chem. Biol. Drug Des.* **67**, 395-408.

Medina-Franco, J. L., Martínez-Mayorga, K., Bender, A. and Scior, T. (2009). Scaffold diversity analysis of compound data sets using an entropy-based measure. *QSAR Comb. Sci.* **28**, 1551-1560.

Megiorni, F., Indovina, P., Mora, B. and Mazzilli, M. C. (2005). Minor expression of fascin-1 gene (*FSCN1*) in NTera2 cells depleted of CREB-binding protein. *Neurosci. Lett.* **381**, 169-174.

Meller, R. (2009). The role of the ubiquitin proteasome system in ischemia and ischemic tolerance. *Neuroscientist* **15**, 243-260.

Miles, W. O., Dyson, N. J. and Walker, J. A. (2011). Modeling tumor invasion and metastasis in *Drosophila*. *Dis. Model. Mech.* **4**, 753-761.

Molli, P. R., Li, D. Q., Murray, B. W., Rayala, S. K. and Kumar, R. (2009). PAK signaling in oncogenesis. *Oncogene* **28**, 2545-2555.

Muldoon, M. F., Ryan, C. M., Sereika, S. M., Flory, J. D. and Manuck, S. B. (2004). Randomized trial of the effects of simvastatin on cognitive functioning in hypercholesterolemic adults. *Am. J. Med.* **117**, 823-829.

Munson, J. M., Fried, L., Rowson, S. A., Bonner, M. Y., Karumbaiah, L., Diaz, B., Courtneidge, S. A., Knaus, U. G., Brat, D. J., Arbiser, J. L. et al. (2012). Anti-invasive adjuvant therapy with imipramine blue enhances chemotherapeutic efficacy against glioma. *Sci. Transl. Med.* **4**, 127ra36.

Myers, J. L. and Well, A. D. (1991). *Research Design and Statistical Analysis*. New York: HarperCollins.

Nagy, S., Ricca, B. L., Norstrom, M. F., Courson, D. S., Brawley, C. M., Smithback, P. A. and Rock, R. S. (2008). A myosin motor that selects bundled actin for motility. *Proc. Natl. Acad. Sci. USA* **105**, 9616-9620.

Narro, M. L., Yang, F., Kraft, R., Wenk, C., Efrat, A. and Restifo, L. L. (2007). NeuronMetrics: software for semi-automated processing of cultured neuron images. *Brain Res.* **1138**, 57-75.

Niemi, M. (2010). Transporter pharmacogenetics and statin toxicity. *Clin. Pharmacol. Ther.* **87**, 130-133.

Ono, S., Yamakita, Y., Yamashiro, S., Matsudaira, P. T., Gnarra, J. R., Obinata, T. and Matsumura, F. (1997). Identification of an actin binding region and a protein kinase C phosphorylation site on human fascin. *J. Biol. Chem.* **272**, 2527-2533.

Opii, W. O., Joshi, G., Head, E., Milgram, N. W., Muggenburg, B. A., Klein, J. B., Pierce, W. M., Cotman, C. W. and Butterfield, D. A. (2008). Proteomic identification of brain proteins in the canine model of human aging following a long-term treatment with antioxidants and a program of behavioral enrichment: relevance to Alzheimer's disease. *Neurobiol. Aging* **29**, 51-70.

Palumbo, A., Facon, T., Sonneveld, P., Bladè, J., Offidani, M., Gay, F., Moreau, P., Waage, A., Spencer, A., Ludwig, H. et al. (2008). Thalidomide for treatment of multiple myeloma: 10 years later. *Blood* **111**, 3968-3977.

Paterson, J. and O'Hare, K. (1991). Structure and transcription of the *singed* locus of *Drosophila melanogaster*. *Genetics* **129**, 1073-1084.

Peraud, A., Mondal, S., Hawkins, C., Mastronardi, M., Bailey, K. and Rutka, J. T. (2003). Expression of fascin, an actin-bundling protein, in astrocytomas of varying grades. *Brain Tumor Pathol.* **20**, 53-58.

Piccioni, F., Roman, B. R., Fischbeck, K. H. and Taylor, J. P. (2004). A screen for drugs that protect against the cytotoxicity of polyglutamine-expanded androgen receptor. *Hum. Mol. Genet.* **13**, 437-446.

Pilling, A. D., Horiuchi, D., Lively, C. M. and Saxton, W. M. (2006). Kinesin-1 and Dynein are the primary motors for fast transport of mitochondria in *Drosophila* motor axons. *Mol. Biol. Cell* **17**, 2057-2068.

Roelfsema, J. H. and Peters, D. J. (2007). Rubinstein-Taybi syndrome: clinical and molecular overview. *Expert Rev. Mol. Med.* **9**, 1-16.

Roma, A. A. and Prayson, R. A. (2005). Fascin expression in 90 patients with glioblastoma multiforme. *Ann. Diagn. Pathol.* **9**, 307-311.

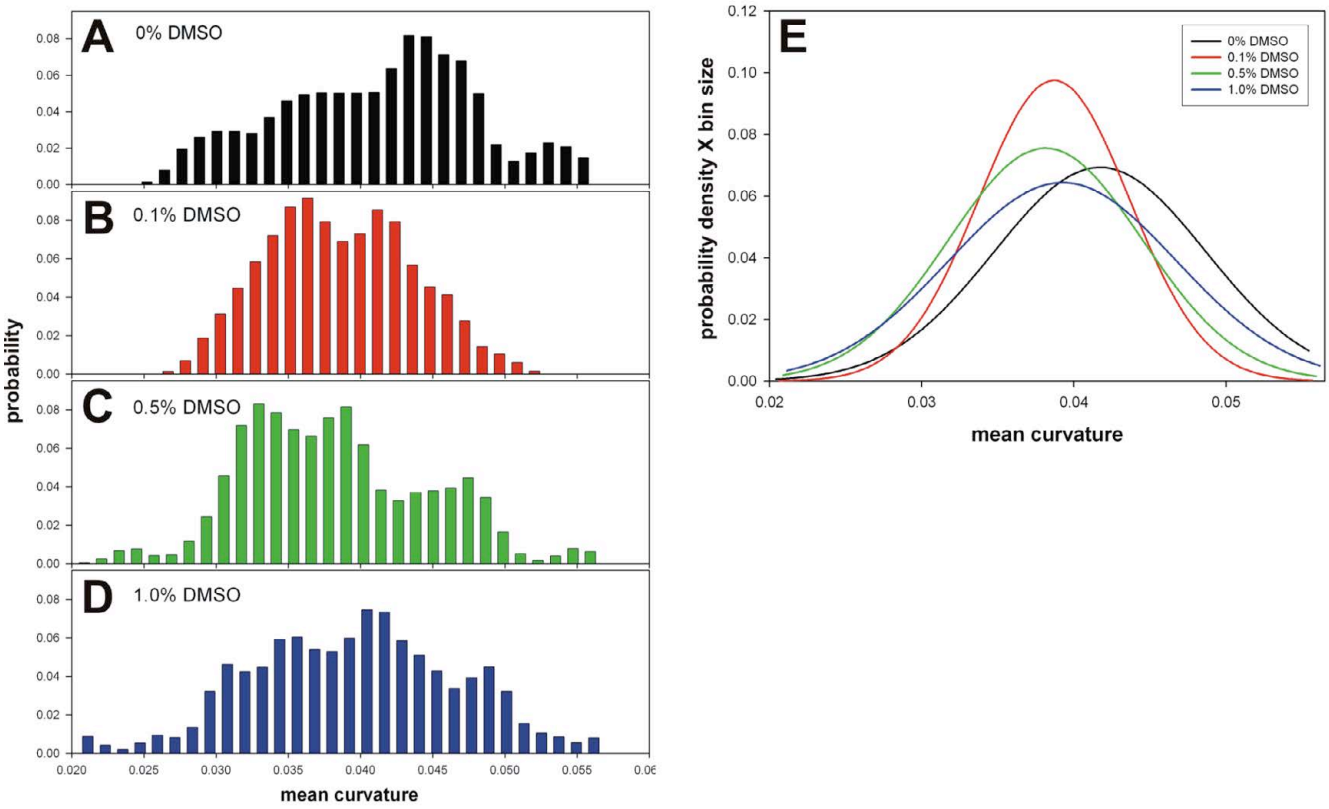
Rothstein, J. D., Patel, S., Regan, M. R., Haenggeli, C., Huang, Y. H., Bergles, D. E., Jin, L., Dykes Hoberg, M., Vidensky, S., Chung, D. S. et al. (2005). Beta-lactam antibiotics offer neuroprotection by increasing glutamate transporter expression. *Nature* **433**, 73-77.

Ryu, M. J., Kim, D., Kang, U. B., Kim, J., Shin, H. S., Lee, C. and Yu, M. H. (2007). Proteomic analysis of gamma-butyrolactone-treated mouse thalamus reveals dysregulated proteins upon absence seizure. *J. Neurochem.* **102**, 646-656.

Ryu, M. J., Lee, C., Kim, J., Shin, H. S. and Yu, M. H. (2008). Proteomic analysis of stargazer mutant mouse neuronal proteins involved in absence seizure. *J. Neurochem.* **104**, 1260-1270.

Safran, N., Haring, R., Gurwitz, D., Shainberg, A., Halili, I., Levy, A., Bogin, E. and Shahar, A. (1996). Selective neurotoxicity induced by the ionophore lasalocid in rat dissociated cerebral cultures, involvement of the NMDA receptor/channel. *Neurotoxicology* **17**, 883-895.

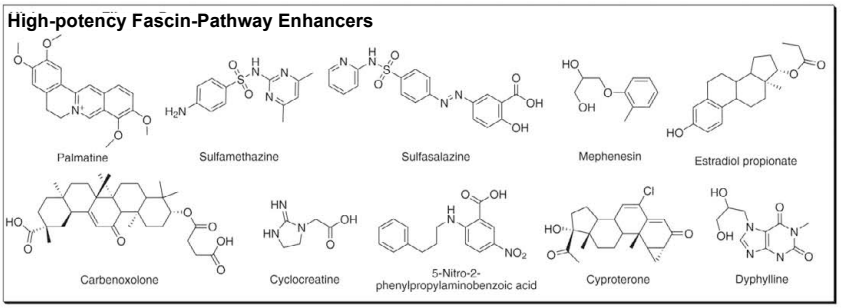
Salhia, B., Tran, N. L., Symons, M., Winkles, J. A., Rutka, J. T. and Berens, M. E. (2006). Molecular pathways triggering glioma cell invasion. *Expert Rev. Mol. Diagn.* **6**, 613-626.
Samuel, F. and Hynds, D. L. (2010). RHO GTPase signaling for axon extension: is prenylation important? *Mol. Neurobiol.* **42**, 133-142.
Sawallisch, C., Berhörster, K., Disanza, A., Mantoani, S., Kintscher, M., Stoenica, L., Dityatev, A., Sieber, S., Kindler, S., Morellini, F. et al. (2009). The insulin receptor substrate of 53 kDa (IRSp53) limits hippocampal synaptic plasticity. *J. Biol. Chem.* **284**, 9225-9236.
Schulz, J. G., Bösel, J., Stoeckel, M., Megow, D., Dirnagl, U. and Endres, M. (2004). HMG-CoA reductase inhibition causes neurite loss by interfering with geranylgeranylpyrophosphate synthesis. *J. Neurochem.* **89**, 24-32.
Sedeh, R. S., Fedorov, A. A., Fedorov, E. V., Ono, S., Matsumura, F., Almo, S. C. and Bathe, M. (2010). Structure, evolutionary conservation, and conformational dynamics of *Homo sapiens* fascin-1, an F-actin crosslinking protein. *J. Mol. Biol.* **400**, 589-604.
Shalaeva, M., Kenseth, J., Lombardo, F. and Bastin, A. (2008). Measurement of dissociation constants (p*K*a values) of organic compounds by multiplexed capillary electrophoresis using aqueous and cosolvent buffers. *J. Pharm. Sci.* **97**, 2581-2606.
Shan, D., Chen, L., Njardarson, J. T., Gaul, C., Ma, X., Danishefsky, S. J. and Huang, X. Y. (2005). Synthetic analogues of migrastatin that inhibit mammary tumor metastasis in mice. *Proc. Natl. Acad. Sci. USA* **102**, 3772-3776.
Shin, J. H., Guedj, F., Delabar, J. M. and Lubec, G. (2007). Dysregulation of growth factor receptor-bound protein 2 and fascin in hippocampus of mice polytransgenic for chromosome 21 structures. *Hippocampus* **17**, 1180-1192.
Shin, J. B., Longo-Guess, C. M., Gagnon, L. H., Saylor, K. W., Dumont, R. A., Spinelli, K. J., Pagana, J. M., Wilmarth, P. A., David, L. L., Gillespie, P. G. et al. (2010). The R109H variant of fascin-2, a developmentally regulated actin crosslinker in hair-cell stereocilia, underlies early-onset hearing loss of DBA/2J mice. *J. Neurosci.* **30**, 9683-9694.
Singh, N., Guha, R., Giulianotti, M. A., Pinilla, C., Houghten, R. A. and Medina-Franco, J. L. (2009). Chemoinformatic analysis of combinatorial libraries, drugs, natural products, and molecular libraries small molecule repository. *J. Chem. Inf. Model.* **49**, 1010-1024.
Slaugenhaupt, S. A., Mull, J., Leyne, M., Cuajungco, M. P., Gill, S. P., Hims, M. M., Quintero, F., Axelrod, F. B. and Gusella, J. F. (2004). Rescue of a human mRNA splicing defect by the plant cytokinin kinetin. *Hum. Mol. Genet.* **13**, 429-436.
Sleeman, J. and Steeg, P. S. (2010). Cancer metastasis as a therapeutic target. *Eur. J. Cancer* **46**, 1177-1180.
Sporn, M. B. (1996). The war on cancer. *Lancet* **347**, 1377-1381.
Stavrovskaya, I. G., Narayanan, M. V., Zhang, W., Krasnikov, B. F., Heemskerk, J., Young, S. S., Blass, J. P., Brown, A. M., Beal, M. F., Friedlander, R. M. et al. (2004). Clinically approved heterocyclics act on a mitochondrial target and reduce stroke-induced pathology. *J. Exp. Med.* **200**, 211-222.
Stella, G. M., Benvenuti, S. and Comoglio, P. M. (2010). Targeting the MET oncogene in cancer and metastases. *Expert Opin. Investig. Drugs* **19**, 1381-1394.
Sun, B. and Salvaterra, P. M. (1995). Characterization of nervana, a *Drosophila melanogaster* neuron-specific glycoprotein antigen recognized by anti-horseradish peroxidase antibodies. *J. Neurochem.* **65**, 434-443.
Svitkina, T. M., Bulanova, E. A., Chaga, O. Y., Vignjevic, D. M., Kojima, S., Vasiliev, J. M. and Borisy, G. G. (2003). Mechanism of filopodia initiation by reorganization of a dendritic network. *J. Cell Biol.* **160**, 409-421.
Tamada, A., Kawase, S., Murakami, F. and Kamiguchi, H. (2010). Autonomous right-screw rotation of growth cone filopodia drives neurite turning. *J. Cell Biol.* **188**, 429-441.
Tang, Z. L., Zhang, X. J., Yang, S. L., Mu, Y. L., Cui, W. T., Ao, H. and Li, K. (2010). The chromosomal localization, expression pattern and polymorphism analysis of porcine *FSCN1* gene differently expressed from LongSAGE library. *Mol. Biol. Rep.* **37**, 2361-2367.
Tatley, M. and Savage, R. (2007). Psychiatric adverse reactions with statins, fibrates and ezetimibe: implications for the use of lipid-lowering agents. *Drug Saf.* **30**, 195-201.
Tilney, L. G., Tilney, M. S. and Guild, G. M. (1995). F actin bundles in *Drosophila* bristles. I. Two filament cross-links are involved in bundling. *J. Cell Biol.* **130**, 629-638.
Tinetti, M. E. (2008). Over-the-counter sales of statins and other drugs for asymptomatic conditions. *N. Engl. J. Med.* **358**, 2728-2732.
Traynor, B. J., Bruijn, L., Conwit, R., Beal, F., O'Neill, G., Fagan, S. C. and Cudkowicz, M. E. (2006). Neuroprotective agents for clinical trials in ALS: a systematic assessment. *Neurology* **67**, 20-27.
Tseng, Y., Kole, T. P., Lee, J. S., Fedorov, E., Almo, S. C., Schafer, B. W. and Wirtz, D. (2005). How actin crosslinking and bundling proteins cooperate to generate an enhanced cell mechanical response. *Biochem. Biophys. Res. Commun.* **334**, 183-192.
Tubb, B. E., Bardien-Kruger, S., Kashork, C. D., Shaffer, L. G., Ramagli, L. S., Xu, J., Siciliano, M. J. and Bryan, J. (2000). Characterization of human retinal fascin gene (FSCN2) at 17q25: close physical linkage of fascin and cytoplasmic actin genes. *Genomics* **65**, 146-156.
Tubb, B., Mulholland, D. J., Vogl, W., Lan, Z. J., Niederberger, C., Cooney, A. and Bryan, J. (2002). Testis fascin (FSCN3): a novel paralog of the actin-bundling protein fascin expressed specifically in the elongate spermatid head. *Exp. Cell Res.* **275**, 92-109.
Verney, C. (2003). Phenotypic expression of monoamines and GABA in the early development of human telencephalon, transient or not transient. *J. Chem. Neuroanat.* **26**, 283-292.
Vignjevic, D., Kojima, S., Aratyn, Y., Danciu, O., Svitkina, T. and Borisy, G. G. (2006). Role of fascin in filopodial protrusion. *J. Cell Biol.* **174**, 863-875.
Vincent, A. M., Backus, C., Taubman, A. A. and Feldman, E. L. (2005). Identification of candidate drugs for the treatment of ALS. *Amyotroph. Lateral Scler. Other Motor Neuron Disord.* **6**, 29-36.
Wagstaff, L. R., Mitton, M. W., Arvik, B. M. and Doraiswamy, P. M. (2003). Statin-associated memory loss: analysis of 60 case reports and review of the literature. *Pharmacotherapy* **23**, 871-880.
Wang, J., Gines, S., MacDonald, M. E. and Gusella, J. F. (2005a). Reversal of a full-length mutant huntingtin neuronal cell phenotype by chemical inhibitors of polyglutamine-mediated aggregation. *BMC Neurosci.* **6**, 1.
Wang, W., Duan, W., Igarashi, S., Morita, H., Nakamura, M. and Ross, C. A. (2005b). Compounds blocking mutant huntingtin toxicity identified using a Huntington's disease neuronal cell model. *Neurobiol. Dis.* **20**, 500-508.
Wang, C. Y., Liu, P. Y. and Liao, J. K. (2008). Pleiotropic effects of statin therapy: molecular mechanisms and clinical results. *Trends Mol. Med.* **14**, 37-44.
White, C. M. (2002). A review of the pharmacologic and pharmacokinetic aspects of rosuvastatin. *J. Clin. Pharmacol.* **42**, 963-970.
Willett, P., Barnard, J. M. and Downs, G. M. (1998). Chemical similarity searching. *J. Chem. Inf. Comput. Sci.* **38**, 983-996.
Wishart, D. S., Knox, C., Guo, A. C., Cheng, D., Shrivastava, S., Tzur, D., Gautam, B. and Hassanali, M. (2008). DrugBank: a knowledgebase for drugs, drug actions and drug targets. *Nucleic Acids Res.* **36**, D901-D906.
Wulfkühle, J. D., Petersen, N. S. and Otto, J. J. (1998). Changes in the F-actin cytoskeleton during neurosensory bristle development in *Drosophila*: the role of singed and forked proteins. *Cell Motil. Cytoskeleton* **40**, 119-132.
Xu, Y. J. and Johnson, M. (2002). Using molecular equivalence numbers to visually explore structural features that distinguish chemical libraries. *J. Chem. Inf. Comput. Sci.* **42**, 912-926.
Yamakita, Y., Matsumura, F. and Yamashiro, S. (2009). Fascin1 is dispensable for mouse development but is favorable for neonatal survival. *Cell Motil. Cytoskeleton* **66**, 524-534.
Yamashiro, S., Yamakita, Y., Ono, S. and Matsumura, F. (1998). Fascin, an actin-bundling protein, induces membrane protrusions and increases cell motility of epithelial cells. *Mol. Biol. Cell* **9**, 993-1006.
Ye, X. and Carew, T. J. (2010). Small G protein signaling in neuronal plasticity and memory formation: the specific role of ras family proteins. *Neuron* **68**, 340-361.
Yoder, B. J., Tso, E., Skacel, M., Pettay, J., Tarr, S., Budd, T., Tubbs, R. R., Adams, J. C. and Hicks, D. G. (2005). The expression of fascin, an actin-bundling motility protein, correlates with hormone receptor-negative breast cancer and a more aggressive clinical course. *Clin. Cancer Res.* **11**, 186-192.
Zanet, J., Stramer, B., Millard, T., Martin, P., Payre, F. and Plaza, S. (2009). Fascin is required for blood cell migration during *Drosophila* embryogenesis. *Development* **136**, 2557-2565.
Zhang, F. R., Tao, L. H., Shen, Z. Y., Lv, Z., Xu, L. Y. and Li, E. M. (2008). Fascin expression in human embryonic, fetal, and normal adult tissue. *J. Histochem. Cytochem.* **56**, 193-199.
Zins, G. R. (1988). The history of the development of minoxidil. *Clin. Dermatol.* **6**, 132-147.

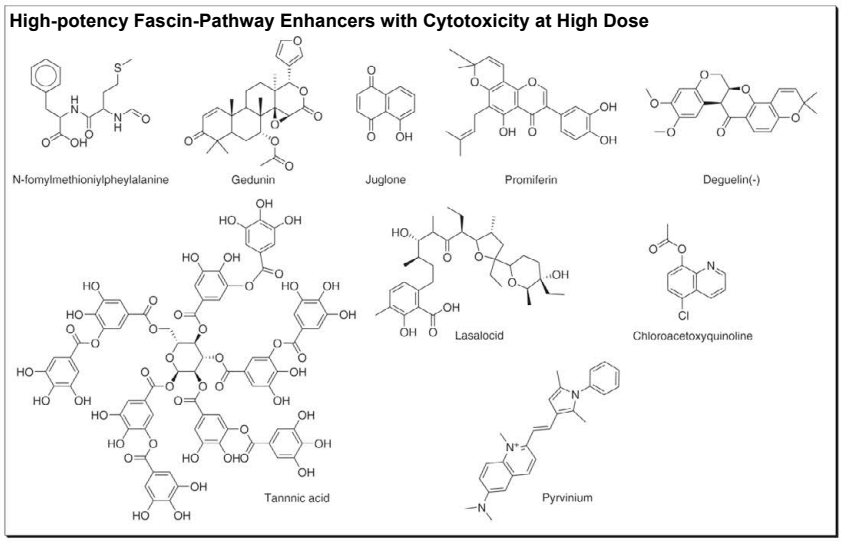


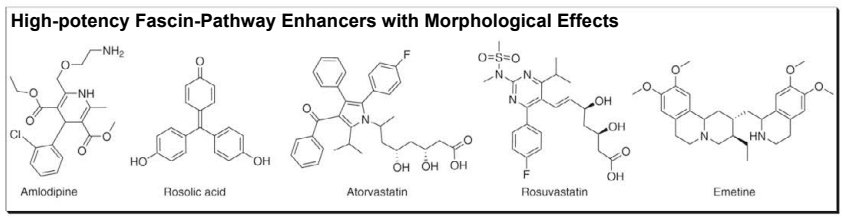
Supplemental Figure 1 (Fig. S1). Effect of DMSO on neurite curvature of cultured Drosophila larval neurons. Curvature profiles of populations of cultured mushroom body (MB) gamma neurons from fascin-deficient sn^3/sn^3 mutant larval CNS. Dissociated neurons from a single CNS were distributed into four culture dishes, each of which was cultured with a different DMSO concentration (0%, 0.1%, 0.5%, or 1.0%) for three days. Gamma neurons were identified using *201Y-GAL4* and *UAS-lacZ*, i.e., based on positive labeling with anti-βgal. Approximately 45 MB gamma neurons were sampled from each dish. Mean curvature for each neuron was calculated from skeletonized images of neurite arbors as described in Kraft et al., 2006, *J. Neurosci.* 26:8734-8747. (A-D) Frequency distributions of mean curvature values for larval MB gamma neurons. The histograms were plotted with soft binning to mitigate the effects of discretization error (see Methods). (A) 0% DMSO. (B) 0.1% DMSO. (C) 0.5% DMSO. (D) 1.0% DMSO. (E) Four scaled normal-distribution curves that were fitted to the data used to generate the histograms in panels A-D. By multiplying the probability density by the bin size, the ordinate axis is scaled to that of the histograms. Each color represents a different concentration of DMSO, as indicated in the legend.

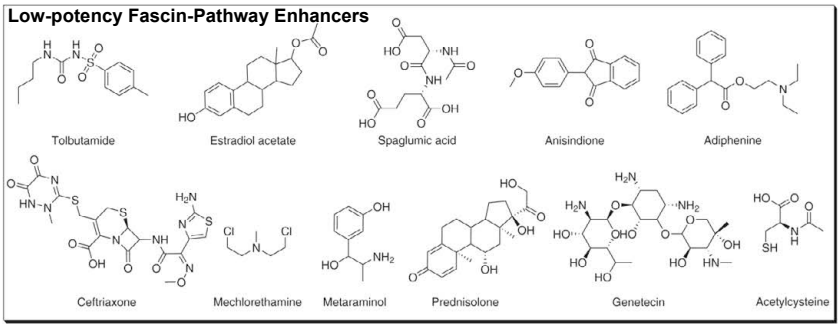
Kraft et al.

Figure S2.
Chemical structures of fascin-pathway modifiers.









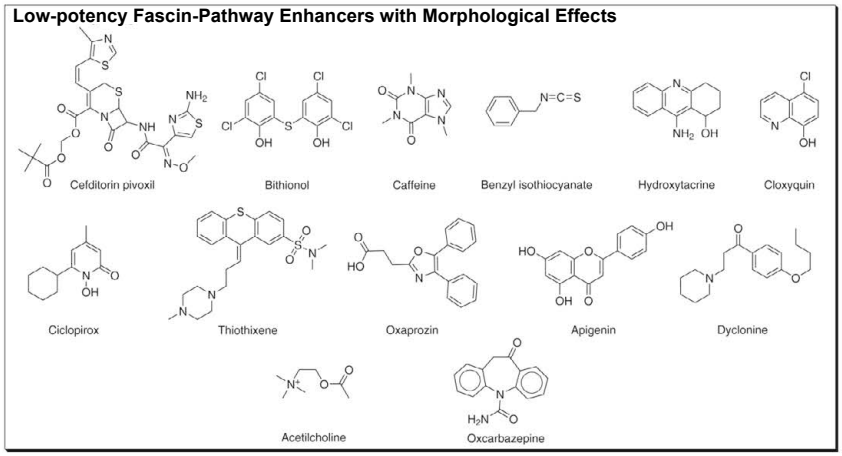
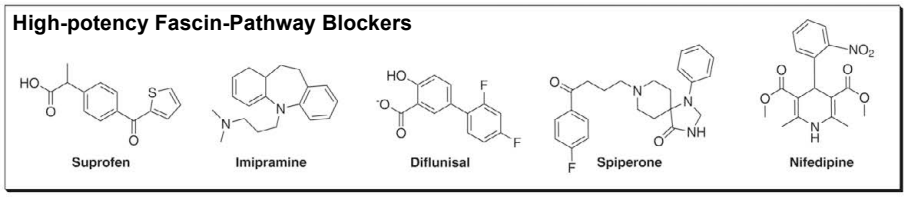
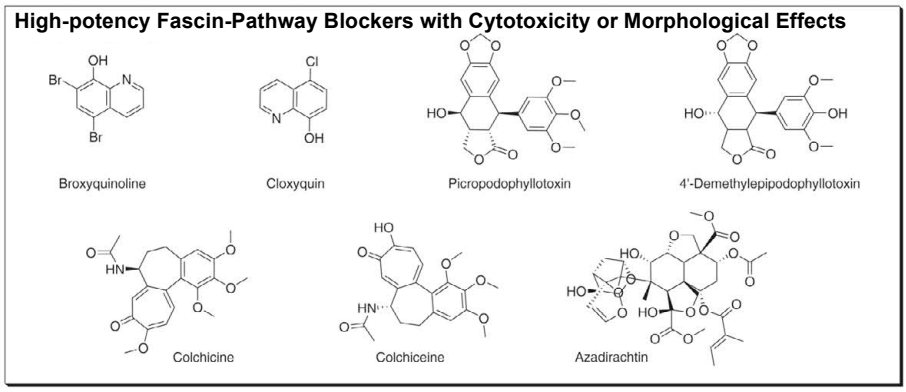
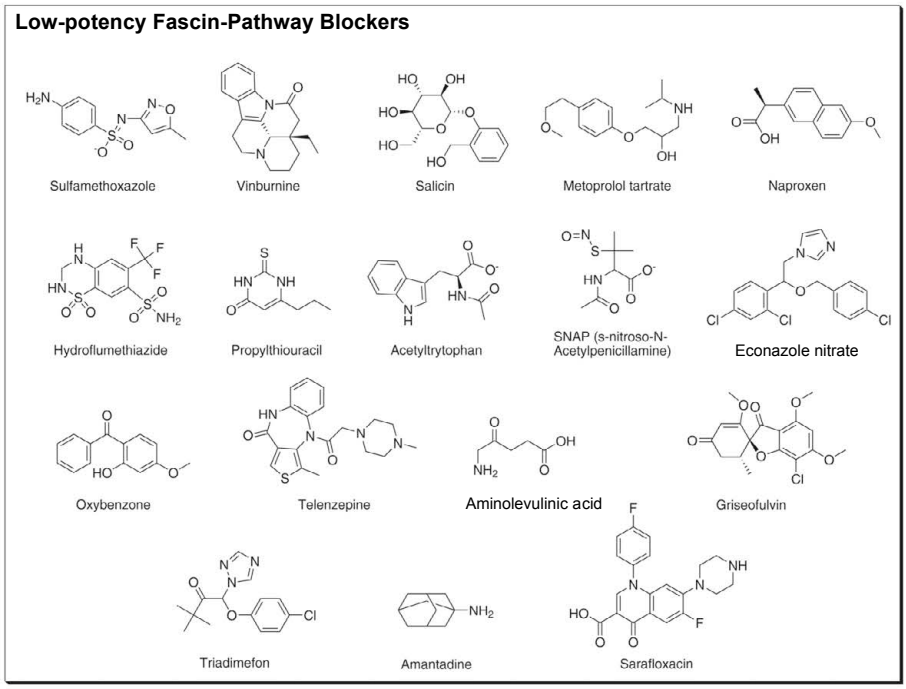
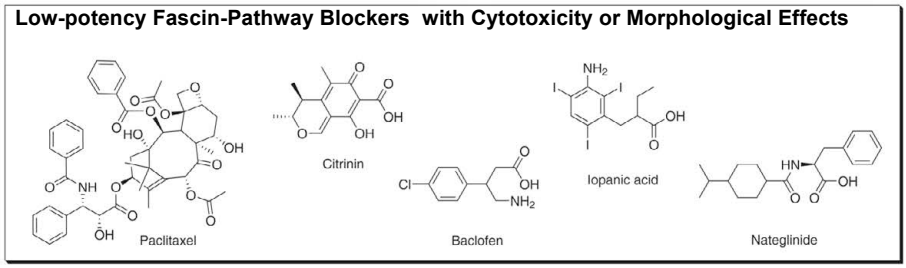


Fig. S2, *continued.*
Chemical structures of fascin-pathway modifiers.









Source:
MicroSource Discovery Systems, Inc.

Kraft et al., TableS1
NINDS Custom Collection II
Compound Library

Yellow: Fascin-pathway enhancer
Blue: Fascin-pathway blocker
Green: Both

COMPOUND NAME	Chamical Abstract Service (CAS) #	FORMULA	MW	STATUS
1- (2-METHOXYPHENYL)PIERAZINE HYDROCHLORIDE		C11H17ClN2O	228.72	experimental
1,2-DIMETHYLHYDRAZINE HYDROCHLORIDE	306-37-6	C2H10Cl2N2	133.02	experimental
1,3-DIPROPYL-8-CYCLOPENTYLXANTHINE [DPCPX]		C16H24N4O2	304.40	experimental
18alpha-GLYCYRRHETINIC ACID		C30H46O4	470.70	experimental
1-BENZYLOXYCARBONYLAMINOPHENETHYL CHLOROMETHYL	26049-94-5	C18H18ClNO3	331.80	experimental
1-METHYLXANTHINE	6136-37-4	C6H6N4O2	166.14	experimental
1-PHENYLBIGUANIDE HYDROCHLORIDE	55-57-2	C8H12ClN5	213.67	experimental
1R,2S-PHENYLPROPYLAMINE	14838-15-4	C9H13NO	151.21	experimental
1R,9S-HYDRASTINE	118-08-1	C21H21NO6	383.40	experimental
1R-CAMPHOR	464-49-3; 76-22-2	C10H16O	152.24	USP, JAN
1S,2R-PHENYLPROPANOLAMINE HYDROCHLORIDE	37577-28-9	C9H14ClNO	187.67	experimental
2- (2,6-DIMETHOXYPHENOXYETHYL)AMINOMETHYL-1,4-		C19H24ClNO5	381.86	experimental
2,3-DIHYDROXY-6,7-DICHLOROQUINOXALINE		C8H4Cl2N2O2	231.04	experimental
2,6-DI-t-BUTYL-4-METHYLPHENOL	128-37-0	C15H24O	220.36	experimental
2-MERCAPTOBENZOTHIAZOLE	149-30-4	C7H5NS2	167.25	experimental
2-THIOURACIL	141-90-2	C4H4N2OS	128.15	BP-1948
3,3'-DIINDOLYLMETHANE	1968-05-4	C17H14N2	246.31	experimental
3,5-DINITROCATECHOL (OR-486)		C6H4N2O6	200.11	experimental
3-AMINOPROPANESULPHONIC ACID	3687-18-1	C3H9NO3S	139.17	experimental
3-ISOBUTYL-1-METHYLXANTHINE (IBMX)	28822-58-4	C10H14N4O2	222.25	experimental
3-METHYL-1-PHENYL-2-PYRAZOLIN-5-ONE (MCI-186)		C10H10N2O	174.20	experimental
3-METHYLXANTHINE	1076-22-8	C6H6N4O2	166.14	experimental
4'-DEMETHYLEPIPODOPHYLLOTOXIN		C21H20O8	400.39	experimental
4-NAPHTHALIMIDOBUTYRIC ACID		C16H13NO4	283.29	experimental
5-AMINOPENTANOIC ACID HYDROCHLORIDE		C5H12ClNO2	153.61	experimental
5-CHLOROINDOLE-2-CARBOXYLIC ACID	10517-21-2	C9H6ClNO2	195.61	experimental
5-FLUORO-5'-DEOXYURIDINE	3094-09-5	C9H11FN2O5	246.20	experimental
5-FLUOROINDOLE-2-CARBOXYLIC ACID	399-76-8	C9H6FNO2	179.15	experimental
5-NITRO-2-(3-PHENYLPROPYLAMINO)-BENZOIC ACID [NPPB]		C16H16N2O4	300.32	experimental
6,7-DICHLORO-3-HYDROXY-2-QUINOXALINECARBOXYLIC ACID		C9H4Cl2N2O3	259.05	experimental
6alpha-METHYLPREDNISOLONE ACETATE		C24H32O6	416.52	experimental
6-AMINOCAPROIC ACID	60-32-2	C6H13NO2	131.18	USP, INN, BAN
6-AMINONICOTINAMIDE	329-89-5	C6H7N3O	137.14	experimental
7-CHLOROKYNURENIC ACID		C10H6ClNO3	223.62	experimental
7-NITROINDAZOLE	2942-42-9	C7H5N3O2	163.14	experimental
8-CYCLOPENTYLTHEOPHYLLINE		C12H16N4O2	248.29	experimental
9-AMINO-1,2,3,4-TETRAHYDROACRIDINE HYDROCHLORIDE		C13H15ClN2	234.73	experimental
ABRINE (L)	526-31-8	C12H14N2O2	218.26	experimental

ACEBUTOLOL HYDROCHLORIDE	34381-68-5, 37517-30-9	C18H29ClN2O4	372.90	USAN, INN, BAN
ACETAMINOPHEN	103-90-2	C8H9NO2	151.17	USP, INN, BAN
ACETAMINOSALOL	118-57-0	C15H13NO4	271.28	INN
ACETANILIDE	103-84-4	C8H9NO	135.17	NF
ACETAZOLAMIDE	59-66-5	C4H6N4O3S2	222.25	USP, INN, BAN, JAN
ACETOHYDROXAMIC ACID	546-88-3	C2H5NO2	75.07	USP, INN
ACETOSYRINGONE	2478-38-8	C10H12O4	196.20	experimental
ACETYL TYROSINE ETHYL ESTER		C13H17NO4	251.28	experimental
ACETYLCARNITINE	3040-38-8	C8H16ClNO4	225.67	experimental
ACETYLCHOLINE	60-31-1, 51-84-3 [acetylcholine]	C7H16ClNO2	181.66	USP
ACETYLCYSTEINE	616-91-1	C5H9NO3S	163.20	USP, INN, BAN, JAN
ACETYLGLUCOSAMINE		C8H15NO6	221.21	experimental
ACETYLGLUTAMIC ACID		C7H11NO5	189.17	experimental
ACETYL-L-LEUCINE	99-15-0	C8H15NO3	173.21	INN
ACETYLTRYPTOPHAN	1218-34-4	C13H14N2O3	246.27	experimental
ACETYLTRYPTOPHANAMIDE		C13H15N3O2	245.28	experimental
ACEXAMIC ACID	57-08-9	C8H15NO3	173.21	INN, BAN
ACIVICIN	42228-92-2	C5H7ClN2O3	178.58	USAN, INN
ACONITINE	302-27-2	C34H47NO11	645.75	BP-1934
ACRIFLAVINIUM HYDROCHLORIDE	8018-07-3	C14H14ClN3	259.74	INN, NF-X
ACRISORCIN	7527-91-5	C25H28N2O2	388.51	USP-XXII, INN
ACYCLOVIR	59277-89-3	C8H11N5O3	225.21	USP, INN, BAN, JAN
ADENOSINE	58-61-7	C10H13N5O4	267.25	USP, BAN
ADIPHENINE HYDROCHLORIDE	50-42-0, 64-95-9 [adiphenine]	C20H26ClNO2	347.89	USAN, INN
ADRENALINE BITARTRATE	51-42-3	C13H19NO9	333.30	USP, JAN
AESCULIN	531-75-9	C15H16O9	340.29	experimental
AGMATINE SULFATE	2482-00-0	C5H16N4O4S	228.27	experimental
AJMALINE	4360-17-7	C20H26N2O2	326.44	JAN
AKLAVINE HYDROCHLORIDE	60504-57-6 (aklavine)	C30H36ClNO10	606.08	experimental
AKLOMIDE	3011-89-0	C7H5ClN2O3	200.58	USAN, INN, BAN
ALAPROCLATE	60719-82-6	C13H18ClNO2	255.75	USAN, INN
ALEXIDINE HYDROCHLORIDE	22573-93-9, 22782-69-0	C26H58Cl2N10	581.73	experimental
ALFLUZOCIN	81403-80-7	C19H27N5O4	389.46	USAN, INN, BAN
ALLANTOIN	97-59-6	C4H6N4O3	158.12	USP, BAN, JAN
ALLOPURINOL	315-30-0	C5H4N4O	136.11	USP, INN, BAN, JAN
ALLOXAN	2244-11-3	C4H2N2O4	142.07	experimental
ALMOTRIPTAN	154323-57-6	C17H25N3O2S	335.47	USAN, INN, BAN
alpha-CYANO-3-HYDROXYCINNAMIC ACID		C10H7NO3	189.17	experimental
alpha-TOCHOPHERYL ACETATE	58-95-7	C31H52O3	472.76	USP
ALTHIAZIDE	5588-16-9	C11H14ClN3O4S3	383.90	USAN, INN
ALTRETAMINE	645-05-6	C9H18N6	210.28	USP, INN, BAN

ALVERINE CITRATE	5560-59-8, 150-59-4 [alverine]	C26H35NO7	473.57	USAN, INN, BAN
AMANTADINE HYDROCHLORIDE	665-66-7, 768-94-5	C10H18ClN	187.71	USP, INN, BAN
AMBROXOL HYDROCHLORIDE	23828-92-4, 18683-91-5	C13H19Br2ClN2O	414.57	INN, BAN, JAN
AMCINONIDE	51022-69-6	C28H35FO7	502.59	USP, INN, BAN, JAN
AMIKACIN SULFATE	39831-55-5, 37517-28-5	C22H47N5O21S2	781.77	USP, JAN
AMILORIDE HYDROCHLORIDE	17440-83-4, 2016-88-8	C6H9Cl2N7O	266.09	USP, INN, BAN
AMINACRINE	90-45-9, 134-50-9 [aminacrine	C13H10N2	194.24	USAN, IN, BAN
AMINOCYCLOPROPANECARBOXYLIC ACID	68781-13-5	C4H7NO2	101.11	experimental
AMINOGLUTETHIMIDE	125-84-8	C13H16N2O2	232.28	USP, INN, BAN
AMINOHIPPURIC ACID	61-78-9, 94-16-6	C9H10N2O3	194.19	USP
AMINOHYDROXYBUTYRIC ACID	924-49-2	C4H9NO3	119.12	JAN
AMINOLEVULINIC ACID HYDROCHLORIDE	5451-09-2	C5H10ClNO3	167.59	USAN
AMINOPHENAZONE	83-07-8, 747-30-8	C11H13N3O	203.25	INN
AMINOPTERIN	54-62-6, 58602-66-7	C19H20N8O5	440.42	INN, BAN
AMINOPYRIDINE	504-24-5	C5H6N2	94.12	experimental
AMINOSALICYLATE SODIUM	6018-19-5	C7H6NNaO3	175.12	USP
AMINOTHIAZOLE	96-50-4	C3H4N2S	100.14	INN
AMIODARONE HYDROCHLORIDE	1951-25-3	C25H30ClI2NO3	681.78	USAN, INN, BAN, JAN
AMIPRILOSE	56824-20-5, 60414-06-4	C14H28ClNO6	341.84	USAN, INN
AMITRAZ	33089-61-1	C19H23N3	293.42	USP, INN, BAN
AMITRIPTYLINE HYDROCHLORIDE	549-18-8, 50-48-6	C20H24ClN	313.87	USP, INN, BAN, JAN
AMLODIPINE BESYLATE	111470-99-6	C26H31ClN2O8S	567.06	USAN, INN, BAN, JAN
AMODIAQUINE DIHYDROCHLORIDE	6398-98-7, 69-44-3	C20H24Cl3N3O	428.79	USP, INN, BAN
AMOXAPINE	14028-44-5	C17H16ClN3O	313.79	USP, INN, BAN, JAN
AMOXICILLIN	61336-70-7, 26787-78-0	C16H19N3O5S	365.41	USP, INN, BAN, JAN
AMPHOTERICIN B	1397-89-3	C47H73NO17	924.10	USP, INN, BAN, JAN
AMPICILLIN SODIUM	69-52-3, 69-53-4 [ampicillin]	C16H18N3NaO4S	371.39	USP, INN, BAN, JAN
AMPROLIUM	121-25-5	C14H20Cl2N4	315.25	USP, INN, BAN
AMYGDALIN	29883-15-6	C20H27NO11	457.44	experimental
ANDROSTERONE SODIUM SULFATE		C19H29NaO5S	392.49	experimental
ANISINDIONE	117-37-3	C16H12O3	252.27	NF-XIII, INN, BAN
ANISODAMINE	17659-49-3	C17H23NO4	305.38	experimental
ANISOMYCIN	22862-76-6	C14H19NO4	265.31	experimental
ANTAZOLINE PHOSPHATE	154-68-7, 91-75-8 [antazoline]	C17H22N3O4P	363.36	USP
ANTHRALIN	480-22-8, 1143-38-0	C14H10O3	226.23	USP
ANTHRAQUINONE	84-65-1	C14H8O2	208.22	experimental
ANTIPYRINE	60-80-0	C11H12N2O	188.23	USP, INN, BAN, JAN
APIGENIN	520-36-5	C15H10O5	270.24	experimental
APOMORPHINE HYDROCHLORIDE	41372-20-7, 314-19-2	C17H18ClNO2	303.79	USP, BAN
APRAMYCIN	37321-09-8	C21H41N5O11	539.59	USAN, INN, BAN
ARECOLINE HYDROBROMIDE	300-08-3, 63-75-2 [arecoline]	C8H14BrNO2	236.11	NF-XIII

ARTEMISININ	63968-64-9	C15H22O5	282.34	INN
ASPARTAME	22839-47-0	C14H18N2O5	294.31	NF, INN, BAN
ASPIRIN	50-78-2	C9H8O4	180.16	USP, BAN, JAN
ASTEMIZOLE	68844-77-9	C28H31FN4O	458.58	USP, INN, BAN, JAN
ATENOLOL	29122-68-7	C14H22N2O3	266.34	USP, INN, BAN, JAN
ATORVASTATIN CALCIUM	134523-03-8, 134523-00-5	C33H33CaFNO5	582.71	USAN, INN, BAN
ATOVAQUONE	95233-18-4	C22H19ClO3	366.85	USP, INN, BAN
ATRACTYLOSIDE POTASSIUM	17754-44-8(acid)	C30H44K2O16S2	803.01	experimental
ATROPINE	51-55-8, 5908-99-6 [atropine	C17H25NO7S	387.46	USP, BAN
AVOBENZONE	70356-09-1	C20H22O3	310.40	USP, INN
AVOCADYNE	34524-38-4	C17H32O3	284.44	experimental
AVOCADYNONE ACETATE	24607-10-1	C19H32O4	324.46	experimental
AZACITIDINE	320-67-2	C8H12N4O5	244.21	USAN, INN
AZADIRACHTIN	11141-17-6	C35H44O16	720.73	experimental
AZAPERONE	1649-18-9	C19H22FN3O	327.41	USP, INN, BAN
AZASERINE	115-02-6	C5H7N3O4	173.13	USAN, INN
AZATHIOPRINE	446-86-6	C9H7N7O2S	277.27	USP, INN, BAN, JAN
AZELAIC ACID	123-99-9	C9H16O4	188.23	USAN, INN
AZELASTINE HYDROCHLORIDE	58581-89-8	C22H25Cl2N3O	418.37	USAN, INN, BAN, JAN
AZITHROMYCIN	83905-01-5, 117772-70-0	C38H72N2O12	749.00	USP, INN, BAN
AZLOCILLIN SODIUM	37091-66-0	C20H22N5NaO6S	483.48	USAN, INN, BAN
AZOBENZENE	103-33-3	C12H10N2	182.23	experimental
BACAMPICILLIN HYDROCHLORIDE	37661-08-8, 50972-17-3	C21H28ClN3O7S	501.99	USP, INN, BAN, JAN
BACITRACIN	1405-87-4	C66H103N17O16S	1422.73	USP, INN, BAN, JAN
BACLOFEN	1134-47-0	C10H12ClNO2	213.67	USP, INN, BAN, JAN
BAICALEIN	491-67-8	C15H10O5	270.24	experimental
BENAZEPRIL HYDROCHLORIDE	86541-74-4	C24H29ClN2O5	460.96	USAN, INN, BAN, JAN
BENDROFUMETHIAZIDE	73-48-3	C15H14F3N3O4S2	421.42	USP, INN, BAN, JAN
BENFLUOREX HYDROCHLORIDE	23602-78-0	C19H21ClF3NO2	387.83	INN, BAN
BENSERAZIDE HYDROCHLORIDE	322-35-0	C10H16ClN3O5	293.71	USAN, INN, BAN, JAN
BENZALKONIUM CHLORIDE	8001-54-5	C22H40ClN	354.02	NF, INN, BAN, JAN
BENZANTHRONE	82-05-3	C17H10O	230.27	experimental
BENZETHONIUM CHLORIDE	121-54-0	C27H42ClNO2	448.09	USP, INN, BAN, JAN
BENZOCAINE	94-09-7	C9H11NO2	165.19	USP, INN, BAN
BENZTHIAZIDE	91-33-8	C15H14ClN3O4S3	431.94	USP-XIII, INN, BAN, JAN
BENZTROPINE	132-17-2, 86-13-5 [benztropine]	C21H27NO5S	405.52	USP, INN, BAN, JAN
BENZYL ISOTHIOCYANATE	622-78-6	C8H7NS	149.22	INN
BENZYL PENICILLIN POTASSIUM	69-57-8, 61-33-6 [penicillin, G]	C16H17KN2O4S	372.49	USP, BAN, JAN
BEPRIDIL HYDROCHLORIDE	74764-40-2	C24H35ClN2O	403.01	USAN, INN, BAN, JAN
BERBAMINE HYDROCHLORIDE	478-61-5 (berbamine)	C37H42Cl2N2O6	681.66	experimental
BERBERINE CHLORIDE	633-65-8, 2086-83-1	C20H18ClNO4	371.82	JAN

BERGAPTEN	484-20-8	C12H8O4	216.20	INN
beta-CAROTENE	7235-40-7	C40H56	536.89	USP, INN
BETAMETHASONE	378-44-9	C22H29FO5	392.47	USP, INN, BAN, JAN
BETAMIPRON	3440-28-6	C10H11NO3	193.20	INN, JAN
beta-PELTATIN	518-29-6	C22H22O8	414.42	experimental
BETA-PROPIOLACTONE	57-57-8	C3H4O2	72.06	USAN, INN
BETHANECHOL CHLORIDE	590-63-6, 674-38-4	C7H17ClN2O2	196.68	USP, BAN, JAN
BETULINIC ACID	472-15-1	C29H46O3	442.69	experimental
BEZAFIBRATE	41859-67-0	C19H20ClNO4	361.83	USAN, INN, BAN, JAN
BIFONAZOLE	60628-96-8	C22H18N2	310.40	USAN, INN, BAN, JAN
BIOTIN	58-85-5	C10H16N2O3S	244.31	USP, INN, JAN
BISACODYL	603-50-9	C22H19NO4	361.40	USP, INN, BAN, JAN
BITHIONOL	97-18-7	C12H4Cl4Na2O2S	400.02	NF-XII,INN, BAN, JAN
BOVINOCIDIN (3-nitropropionic acid)	504-88-1	C3H5NO4	119.08	experimental
BRETYLIUM TOSYLATE	61-75-6, 59-41-6 [bretylium]	C18H24BrNO3S	414.36	USP, INN, BAN
BROMHEXINE HYDROCHLORIDE	611-75-6, 3572-43-8	C14H21Br2ClN2	412.60	USAN, INN, BAN, JAN
BROMOPRIDE	4093-35-0	C14H22BrN3O2	344.25	INN
BROMPHENIRAMINE MALEATE	980-71-2, 86-22-6	C20H23BrN2O4	435.32	USP, INN, BAN
BROXYQUINOLINE	521-74-4	C9H5Br2NO	302.95	INN
BUCLADESINE	362-74-3	C18H24N5O8P	469.39	INN, JAN
BUDESONIDE	51333-22-3 [11(gr b), 16(gr a)]	C25H34O6	430.55	USAN, INN, BAN, JAN
BUMETANIDE	28395-03-1	C17H20N2O5S	364.42	USP, INN, BAN, JAN
BUPIVACAINE HYDROCHLORIDE	14252-80-3, 2180-92-9	C18H29ClN2O	324.90	USP, INN, BAN, JAN
BUPROPION	31677-93-7, 34911-55-2	C13H19Cl2NO	276.21	USP, INN, BAN
BUSULFAN	55-98-1	C6H14O6S2	246.30	USP, INN, BAN, JAN
BUTACAINE	149-15-5, 149-16-6 [butacaine]	C18H30N2O2	306.45	USP-XX, INN, BAN
BUTAMBEN	94-25-7	C11H15NO2	193.25	USP
CACODYLIC ACID	75-60-5	C2H7AsO2	138.00	experimental
CAFFEINE	58-08-2, 5743-12-4	C8H10N4O2	194.19	USP, INN, BAN, JAN
CALCEIN	1461-15-0	C30H26N2O13	622.55	experimental
CAMPTOTHECIN	7689-03-4	C20H16N2O4	348.36	experimental
CANDESARTAN CILEXTIL	139481-59-7	C33H34N6O6	610.68	USAN, INN
CANRENOIC ACID, POTASSIUM SALT	2181-04-6, 4138-96-9	C22H29KO4	396.58	USAN, INN, BAN, JAN
CANRENONE	976-71-6	C22H28O3	340.47	USAN, INN
CAPREOMYCIN SULFATE	1405-37-4, 11003-38-6	C25H46N14O12S	766.80	USP, INN, BAN, JAN
CAPSANTHIN	465-42-9	C40H56O3	584.89	experimental
CAPTOPRIL	62571-86-2	C9H15NO3S	217.29	USP, INN, BAN, JAN
CARBACHOL	51-83-2	C6H15ClN2O2	182.65	USP, INN, BAN, JAN
CARBADOX	6804-07-5	C11H10N4O4	262.23	USAN, INN, BAN
CARBAMAZEPINE	298-46-4	C15H12N2O	236.28	USP, INN, BAN, JAN
CARBENICILLIN DISODIUM	4800-94-6, 4697-36-3	C17H16N2Na2O6S	422.37	USP, INN, BAN, JAN

CARBENOXOLONE SODIUM	7421-40-1, 5697-56-3	C34H48Na2O7	614.74	USAN, INN, BAN, JAN
CARBETAPENTANE CITRATE	23142-01-0, 77-23-6	C26H39NO10	525.60	NF-XIII, INN, BAN
CARBIMAZOLE	22232-54-8	C7H10N2O2S	186.23	INN, BAN
CARBINOXAMINE MALEATE	3505-38-2, 486-16-8	C20H23ClN2O5	406.87	USP, INN, BAN, JAN
CARBOPLATIN	41575-94-4	C6H12N2O4Pt	371.26	USP, INN, BAN, JAN
CARISOPRODOL	78-44-4	C12H24N2O4	260.34	USP, INN, BAN
CARMOFUR	61422-45-5	C11H16FN3O3	257.27	INN, JAN
CARMUSTINE	154-93-8	C5H9Cl2N3O2	214.05	USAN, INN, BAN
CARNITINE HYDROCHLORIDE	461-06-3	C7H16ClNO3	197.66	INN, JAN
CARPROFEN	53716-49-7	C15H12ClNO2	273.72	USAN, INN, BAN
CARVEDILOL TARTRATE	72956-09-3 (carvedilol)	C28H32N2O10	556.57	USAN, INN, BAN, JAN
CEFACLOR	70356-03-5, 53994-73-3	C15H14ClN3O4S	367.81	USP, INN, BAN, JAN
CEFADROXIL	66592-87-8, 50370-12-2	C16H17N3O5S	363.39	USP, INN, BAN, JAN
CEFAMANDOLE NAFATE	42540-40-9, 34444-01-4	C19H17N6NaO6S2	512.50	USP, BAN
CEFAZOLIN SODIUM	27164-46-1, 25953-19-9	C14H13N8NaO4S3	476.49	USP, INN, BAN
CEFDINIR	91832-40-5	C14H13N5O5S2	395.42	USAN, INN, BAN
CEFDITORIN PIVOXIL	117467-28-4	C25H28N6O7S3	620.73	INN, JAN
CEFMETAZOLE SODIUM	56796-39-5	C15H16N7NaO5S3	493.52	USP, INN
CEFOPERAZONE SODIUM	62893-20-3, 62893-19-0	C25H26N9NaO8S2	667.66	USP, INN, BAN, JAN
CEFOTAXIME SODIUM	64485-93-4, 63527-52-6	C16H16N5NaO7S2	477.45	USP, INN, BAN, JAN
CEFOXITIN SODIUM	66309-69-1, 61622-34-2	C16H16N3NaO7S2	449.44	USP, INN, BAN, JAN
CEFTIBUTEN	97519-39-6	C15H14N4O6S2	410.43	USAN, INN, BAN
CEFTRIAXONE SODIUM	73384-59-5 [ceftriaxone],	C18H16N8Na2O7S3	598.55	USP, INN, BAN, JAN
CEFUROXIME SODIUM	56238-63-2	C16H15N4NaO8S	446.37	USAN, INN, BAN
CELASTROL	34157-83-0	C29H38O4	450.62	experimental
CELECOXIB	169590-42-5	C17H14F3N3O2S	381.38	USAN, INN, BAN
CEPHALEXIN	23325-78-2, 15686-71-2	C16H17N3O4S	347.40	USP, INN, BAN, JAN
CEPHALORIDINE	50-59-9	C19H17N3O4S2	415.49	USAN, INN, BAN, JAN
CEPHALOTHIN SODIUM	58-71-9, 153-61-7 [cephalothin]	C16H15N2NaO6S2	418.43	USP, INN, BAN, JAN
CEPHAPIRIN SODIUM	24356-60-3, 21593-23-7	C17H16N3NaO6S2	445.45	USP, INN, BAN, JAN
CEPHARANTHINE	481-49-2	C37H38N2O6	606.73	JAN
CEPHRADINE	38821-53-3 [anhydrous], 58456-	C16H19N3O4S	349.41	USP, INN, BAN, JAN
CETRIMONIUM BROMIDE	57-09-0, 6899-10-1	C19H42BrN	364.46	INN, BAN
CETYLPYRIDINIUM CHLORIDE	6004-24-6, 123-03-5	C21H38ClN	340.00	USP, INN, BAN, JAN
CEVADINE	62-59-9	C32H49NO9	591.75	experimental
CHAULMOSULFONE	473-32-5	C48H76N2O4S	777.22	INN
CHLORAMPHENICOL	56-75-7	C11H12Cl2N2O5	323.13	USP, INN, BAN, JAN
CHLORAMPHENICOL HEMISUCCINATE	982-57-0, 56-75-7	C15H16Cl2N2O8	423.21	USP, BAN, JAN
CHLORANIL	118-75-2	C6Cl4O2	245.88	experimental
CHLORMADINONE ACETATE	302-22-7	C23H29ClO4	404.94	USAN, INN, BAN, JAN
CHLORMEZANONE	80-77-3	C11H12ClNO3S	273.74	INN, BAN, JAN

CHLOROACETOXYQUINOLINE		C11H8ClNO2	221.64	experimental
CHLOROCRESOL	59-50-7	C7H7ClO	142.59	NF, INN
CHLOROGUANIDE HYDROCHLORIDE	637-32-1	C11H17Cl2N5	290.20	USP-XIV, INN, BAN
CHLOROPHYLLIDE Cu COMPLEX Na SALT	15611-43-5	C34H28CuN4Na2O5	682.15	USP, JAN
CHLOROQUINE DIPHOSPHATE	54-05-7	C18H32ClN3O8P2	515.87	USP, BAN
CHLOROTHIAZIDE	58-94-6	C7H6ClN3O4S2	295.72	USP, INN, BAN
CHLOROTRIANISENE	569-57-3	C23H21ClO3	380.88	USP-XIII, INN, BAN
CHLOROXINE	773-76-2	C9H5Cl2NO	214.05	USAN
CHLOROXYLENOL	88-04-0	C8H9ClO	156.61	USP, INN, BAN
CHLORPHENIRAMINE (S) MALEATE	113-92-8, 132-22-9	C20H23ClN2O4	390.87	USP, INN, BAN
CHLORPROMAZINE	50-53-3	C17H19ClN2S	318.87	USP, INN, BAN, JAN
CHLORPROPAMIDE	94-20-2	C10H13ClN2O3S	276.74	USP, INN, BAN, JAN
CHLORTETRACYCLINE HYDROCHLORIDE	64-72-2	C22H24Cl2N2O8	515.35	USP, BAN
CHLORTHALIDONE	77-36-1	C14H11ClN2O4S	338.77	USP, INN, BAN, JAN
CHLORZOXAZONE	95-25-0	C7H4ClNO2	169.57	USP, INN, BAN, JAN
CHRYSANTHEMIC ACID	10453-89-1	C10H16O2	168.24	experimental
CHRYSIN	480-40-0	C15H10O4	254.24	experimental
CICLOPIROX OLAMINE	41621-49-2	C14H24N2O3	268.36	USP, INN, BAN
CILOSTAZOL	73963-72-1	C20H27N5O2	369.47	USAN, INN, BAN, JAN
CIMETIDINE	51481-61-9	C10H16N6S	252.34	USP, INN, BAN, JAN
CINEOLE	470-82-6	C10H18O	154.25	experimental
CINNARAZINE	298-57-7	C26H28N2	368.53	USAN, INN, BAN, JAN
CINOXACIN	28657-80-9	C12H10N2O5	262.22	USP, INN, BAN, JAN
CIPROFLOXACIN	85721-33-1	C17H18FN3O3	331.35	USP, INN, BAN
CISPLATIN	15663-27-1	H6Cl2N2Pt	300.06	USP, INN, BAN, JAN
CITICOLINE	987-78-0	C14H26N4O11P2	488.33	USAN, INN, JAN
CITIOLONE	1195-16-0	C6H9NO2S	159.21	INN
CITRININ	518-75-2	C13H14O5	250.25	experimental
CITROPTEN	487-06-9	C11H10O4	206.20	experimental
CLARITHROMYCIN	81103-11-9	C38H69NO13	747.97	USP, INN, BAN, JAN
CLEBOPRIDE MALEATE	55905-53-8	C24H28ClN3O6	489.96	USAN, INN, BAN, JAN
CLEMASTINE	15686-51-8	C25H30ClNO5	459.97	USAN, BAN
CLIDINIUM BROMIDE	3485-62-9	C22H26BrNO3	432.36	USP, INN, BAN
CLINDAMYCIN HYDROCHLORIDE	21462-39-5, 58207-19-5	C18H34Cl2N2O5S	461.45	USAN, INN, BAN
CLOBETASOL PROPIONATE	25122-46-7, 25122-41-2	C25H32ClFO5	466.98	USP, INN, BAN, JAN
CLOFIBRIC ACID	882-09-7	C10H11ClO3	214.65	INN
CLOFOCTOL	37693-01-9	C21H26Cl2O	365.35	INN
CLOMIPHENE CITRATE	50-41-9, 911-45-5 [clomiphene]	C32H36ClNO8	598.10	USP, INN, BAN
CLOMIPRAMINE HYDROCHLORIDE	17321-77-6, 303-49-1	C19H24Cl2N2	351.32	USP, INN, BAN, JAN
CLONIDINE HYDROCHLORIDE	4205-91-8, 4205-90-7	C9H10Cl3N3	266.56	USP, INN, BAN
CLOPERASTINE HYDROCHLORIDE	3703-76-2	C20H25Cl2NO	366.33	INN, JAN

CLOPIDOGREL SULFATE	113665-84-2	C16H18ClNO6S2	419.91	USP, INN, BAN
CLOPIDOL	2971-90-6	C7H7Cl2NO	192.05	USAN, INN, BAN
CLOTRIMAZOLE	23593-75-1	C22H17ClN2	344.85	USP, INN, BAN, JAN
CLOXACILLIN SODIUM	7081-44-9, 642-78-4	C19H17ClN3NaO5S	457.87	USP, INN, BAN, JAN
CLOXYQUIN	130-16-5	C9H6ClNO	179.61	USAN, INN
CLOZAPINE	5786-21-0	C18H19ClN4	326.83	USP, INN, BAN
COLCHICEINE	477-27-0	C21H23NO6	385.42	experimental
COLCHICINE	64-86-8	C22H25NO6	399.45	USP, JAN
COLFORSIN	66575-29-9	C22H34O7	410.51	USAN, INN
COLISTIMETHATE SODIUM	8068-28-8, 21362-08-3	C57H103N16Na5O28S	1735.82	USP, INN, BAN, JAN
CONVALLATOXIN	508-75-8	C29H42O10	550.65	experimental
CORALYNE CHLORIDE	38989-38-7	C22H22ClNO4	399.88	experimental
CORTISONE ACETATE	50-04-4, 53-06-5 [cortisone]	C23H30O6	402.49	USP, INN, BAN, JAN
COTININE	5695-98-7, 486-56-6 [cotinine]	C10H12N2O	176.22	experimental
CREATININE	60-27-5	C4H7N3O	113.12	undetermined activity
CRESOL	1319-77-3	C7H8O	108.14	NF, JAN
CROMOLYN SODIUM	15826-37-6, 16110-51-3	C23H14Na2O11	512.34	USP, INN, BAN, JAN
CROTAMITON	483-63-6	C13H17NO	203.29	USP, INN, BAN, JAN
CRUSTECDYSONE	5289-74-7	C27H44O7	480.65	experimental
CURCUMIN	458-37-7	C21H20O6	368.39	experimental
CYCLIZINE	82-92-8	C18H22N2	266.39	USP, BAN
CYCLOBENZAPRINE HYDROCHLORIDE	6202-23-9, 303-53-7	C20H22ClN	311.86	USP, INN
CYCLOCREATINE	35404-50-3	C5H9N3O2	143.15	experimental
CYCLOHEXIMIDE	66-81-9	C15H23NO4	281.35	USAN, INN
CYCLOLEUCINE	52-52-8	C6H11NO2	129.16	experimental
CYCLOPENTOLATE HYDROCHLORIDE	5870-29-1, 512-15-2	C17H26ClNO3	327.85	USP, INN, BAN, JAN
CYCLOPHOSPHAMIDE HYDRATE	6055-19-2, 50-18-0 [anhydrous]	C7H17Cl2N2O3P	279.10	USP, INN, BAN, JAN
CYCLOSERINE	68-41-7	C3H6N2O2	102.09	USP, INN, BAN, JAN
CYCLOSPORINE	59865-13-3	C62H111N11O12	1202.64	USP, INN, BAN, JAN
CYPROTERONE	2098-66-0	C22H27ClO3	374.91	INN, BAN, JAN
CYSTAMINE DIHYDROCHLORIDE	56-17-7	C4H14Cl2N2S2	225.20	experimental
CYTARABINE	147-94-4	C9H13N3O5	243.22	USP, INN, BAN, JAN
CYTISINE	485-35-8	C11H14N2O	190.25	INN
d[-Arg-2]KYOTORPHAN ACETATE		C17H27N5O6	397.43	experimental
DANAZOL	17230-88-5	C22H27NO2	337.47	USP, INN, BAN, JAN
DAPSONE	80-08-0	C12H12N2O2S	248.31	USP, INN, BAN
DEFEROXAMINE MESYLATE	138-14-7, 70-51-9	C26H52N6O11S	656.80	USAN, INN, BAN
DEGUELIN(-)	522-17-8	C23H22O6	394.43	experimental
DELTALINE	6836-11-9	C24H37NO7	451.56	experimental
DEMECLOCYCLINE HYDROCHLORIDE	127-33-3	C21H22Cl2N2O8	501.32	USP, BAN, JAN
DEQUALINIUM CHLORIDE	522-51-0, 6707-58-0	C30H40Cl2N4	527.59	INN, BAN, JAN

DERACOXIB	169590-41-4	C17H14F3N3O3S	397.38	USAN, INN
DESIPRAMINE HYDROCHLORIDE	58-28-6, 50-47-5 [desipramine]	C18H23ClN2	302.85	USP, INN, BAN, JAN
DESMETHYLDIHYDROCAPSAICIN		C17H27NO3	293.41	experimental
DESOXYCORTICOSTERONE ACETATE	56-47-3	C23H32O4	372.51	USP, INN, BAN
DEXAMETHASONE	50-02-2	C22H29FO5	392.47	USP, INN, BAN, JAN
DEXAMETHASONE ACETATE	55812-90-3, 1177-87-3	C24H31FO6	434.51	USP, INN, BAN, JAN
DEXAMETHASONE SODIUM PHOSPHATE	2392-39-4, 312-93-6	C22H28FNa2O8P	516.42	USP, BAN, JAN
DEXPROPRANOLOL HYDROCHLORIDE	13071-11-9	C16H22ClNO2	295.81	USAN, INN, BAN
DEXTROMETHORPHAN HYDROBROMIDE	6700-34-1, 125-69-9	C18H26BrNO	352.32	USP, INN, BAN
DIALLYL SULFIDE	592-88-1	C6H10S	114.21	experimental
DIAZOXIDE	364-98-7	C8H7ClN2O2S	230.67	USP, INN, BAN
DIBENZOTHIOPHENE	132-65-0	C12H8S	184.26	USAN
DIBENZOYLMETHANE	120-46-7	C15H12O2	224.26	experimental
DIBUCAINE HYDROCHLORIDE	61-12-1, 85-79-0 [dibucaine]	C20H30ClN3O2	379.93	USP, INN, BAN
DICLOFENAC SODIUM	15307-79-6	C14H10Cl2NNaO2	318.14	USP, JAN
DICLOXACILLIN SODIUM	13412-64-1, 343-55-5	C19H16Cl2N3NaO5S	492.32	USAN, INN, BAN
DICUMAROL	66-76-2	C19H12O6	336.30	USAN, INN
DIENESTROL	84-17-3, 13029-44-2 [//E,E//]	C18H18O2	266.34	USP, INN, BAN
DIETHYLCARBAMAZINE CITRATE	1642-54-2, 90-89-1	C16H29N3O8	391.42	USP, INN, BAN, JAN
DIETHYLSTILBESTROL	56-53-1	C18H20O2	268.36	USP, INN, BAN
DIETHYLTOLUAMIDE	134-62-3	C12H17NO	191.28	USP, INN, BAN
DIFLUNISAL	22494-42-4	C13H8F2O3	250.20	USP, INN, BAN, JAN
DIGITOXIN	71-63-6	C41H64O13	764.96	USP, INN, BAN, JAN
DIGOXIN	20830-75-5	C41H64O14	780.96	USP, INN, BAN, JAN
DIHYDROJASMONIC ACID	98674-52-3	C12H20O3	212.29	experimental
DIHYDROJASMONIC ACID, METHYL ESTER	24851-98-7	C13H22O3	226.32	experimental
DIHYDROSTREPTOMYCIN SULFATE	5490-27-7, 128-46-1	C21H43N7O16S	681.68	USP, INN, BAN, JAN
DILTIAZEM HYDROCHLORIDE	33286-22-5, 42399-41-7	C22H27ClN2O4S	450.99	USP, INN, BAN, JAN
DIMENHYDRINATE	523-87-5	C24H28ClN5O3	469.98	USP, INN, BAN, JAN
DIMETHADIONE	695-53-4	C5H7NO3	129.12	USAN, INN
DINITOLMIDE	148-01-6	C8H7N3O5	225.16	INN, BAN
DIOXYBENZONE	131-53-3	C14H12O4	244.25	USP, INN
DIPHENHYDRAMINE HYDROCHLORIDE	147-24-0	C17H22ClNO	291.82	USP, INN, BAN, JAN
DIPHENYLPYRALINE HYDROCHLORIDE	132-18-3 147-20-6	C19H24ClNO	317.86	USP-XXI, INN, BAN,
DIPLOSALSALATE	530-75-6	C16H12O6	300.27	experimental
DIPYRIDAMOLE	58-32-2	C24H40N8O4	504.64	USP, INN, BAN, JAN
DIPYRONE	5907-38-0, 68-89-3 [anhydrous]	C13H16N3NaO4S	333.34	USAN, INN, BAN, JAN
DIRITHROMYCIN	62013-04-1	C42H78N2O14	835.09	USP, INN, BAN
DISOPYRAMIDE PHOSPHATE	3737-09-5	C21H32N3O5P	437.48	USP, INN, BAN, JAN
DISULFIRAM	97-77-8	C10H20N2S4	296.54	USP, INN, BAN, JAN
DOPAMINE HYDROCHLORIDE	62-31-7, 51-61-6 [dopamine]	C8H12ClNO2	189.64	USP, INN, BAN, JAN

DOXEPIN HYDROCHLORIDE	1229-29-4, 1668-19-5	C19H22ClNO	315.85	USP, INN, BAN
DOXYCYCLINE HYDROCHLORIDE	17086-28-1, 564-25-0	C22H25ClN2O8	480.91	USP, INN, BAN
DOXYLAMINE SUCCINATE	562-10-7, 469-21-6	C21H28N2O5	388.47	USP, INN, BAN
D-PHENYLALANINE	673-06-3	C9H11NO2	165.19	INN
DROPERIDOL	548-73-2	C22H22FN3O2	379.44	USP, INN, BAN, JAN
DROPROPIZINE	17692-31-8	C13H20N2O2	236.32	INN, BAN
DYCLONINE HYDROCHLORIDE	536-43-6, 586-60-7 [dyclonine]	C18H28ClNO2	325.88	USP, INN, BAN
DYPHYLLINE	479-18-5	C10H14N4O4	254.25	USP, INN, BAN, JAN
EBSELEN	60940-34-3	C13H9NOSe	274.18	INN
ECONAZOLE NITRATE	68797-31-9, 27220-47-9	C18H16Cl3N3O4	444.70	USP, INN, BAN, JAN
EDROPHONIUM CHLORIDE	116-38-1, 312-48-1	C10H16ClNO	201.70	USP, INN, BAN, JAN
ELAIDYLPHOSPHOCHOLINE		C23H48NO4P	433.62	experimental
ELLAGIC ACID	476-66-4	C14H6O8	302.20	INN
EMETINE	316-42-7, 483-18-1 [emetine]	C29H42Cl2N2O4	553.58	USP, BAN
EMODIC ACID	578-45-5	C15H8O7	300.23	experimental
ENALAPRIL MALEATE	76095-16-4, 75847-73-3	C24H32N2O9	492.53	USP, INN, BAN, JAN
ENOXACIN	74011-58-8	C15H17FN4O3	320.33	USAN, INN, BAN, JAN
EPHEDRINE (1R,2S) HYDROCHLORIDE	50-98-6 [((-))-ephedrine,	C10H16ClNO	201.70	USAN, INN, BAN, JAN
ERGOCALCIFEROL	50-14-6	C28H44O	396.66	USP, INN, BAN, JAN
ERGONOVINE MALEATE	129-51-1, 60-79-7 [ergonovine]	C23H27N3O6	441.49	USP, INN, BAN, JAN
ERYTHROMYCIN ESTOLATE	134-36-1, 114-07-8	C52H97NO18S	1056.41	USP, INN, BAN, JAN
ESERINE	57-47-6	C15H21N3O2	275.35	USP, BAN
ESTRADIOL	50-28-2	C18H24O2	272.39	USP, INN, BAN
ESTRADIOL ACETATE	4245-41-4	C20H26O3	314.43	USAN
ESTRADIOL CYPIONATE	313-06-4	C26H36O3	396.58	USP
ESTRADIOL DIACETATE	34334-88-6	C22H28O4	356.47	experimental
ESTRADIOL METHYL ETHER	1035-77-4	C19H26O2	286.42	experimental
ESTRADIOL PROPIONATE	113-38-2	C21H28O3	328.46	NF-XIV, JAN
ESTRADIOL VALERATE	979-32-8	C23H32O3	356.51	USP
ESTRADIOL-3-SULFATE, SODIUM SALT		C18H23NaO5S	374.43	experimental
ESTRIOL	50-27-1, 514-68-1 [as,	C18H24O3	288.39	USP, INN, BAN, JAN
ESTRIOL BENZYL ETHER		C25H30O3	378.52	experimental
ESTRIOL METHYL ETHER	1474-53-9	C19H26O3	302.42	experimental
ESTRONE	53-16-7	C18H22O2	270.37	USP, INN, BAN
ESTRONE ACETATE		C20H24O3	312.41	experimental
ESTRONE HEMISUCCINATE		C22H26O5	370.45	experimental
ETANIDAZOLE	22668-01-5	C7H10N4O4	214.18	USAN, INN
ETHAMBUTOL HYDROCHLORIDE	1070-11-7, 74-55-5	C10H26Cl2N2O2	277.24	USP, INN, BAN, JAN
ETHAVERINE HYDROCHLORIDE	985-13-7, 486-47-5 [ethaverine]	C24H30ClNO4	431.96	INN
ETHINYL ESTRADIOL	57-63-6	C20H24O2	296.41	USP, INN, BAN, JAN
ETHIONAMIDE	536-33-4	C8H10N2S	166.25	USP, INN, BAN, JAN

ETHISTERONE	434-03-7	C21H28O2	312.46	NF-XIII, INN, BAN
ETHOPROPAZINE HYDROCHLORIDE	1094-08-2, 522-00-9	C19H25ClN2S	348.94	USP-XXIII, INN, BAN
ETHOSUXIMIDE	77-67-8	C7H11NO2	141.17	USP, INN, BAN, JAN
ETHYL 1-BENZYL-3-HYDROXY- 2-OXO[5H]PYRROLE-4-CARBOXYLATE		C14H15NO4	261.28	experimental
ETHYLNOREPINEPHRINE HYDROCHLORIDE	3198-07-0, 536-24-3	C10H16ClNO3	233.70	INN
ETODOLAC	41340-25-4	C17H21NO3	287.36	USP, INN, BAN
EUCATROPINE HYDROCHLORIDE	536-93-6, 100-91-4	C17H26ClNO3	327.85	USP, INN, BAN
EUGENOL	97-53-0	C10H12O2	164.21	USP
EXALAMIDE	53370-90-4	C13H19NO2	221.30	INN, JAN
EZETIMIBE	163222-33-1	C24H21F2NO3	409.44	USAN, INN, BAN
FAMCICLOVIR	104227-87-4	C14H19N5O4	321.34	USAN, INN, BAN
FAMOTIDINE	76824-35-6	C8H15N7O2S3	337.45	USP, INN, BAN, JAN
FENBENDAZOLE	43210-67-9	C15H13N3O2S	299.35	USAN, INN, BAN
FENBUFEN	36330-85-5	C16H14O3	254.29	USAN, INN, BAN, JAN
FENBUTYRAMIDE	90-26-6	C10H13NO	163.22	experimental
FENDILINE HYDROCHLORIDE	113042-18-7	C23H26ClN	351.92	INN
FENOFIBRATE	49562-28-9	C20H21ClO4	360.84	INN, BAN
FENOPROFEN	31879-05-7	C15H14O3	242.28	USAN, INN, BAN
FENOTEROL HYDROBROMIDE	13392-18-2	C17H22BrNO4	384.27	USAN, INN, BAN, JAN
FENSPIRIDE HYDROCHLORIDE	5053-08-7, 5053-06-5	C15H21ClN2O2	296.80	USAN, INN
FIPEXIDE HYDROCHLORIDE	34161-24-5	C20H22Cl2N2O4	425.32	INN
FLOXURIDINE	50-91-9	C9H11FN2O5	246.20	USP
FLUDROCORTISONE ACETATE	514-36-3, 127-31-1	C23H31FO6	422.50	USP, INN, BAN, JAN
FLUFENAMIC ACID	530-78-9	C14H10F3NO2	281.24	USAN, INN, BAN, JAN
FLUMEQUINE	42835-25-6	C14H12FNO3	261.26	USAN, INN, BAN
FLUMETHAZONE PIVALATE	2002-29-1, 2135-17-3	C27H36F2O6	494.58	USP, INN, BAN, JAN
FLUNARIZINE HYDROCHLORIDE	30484-77-6, 52468-60-7	C26H28Cl2F2N2	477.43	USAN, INN, BAN, JAN
FLUNISOLIDE	77326-96-6, 3385-03-3	C24H31FO6	434.51	USP, INN, BAN, JAN
FLUOCINONIDE	356-12-7	C26H32F2O7	494.54	USP, INN, BAN, JAN
FLUOROMETHOLONE	426-13-1	C22H29FO4	376.47	USP, INN, BAN, JAN
FLUOROURACIL	51-21-8	C4H3FN2O2	130.08	USP, INN, BAN, JAN
FLUOXETINE	54910-89-3	C17H19ClF3NO	345.80	USAN, INN, BAN
FLUPHENAZINE HYDROCHLORIDE	146-56-5	C22H28Cl2F3N3OS	510.45	USP, BAN, JAN
FLURANDRENOLIDE	1524-88-5	C24H33FO6	436.53	USP, INN, BAN, JAN
FLURBIPROFEN	5104-49-4	C15H13FO2	244.27	USP, INN, BAN, JAN
FLUTAMIDE	13311-84-7	C11H11F3N2O3	276.22	USP, INN, BAN
FOLIC ACID	59-30-3	C19H19N7O6	441.41	USP, INN, BAN, JAN
FORMESTANE	566-48-3	C20H28O2	300.44	INN, BAN
FOSCARNET SODIUM	63585-09-1	CNa3O5P	191.95	USAN, INN, BAN
FOSFOMYCIN	26472-47-9, 23112-90-5(acid)	C3H5CaO4P	176.12	USAN, INN, BAN
FOSFOSAL	6064-83-1	C7H7O6P	218.10	INN

FURAZOLIDONE	67-45-8	C8H7N3O5	225.16	USP, INN, BAN
FUREGRELATE SODIUM	87463-91-0, 85666-24-6	C15H10NNaO3	275.24	USAN, INN
FUROSEMIDE	54-31-9	C12H11ClN2O5S	330.75	USP, INN, BAN, JAN
FUSIDIC ACID	6990-06-3	C31H48O6	516.72	USAN, INN, BAN
GABOXADOL HYDROCHLORIDE	64603-91-4	C6H9ClN2O2	176.60	INN
GALANTHAMINE HYDROBROMIDE	357-70-0, 1953-04-4	C17H22BrNO3	368.27	USAN
GALLAMINE TRIETHIODIDE	65-29-2, 153-76-4 [gallamine]	C30H60I3N3O3	891.54	USP, INN
GAMBOGIC ACID	2752-65-0	C38H44O8	628.77	experimental
gamma-AMINOBUTYRIC ACID	56-12-2	C4H9NO2	103.12	JAN
GATIFLOXACIN	160738-57-8	C19H22FN3O4	375.40	USAN, INN
GEDUNIN	2753-30-2	C28H34O7	482.58	experimental
GEMFIBROZIL	25812-30-0	C15H22O3	250.34	USP, INN, BAN
GEMIFLOXACIN MESYLATE	204519-65-3	C19H24FN5O7S	485.49	USAN
GENETICIN	108321-42-2, 49863-47-	C20H44N4O18S2	692.72	experimental
GENTAMICIN SULFATE	1405-41-0, 1403-66-3	C21H45N5O11S	575.68	USP, INN, BAN, JAN
GENTIAN VIOLET	548-62-9	C25H30ClN3	407.99	USP, INN, BAN, JAN
GINKGOLIC ACID	22910-60-7	C22H34O3	346.51	experimental
GLAFENINE	3820-67-5	C19H17ClN2O4	372.81	INN, JAN
GLICLAZIDE	21187-98-4	C15H21N3O3S	323.42	INN, BAN, JAN
GLUCONOLACTONE	90-80-2	C6H10O6	178.14	USP
GLUCOSAMINE HYDROCHLORIDE	3416-24-8	C6H14ClNO5	215.64	NF-XXI
GLUTATHIONE	70-18-8	C10H17N3O6S	307.33	JAN
GLYBURIDE	10238-21-8	C23H28ClN3O5S	494.01	USP, INN, BAN, JAN
GLYCYLLEUCYLPHENYLALANINE		C17H25N3O4	335.41	experimental
GOSSYPOL	303-45-7	C30H30O8	518.57	experimental
GRISEOFULVIN	126-07-8	C17H17ClO6	352.77	USP, INN, BAN, JAN
GUAIFENESIN	93-14-1	C10H14O4	198.22	USP, INN, BAN, JAN
GUANABENZ ACETATE	23256-50-0	C10H12Cl2N4O2	291.14	USP, JAN
GUANETHIDINE SULFATE	60-02-6, 55-65-2 [guanethidine]	C10H24N4O4S	296.39	USP, INN, BAN
GUANIDINE CARBONATE	593-85-1	C2H7N3O3	121.10	experimental
GUVACINE HYDROCHLORIDE	498-96-4	C6H10ClNO2	163.61	experimental
HALAZONE	80-13-7	C7H5Cl2NO4S	270.09	USP, INN
HALCINONIDE	3093-35-4	C24H32ClFO5	454.97	USP, INN, BAN, JAN
HALOPERIDOL	52-86-8	C21H23ClFNO2	375.87	USP, INN, BAN, JAN
HARMALINE	304-21-2	C13H14N2O	214.27	experimental
HARMALOL HYDROCHLORIDE	6028-07-5	C12H13ClN2O	236.70	experimental
HARMINE	442-51-3	C13H12N2O	212.25	experimental
HARMOL HYDROCHLORIDE	40580-83-4	C12H11ClN2O	234.69	experimental
HECOGENIN	467-55-0	C27H42O4	430.63	experimental
HETACILLIN POTASSIUM	5321-32-4, 3511-16-8	C19H22KN3O4S	427.57	USP-XIII, JAN
HEXACHLOROPHENE	70-30-4	C13H6Cl6O2	406.91	USP, INN, BAN

HEXAMETHONIUM BROMIDE	55-97-0, 60-26-4	C12H30Br2N2	362.19	INN, BAN, JAN
HEXESTROL	5635-50-7	C18H22O2	270.37	NF-XI, INN
HEXETIDINE	141-94-6	C21H45N3	339.61	BAN
HEXYLRESORCINOL	136-77-6	C12H18O2	194.28	USP, BAN
HISTAMINE DIHYDROCHLORIDE	51-45-6 [histamine]	C5H11Cl2N3	184.07	USAN
HOMATROPINE BROMIDE	51-56-9, 87-00-3 [homatropine]	C16H22BrNO3	356.26	USP, JAN
HOMATROPINE METHYLBROMIDE	80-49-9, 87-00-3 [homatropine]	C17H24BrNO3	370.29	USP, INN, BAN
HUPERZINE A	102518-79-6	C15H18N2O	242.32	experimental
HYCANTHONE	3105-97-3	C20H24N2O2S	356.49	USAN, INN
HYDRALAZINE HYDROCHLORIDE	304-20-1, 86-54-4 [hydralazine]	C8H9ClN4	196.64	USP, INN, BAN
HYDROCHLOROTHIAZIDE	58-93-5	C7H8ClN3O4S2	297.74	USP, INN, BAN, JAN
HYDROCORTISONE	50-23-7	C21H30O5	362.47	USP, INN, BAN, JAN
HYDROCORTISONE ACETATE	50-03-3	C23H32O6	404.51	USP, INN, BAN, JAN
HYDROCORTISONE BUTYRATE	13609-67-1	C25H36O6	432.56	USP, INN, BAN, JAN
HYDROCORTISONE HEMISUCCINATE	83784-20-7, 2203-97-6	C25H34O8	462.54	USP, JAN
HYDROFLUMETHIAZIDE	135-09-1	C8H8F3N3O4S2	331.29	USP, INN, BAN, JAN
HYDROQUINIDINE	1435-55-8	C20H26N2O2	326.44	INN
HYDROQUINONE	123-31-9	C6H6O2	110.11	USP
HYDROXYCHLOROQUINE SULFATE	747-36-4, 118-42-3	C18H28ClN3O5S	433.96	USP-XXII, INN
HYDROXYPROGESTERONE CAPROATE	630-56-8, 68-96-2	C27H40O4	428.62	USP, INN, JAN
HYDROXYTACRINE MALEATE		C17H18N2O5	330.34	experimental
HYDROXYUREA	127-07-1	CH4N2O2	76.06	USP, INN, BAN
HYDROXYZINE PAMOATE	10246-75-0, 68-88-2	C44H43ClN2O8	763.29	USP, JAN
HYOSCYAMINE	101-31-5	C17H23NO3	289.38	USP, BAN
IBUPROFEN	15687-27-1, 58560-75-1 [(+/-)	C13H18O2	206.29	USP, INN, BAN, JAN
ICARIIN	489-32-7	C33H40O15	676.68	experimental
IMIDACLOPRID	13826-41-3	C10H11ClN4O2	254.68	agricultural use
IMIPRAMINE HYDROCHLORIDE	113-52-0, 50-49-7 [imipramine]	C19H25ClN2	316.88	USP, INN, BAN, JAN
INDAPAMIDE	26807-65-8	C16H16ClN3O3S	365.84	USP, INN, BAN, JAN
INDOLE-2-CARBOXYLIC ACID	1477-50-5	C9H7NO2	161.16	experimental
INDOLE-3-CARBINOL	700-06-1	C9H9NO	147.18	experimental
INDOMETHACIN	53-86-1	C19H16ClNO4	357.80	USP, INN, BAN, JAN
INDOPROFEN	31842-01-0	C17H15NO3	281.31	USAN, INN, BAN
IODIPAMIDE	606-17-7, 2618-26-0	C12H11I3N2O4	627.95	USAN, INN, BAN, JAN
IODOQUINOL	83-73-8	C9H5I2NO	396.96	USP, INN, BAN
IOPANIC ACID	96-83-3	C11H12I3NO2	570.94	USP, INN, BAN, JAN
IPRATROPIUM BROMIDE	66985-17-9, 22254-24-6	C20H30BrNO3	412.37	USAN, INN, BAN, JAN
IPRONIAZID SULFATE	54-92-2, 305-33-9 [as	C9H15N3O5S	277.30	INN, BAN
IRBESARTAN	138402-11-6	C25H28N6O	428.54	USP, INN, BAN
ISOBUTYLMETHYLXANTHINE		C10H14N4O2	222.25	experimental
ISOLIQUIRITIGENIN	961-29-5	C15H12O4	256.26	experimental

ISONIAZID	54-85-3	C6H7N3O	137.14	USP, INN, BAN, JAN
ISOPROPAMIDE IODIDE	71-81-8, 7492-32-2	C23H33IN2O	480.44	USP, INN, BAN, JAN
ISOPROTERENOL HYDROCHLORIDE	51-30-9, 7683-59-2	C11H18ClNO3	247.72	USP, INN, BAN, JAN
ISORESERPINE	482-85-9	C33H40N2O9	608.69	experimental
ISOSORBIDE DINITRATE	87-33-2	C6H8N2O8	236.14	USP, INN, BAN, JAN
ISOXICAM	34552-84-6	C14H13N3O5S	335.34	USAN, INN, BAN
ISOXSUPRINE HYDROCHLORIDE	579-56-6, 395-28-8	C18H24ClNO3	337.85	USP, INN, BAN, JAN
JUGLONE	481-39-0	C10H6O3	174.16	experimental
KAINIC ACID	487-79-6	C10H15NO4	213.24	INN, JAN
KANAMYCIN SULFATE	25389-94-0, 133-92-6	C18H38N4O15S	582.59	USP, INN, BAN, JAN
KETOCONAZOLE	65277-42-1	C26H28Cl2N4O4	531.44	USP, INN, BAN, JAN
KETOPROFEN	22071-15-4	C16H14O3	254.29	USP, INN, BAN, JAN
KETOROLAC TROMETHAMINE	74103-07-4, 74103-06-3	C19H24N2O6	376.41	USP, INN, BAN
KETOTIFEN FUMARATE	34580-14-8, 34580-13-7	C23H23NO5S	425.51	USAN, INN, BAN, JAN
KINETIN	525-79-1	C10H9N5O	215.22	experimental
KOJIC ACID	501-30-4	C6H6O4	142.11	experimental
KYNURENIC ACID		C10H7NO3	189.17	experimental
LABETALOL HYDROCHLORIDE	32780-64-6, 36894-69-6	C19H25ClN2O3	364.88	USP, INN, BAN, JAN
LACTULOSE	4618-18-2	C12H22O11	342.30	USP, INN, BAN, JAN
LANSOPRAZOLE	103577-45-3	C16H14F3N3O2S	369.37	USP, INN, BAN
LAPACHOL	84-79-7	C15H14O3	242.28	experimental
LASALOCID SODIUM	25999-31-9; 25999-20-6?	C34H53NaO8	612.79	USAN, INN, BAN
LEFUNOMIDE	75706-12-6	C12H9F3N2O2	270.21	USAN, INN, BAN
LEUCINE ENKEPHALIN		C28H37N5O7	555.64	experimental
LEUCOVORIN CALCIUM	1492-18-8	C20H21CaN7O7	511.51	USP, INN, BAN, JAN
LEVAMISOLE HYDROCHLORIDE	16595-80-5, 14769-73-4	C11H13ClN2S	240.76	USP, INN, BAN
LEVODOPA	59-92-7	C9H11NO4	197.19	USP, INN, BAN, JAN
LEVOFLOXACIN	138199-71-0	C18H20FN3O4	361.38	USAN, INN, BAN, JAN
LEVONORDEFRIN	829-74-3, 18829-78-2	C9H13NO3	183.21	USP, INN
LIDOCAINE HYDROCHLORIDE	6108-05-0, 73-78-9	C14H23ClN2O	270.81	USP, INN, JAN
LINCOMYCIN HYDROCHLORIDE	7179-49-9, 859-18-7	C18H35ClN2O6S	443.01	USAN, INN, BAN
LIOTHYRONINE SODIUM	55-06-1, 6893-02-3	C15H11I3NNaO4	672.96	USP, BAN, JAN
LISINOPRIL	83915-83-7, 76547-98-3	C21H31N3O5	405.50	USP, INN, BAN, JAN
L-LEUCYL-L-ALANINE	7298-84-2	C9H18N2O3	202.26	experimental
LOBELINE HYDROCHLORIDE	90-69-7	C22H28ClNO2	373.93	INN, BAN, JAN
LOMEFLOXACIN HYDROCHLORIDE	98079-52-8, 98079-51-7	C17H20ClF2N3O3	387.82	USAN, JAN
LOPERAMIDE HYDROCHLORIDE	34552-83-5, 53179-11-6	C29H34Cl2N2O2	513.51	USP, INN, BAN, JAN
LORATADINE	79794-75-5	C22H23ClN2O2	382.89	USP, INN, BAN
LOSARTAN	124750-99-8, 114798-26-4	C22H23ClN6O	422.92	USAN, INN, BAN
LOVASTATIN	75330-75-5	C24H36O5	404.55	USP, INN, BAN
LOXAPINE SUCCINATE	27833-64-3, 1977-10-2	C22H24ClN3O5	445.91	USP

L-PHENYLALANINOL	3182-95-4	C9H13NO	151.21	experimental
LUPININE	486-70-4	C10H19NO	169.27	experimental
LYSYLPHENYLALANYLTYROSINE		C24H32N4O5	456.55	experimental
LYSYL-TYROSYL-LYSINE ACETATE		C23H39N5O7	497.60	experimental
MADECASSIC ACID	18449-41-7	C30H48O6	504.71	experimental
MAFENIDE HYDROCHLORIDE	138-39-6	C7H11ClN2O2S	222.69	USAN, INN, BAN
MAPROTILINE HYDROCHLORIDE	10347-81-6, 10262-69-8	C20H24ClN	313.87	USAN, INN, BAN
MEBENDAZOLE	31431-39-7	C16H13N3O3	295.30	USP, INN, BAN, JAN
MEBEVERINE HYDROCHLORIDE	2753-45-9, 3625-06-7	C25H36ClNO5	466.02	USAN, INN, BAN
MEBHYDROLIN NAPHTHALENESULFONATE	524-81-2	C29H28N2O6S2	564.68	INN, BAN, JAN
MECAMYLAMINE HYDROCHLORIDE	826-39-1, 60-40-2	C11H22ClN	203.76	USP, INN, BAN
MECHLORETHAMINE	55-86-7, 51-75-2	C5H11Cl2N	156.06	USP, INN, BAN, JAN
MECLIZINE HYDROCHLORIDE	31884-77-2, 1104-22-9	C25H29Cl3N2	463.88	USP, INN, BAN, JAN
MECLOCYCLINE SULFOSALICYLATE	73816-42-9, 2013-58-3	C29H27ClN2O14S	695.06	USAN, INN, BAN
MECLOFENAMATE SODIUM	6385-02-0	C14H10Cl2NNaO2	318.14	USP
MEDROXYPROGESTERONE ACETATE	71-58-9, 520-85-4	C24H34O4	386.54	USP, INN, BAN, JAN
MEDRYSONE	2668-66-8	C22H32O3	344.50	USAN, INN
MEFENAMIC ACID	61-68-7	C15H15NO2	241.29	USP, INN, BAN, JAN
MEFEXAMIDE	1227-61-8	C15H25ClN2O3	316.83	USAN, INN
MEFLOQUINE	53230-10-7	C17H16F6N2O	378.32	USAN, INN, BAN
MEGESTROL ACETATE	595-33-5, 3562-63-8	C24H32O4	384.52	USP, INN, BAN
MELATONIN	73-31-4	C13H16N2O2	232.28	experimental
MELOXICAM	71125-38-7	C14H13N3O4S2	351.41	USAN, INN, BAN
MEMANTINE HYDROCHLORIDE	19982-08-2	C12H22ClN	215.77	USAN
MENADIONE	58-27-5	C11H8O2	172.19	USP, BAN
MENTHOL(-)	1490-04-6	C10H20O	156.27	USP, JAN
MEPENZOLATE BROMIDE	76-90-4, 25990-43-6	C21H26BrNO3	420.35	USP-XXIII, INN, BAN
MEPHENESIN	59-47-2	C10H14O3	182.22	NF-XII, INN, BAN
MEPHENTERMINE SULFATE	1212-72-2, 6190-60-9	C11H19NO4S	261.34	USP-XXIII, INN, BAN
MEPIVACAINE HYDROCHLORIDE	1722-62-9, 96-88-8	C15H23ClN2O	282.82	USP, INN, BAN, JAN
MERBROMIN	129-16-8	C20H8Br2HgNa2O6	750.66	NF-XII, INN, BAN
MERCAPTAMINE HYDROCHLORIDE	60-23-1	C2H8ClNS	113.61	INN, BAN
MERCAPTOPURINE	6112-76-1, 50-44-2 [anhydrous]	C5H4N4S	152.18	USP, INN, BAN, JAN
MESNA	19767-45-4, 3375-50-6 [2-	C2H5NaO3S2	164.18	USAN, INN, BAN
METAMPICILLIN SODIUM	6489-97-0	C17H18N3NaO4S	383.40	INN
METAPROTERENOL	586-06-1, 5874-97-5	C11H17NO3	211.26	USP, JAN
METARAMINOL BITARTRATE	33402-03-8	C13H19NO8	317.30	USP, INN, BAN, JAN
METAXALONE	1665-48-1	C12H15NO3	221.26	USAN, INN, BAN
METERGOLINE	17692-51-2	C25H29N3O2	403.53	INN, BAN
METHACHOLINE CHLORIDE	62-51-1, 55-92-5	C8H18ClNO2	195.69	USP, INN, BAN
METHACYCLINE HYDROCHLORIDE	3963-95-9, 914-00-1	C22H23ClN2O8	478.89	USAN, INN, BAN

METHAPYRILENE HYDROCHLORIDE	135-23-9, 91-80-5	C14H20ClN3S	297.85	USP-XX, INN, BAN
METHAZOLAMIDE	554-57-4	C5H8N4O3S2	236.27	USP, INN, BAN, JAN
METHENAMINE	100-97-0	C6H12N4	140.19	USP, INN, JAN
METHICILLIN SODIUM	7246-14-2, 132-92-3	C17H19N2NaO6S	402.40	USAN, INN, BAN, JAN
METHIMAZOLE	60-56-0	C4H6N2S	114.17	USP, INN, BAN, JAN
METHIONYL-LEUCYLPHENYLALANINE ACETATE		C22H35N3O6S	469.60	experimental
METHIOTHEPIN MALEATE	20229-30-5	C24H28N2O4S2	472.63	INN
METHOCARBAMOL	532-03-6	C11H15NO5	241.25	USP, INN, BAN, JAN
METHOTREXATE	59-05-2	C20H22N8O5	454.45	USP, INN, BAN, JAN
METHOXAMINE HYDROCHLORIDE	61-16-5, 390-28-3	C11H18ClNO3	247.72	USP-XXII, INN, BAN,
METHOXSALEN	298-81-7	C12H8O4	216.20	USP, BAN, JAN
METHOXYAMINE HYDROCHLORIDE	593-56-6	CH6ClNO	83.52	experimental
METHSCOPOLAMINE BROMIDE	155-41-9	C18H24BrNO4	398.30	USP-XXII, BAN, JAN
METHYLBENZETHONIUM CHLORIDE	1320-44-1, 25155-18-4	C28H44ClNO2	462.12	USP, INN, BAN
METHYLDOPA	41372-08-1, 555-30-6	C10H13NO4	211.22	USP, INN, BAN, JAN
METHYLERGONOVINE MALEATE	57432-61-8, 7054-07-1	C24H29N3O6	455.52	USP, INN, BAN, JAN
METHYLPREDNISOLONE	83-43-2	C22H30O5	374.48	USP, INN, BAN, JAN
METHYLTHIOURACIL	56-04-2	C5H6N2OS	142.18	USP-XXI, INN
METOCLOPRAMIDE HYDROCHLORIDE	54143-57-6, 7232-21-5	C14H23Cl2N3O2	336.26	USP, INN, BAN, JAN
METOLAZONE	17560-51-9	C16H16ClN3O3S	365.84	USP, INN, BAN, JAN
METOPROLOL TARTRATE	56392-17-7, 37350-58-6	C19H31NO9	417.46	USP, JAN
METRONIDAZOLE	443-48-1, 69198-10-3	C6H9N3O3	171.16	USP, INN, BAN, JAN
MEXAMINE	608-07-1	C11H15ClN2O	226.71	experimental
MICONAZOLE NITRATE	22832-87-7, 22916-47-8	C18H15Cl4N3O4	479.15	USP, JAN
MIDODRINE HYDROCHLORIDE	3092-17-9, 42794-76-3	C12H19ClN2O4	290.75	USAN, INN, BAN, JAN
MIGLITOL	72432-03-2	C8H17NO5	207.23	USAN, INN, BAN
MILTEFOSINE	58066-85-6	C21H46NO4P	407.58	INN, BAN
MIMOSINE		C8H10N2O4	198.18	experimental
MINAPRINE HYDROCHLORIDE	25953-17-7, 25905-77-5	C17H24Cl2N4O	371.31	USAN
MINOXIDIL	38304-91-5	C9H15N5O	209.25	USP, INN, BAN
MITOXANTHRONE HYDROCHLORIDE	70476-82-3, 65271-80-9	C22H30Cl2N4O6	517.41	USP, INN, BAN, JAN
MIZORIBINE	50924-49-7	C9H13N3O6	259.22	INN, JAN
MODAFINIL	68693-11-8	C15H15NO2S	273.36	USAN, INN, BAN
MOLSIDOMINE	25717-80-0	C9H14N4O4	242.24	USAN, INN, BAN, JAN
MONENSIN SODIUM (monensin A is shown)	22373-78-0, 17090-79-8	C37H63NaO10	690.90	USP, INN, BAN
MONOCROTALINE	315-22-0	C16H23NO6	325.36	experimental
MORANTEL CITRATE	26155-31-7, 20574-50-9	C18H24N2O7S	412.47	USAN, INN, BAN
MORIN	480-16-0	C15H10O7	302.24	experimental
MOXALACTAM DISODIUM	8031-09-2	C20H18N6Na2O9S	564.44	USAN, INN, BAN
MOXIFLOXACIN HYDROCHLORIDE	186826-86-8	C23H29ClFN3O4	465.96	USAN
MYCOPHENOLIC ACID	24280-93-1	C17H20O6	320.35	USAN, INN, BAN

N- (3-TRIFLUOROMETHYLPHENYL)PIPERAZINE HYDROCHLORIDE		C11H14ClF3N2	266.70	experimental
N- (9-FLUORENYLMETHOXYCARBONYL)-L-LEUCINE	35661-60-0	C21H23NO4	353.42	experimental
N (g)-NITRO-L-ARGININE	2149-70-4	C6H13N5O4	219.20	experimental
N,N-HEXAMETHYLENEAMILORIDE		C12H18ClN7O	311.78	experimental
NABUMETONE	42924-53-8	C15H16O2	228.29	USP, INN, BAN, JAN
N-ACETYLASPARTIC ACID	997-55-7	C6H9NO5	175.14	experimental
N-ACETYLNEURAMIC ACID	131-48-6	C11H19NO9	309.28	experimental
N-ACETYLPROLINE		C7H11NO3	157.17	experimental
NADOLOL	42200-33-9	C17H27NO4	309.41	USP, INN, BAN, JAN
NAFCILLIN SODIUM	7177-50-6, 985-16-0	C21H21N2NaO5S	436.47	USP, INN, BAN
NAFRONYL OXALATE	3200-06-4, 31329-57-4	C26H35NO7	473.57	USAN, INN, BAN
NALBUPHINE HYDROCHLORIDE	23277-43-2, 20594-83-6	C21H28ClNO4	393.91	USAN, INN, BAN
NALIDIXIC ACID	389-08-2, 3374-05-8	C12H12N2O3	232.24	USP, INN, BAN, JAN
NALOXONE HYDROCHLORIDE	357-08-4, 51481-60-8	C19H22ClNO4	363.84	USP, INN, BAN, JAN
NALTREXONE HYDROCHLORIDE	16676-29-2, 16590-41-3	C20H23NO4	341.41	USP
N-AMINOHEXYL-5-CHLORO-1-NAPTHALENESULFONAMIDE		C16H22Cl2N2O2S	377.34	experimental
NAPHAZOLINE HYDROCHLORIDE	550-99-2, 835-31-4	C14H15ClN2	246.74	USP, INN, BAN, JAN
NAPROXEN(+)	22204-53-1	C14H14O3	230.27	USP, INN, BAN, JAN
NAPROXOL	26159-36-4	C14H16O2	216.28	USAN, INN
NARASIN	55134-13-9	C43H72O11	765.05	USP, INN, BAN
NARINGENIN	480-41-1	C15H12O5	272.26	experimental
NARINGIN	10236-47-2	C27H32O14	580.55	experimental
NATEGLINIDE	105816-04-4	C19H27NO3	317.43	USAN, INN, BAN
N-CHLOROETHYL-N-ETHYL-2'-METHYLBENZYLAMINE HYDROCHLORIDE		C12H19Cl2N	248.20	experimental
NEFOPAM	23327-57-3, 13669-70-0	C17H19NO	253.35	USAN, INN, BAN
NEOHESPERIDIN DIHYDROCHALCONE		C28H36O15	612.59	experimental
NEOMYCIN SULFATE	1405-10-3, 1404-04-2	C23H48N6O17S	712.73	USP, JAN
NEOSTIGMINE BROMIDE	114-80-7, 59-99-4	C12H19BrN2O2	303.20	USP, INN, BAN, JAN
NEROL	106-25-2	C10H18O	154.25	experimental
N-FORMYLMETHIONYL-LEUCYLPHENYLALANINE		C21H31N3O5S	437.56	experimental
N-FORMYLMETHIONYLPHENYLALANINE	22008-60-2	C15H20N2O4S	324.40	experimental
Ng-METHYL-L-ARGININE ACETATE		C9H20N4O4	248.28	experimental
N-HISTIDYL-2-AMINONAPHTHALENE (betaNA)	7424-15-9	C16H16N4O	280.33	experimental
N-HYDROXYMETHYLNICOTINAMIDE	3569-99-1	C7H8N2O2	152.15	experimental
NIACIN	59-67-6	C6H5NO2	123.11	USP, INN, JAN
NICARDIPINE HYDROCHLORIDE	54527-84-3, 55985-32-5	C26H30ClN3O6	516.00	USAN, INN, BAN, JAN
NICERGOLINE	27848-84-6	C24H26BrN3O3	484.40	USAN, INN, BAN, JAN
NICOTINE DITARTRATE	65-31-6	C18H26N2O12	462.41	USAN
NICOTINYL TARTRATE	100-55-0	C10H13NO7	259.22	USAN, JAN
NIFEDIPINE	21829-25-4	C17H18N2O6	346.34	USP, INN, BAN, JAN
NIFENAZONE	2139-47-1	C17H16N4O2	308.34	INN, BAN

NIGERICIN SODIUM	28380-24-7	C40H67NaO11	746.96	experimental
NILUTAMIDE	63612-50-0	C12H10F3N3O4	317.23	USAN, INN, BAN
NIMESULIDE	51803-78-2	C13H12N2O5S	308.31	INN, BAN
NIMODIPINE	66085-59-4	C21H26N2O7	418.45	USP, INN, BAN
NIMUSTINE	42471-28-3	C9H13ClN6O2	272.70	INN, JAN
NIPECOTIC ACID	498-95-3	C6H11NO2	129.16	experimental
NITRENDIPINE	84845-75-0	C18H20N2O6	360.37	USAN, INN, BAN, JAN
NITROFURANTOIN	67-20-9, 54-87-5 [nitrofurantoin	C8H6N4O5	238.16	USP, INN, BAN, JAN
NITROFURAZONE	59-87-0	C6H6N4O4	198.14	USP, INN, BAN
NITROMIDE	121-81-3	C7H5N3O5	211.14	USAN
NOMIFENSINE MALEATE	32795-47-4, 24526-64-5	C20H22N2O4	354.41	USAN, INN, BAN
NORCANTHARIDIN		C8H8O4	168.15	experimental
NOREPINEPHRINE	69815-49-2, 51-40-1	C8H11NO3	169.18	USP, INN, BAN
NORETHINDRONE ACETATE	51-98-9	C22H28O3	340.47	USP
NORETHYNODREL	68-23-5	C20H26O2	298.43	USP
NORFLOXACIN	70458-96-7	C16H18FN3O3	319.34	USP, INN, BAN, JAN
NORGESTREL	6533-00-2	C21H28O2	312.46	USP, INN, BAN, JAN
NORHARMAN	244-63-3	C11H8N2	168.20	experimental
NORTRIPTYLINE	894-71-3, 72-69-5 [nortriptyline]	C19H21N	263.39	USP, INN, BAN, JAN
NOSCAPINE HYDROCHLORIDE	912-60-7, 128-62-1 [noscapine]	C22H24ClNO7	449.89	USP, INN, BAN, JAN
NOVOBIOCIN SODIUM	1476-53-5, 303-81-1	C31H35N2NaO11	634.62	USP
NYLIDRIN HYDROCHLORIDE	1400-61-9	C19H26ClNO2	335.88	USP-XII, INN, BAN
NYSTATIN	114-90-9	C47H75NO17	926.12	USP, INN, BAN, JAN
OCTOPAMINE HYDROCHLORIDE	104-14-3	C8H12ClNO2	189.64	INN
OFLOXACIN	82419-36-1	C18H20FN3O4	361.38	USP, INN, BAN, JAN
OLEANDOMYCIN PHOSPHATE	3922-90-5 (base)	C35H64NO16P	785.87	NF-XIII, INN, BAN, JAN
OLMESARTAN MEDOXOMIL	144689-63-4	C29H30N6O6	558.60	USAN, INN, BAN
ORLISTAT	96829-58-2	C29H53NO5	495.75	USAN, INN, BAN
ORPHENADRINE CITRATE	4682-36-4, 83-98-7	C24H31NO8	461.52	USP, INN, BAN
OUABAIN	11018-89-6, 630-60-4	C29H44O12	584.67	USP-XX, JAN
OXACILLIN SODIUM	7240-38-2, 1173-88-2	C19H18N3NaO5S	423.43	USP, INN, BAN, JAN
OXAPROZIN	21256-18-8	C18H15NO3	293.33	USP, INN, BAN, JAN
OXCARBAZEPINE	28721-07-5	C15H12N2O2	252.28	USAN, INN, BAN
OXFENDAZOLE	53716-50-0	C15H13N3O3S	315.35	USP, INN, BAN
OXICONAZOLE NITRATE	64211-46-7	C18H14Cl4N4O4	492.15	USAN, INN, BAN, JAN
OXIDOPAMINE HYDROCHLORIDE	1199-18-4	C8H12ClNO3	205.64	USAN, INN
OXOTREMORINE SESQUIFUMARATE	17360-35-9	C16H22N2O5	322.36	experimental
OXYBENZONE	131-57-7	C14H12O3	228.25	USP, INN
OXYMETAZOLINE HYDROCHLORIDE	2315-02-8, 1491-59-4	C16H25ClN2O	296.84	USP, INN, BAN, JAN
OXYPHENBUTAZONE	7081-38-1, 129-20-4	C19H20N2O3	324.38	USP-XXIII, INN, BAN
OXYPHENCYCLIMINE HYDROCHLORIDE	125-52-0, 125-53-1	C20H29ClN2O3	380.92	USP-XXII, INN, BAN,

OXYQUINOLINE HEMISULFATE	148-24-3	C9H9NO5S	243.24	USAN
OXYTETRACYCLINE	6153-64-6, 79-57-2 [anhydrous]	C22H25ClN2O9	496.91	USP, INN, BAN, JAN
PACLITAXEL	33069-62-4	C47H51NO14	853.93	USP, INN, BAN
PAEONOL	552-41-0	C9H10O3	166.18	experimental
PALMATINE	3486-67-7	C21H22NO5	368.41	experimental
PALMATINE CHLORIDE	10605-02-4	C21H22ClNO4	387.87	experimental
PAPAVERINE HYDROCHLORIDE	61-25-6, 58-74-2 [papaverine]	C20H22ClNO4	375.86	USP, BAN, JAN
PARACHLOROPHENOL	106-48-9	C6H5ClO	128.56	USP
PARAROSANILINE PAMOATE	7232-51-1, 569-61-9	C42H33N3O6	675.75	USAN, INN
PARAXANTHINE		C7H8N4O2	180.17	experimental
PAROMOMYCIN SULFATE	1263-89-4, 7542-37-2	C23H47N5O18S	713.72	USP, INN, BAN
PATULIN	149-29-1	C7H6O4	154.12	experimental
p-CHLOROPHENYLALANINE	7424-00-2(dl); 14173-39-8(l)	C9H10ClNO2	199.64	experimental
PEFLOXACINE MESYLATE	149676-40-4	C18H24FN3O6S	429.47	USAN, INN, BAN
PENICILLAMINE	52-67-5	C5H11NO2S	149.21	USP, INN, BAN, JAN
PENICILLIN V POTASSIUM	132-98-9, 87-08-1 [penicillin, V]	C16H17KN2O5S	388.49	USP, JAN
PENTAMIDINE ISETHIONATE	100-33-4	C23H36N4O10S2	592.69	INN, BAN, JAN
PENTETRAZOL	54-95-5	C6H10N4	138.17	NF-XIII, INN, BAN
PENTOLINIUM TARTRATE	52-62-0, 144-44-5 [pentolinium]	C23H42N2O12	538.60	NF-XIV, INN, BAN
PENTOXIFYLLINE	6493-05-6	C13H18N4O3	278.31	USP, INN, BAN, JAN
PEONIFLORIN	23180-57-6	C23H30O11	482.49	experimental
PERHEXILINE MALEATE	6724-53-4, 6621-47-2	C23H39NO4	393.57	USAN, INN, BAN
PERICIAZINE	2622-26-6	C21H23N3OS	365.50	BAN, JAN
PERILLIC ACID (-)	7694-45-3	C10H14O2	166.22	experimental
PERILLYL ALCOHOL	536-59-4, 18457-55-1	C10H16O	152.24	experimental
PERINDOPRIL ERBUMINE	107133-36-8; 82834-16-0	C23H43N3O5	441.62	USAN
PERPHENAZINE	58-39-9	C21H26ClN3OS	403.98	USP, INN, BAN, JAN
PERUVOSIDE	1182-67-2	C30H44O9	548.68	experimental
PHENACETIN	62-44-2	C10H13NO2	179.22	USP-XX, INN, BAN
PHENAZOPYRIDINE HYDROCHLORIDE	136-40-3, 94-78-0	C11H12ClN5	249.70	USP, INN, BAN
PHENELZINE SULFATE	156-51-4, 51-71-8 [phenelzine]	C8H14N2O4S	234.28	USP, INN, BAN
PHENETHYL CAFFEATE (CAPE)	104594-70-9	C17H16O4	284.31	experimental
PHENINDIONE	83-12-5	C15H10O2	222.25	USP-XXII, INN, BAN
PHENIRAMINE MALEATE	132-20-7, 86-21-5	C20H24N2O4	356.43	USP, INN, BAN
PHENOTHRIN	26002-80-2	C23H26O3	350.46	INN, BAN
PHENOXYBENZAMINE HYDROCHLORIDE	63-92-3, 59-96-1	C18H23Cl2NO	340.30	USP
PHENYLALANYLTYROSINE	17355-18-9	C18H20N2O4	328.37	experimental
PHENYLBUTYRATE SODIUM	90-27-7 (phenylbutyric acid)	C10H11NaO2	186.19	experimental
PHENYLEPHRINE HYDROCHLORIDE	61-76-7, 59-42-7	C9H14ClNO2	203.67	USP, INN, BAN, JAN
PHENYLMERCURIC ACETATE	62-38-4	C8H8HgO2	336.74	NF
PHENYTOIN SODIUM	630-93-3, 57-41-0 [phenytoin]	C15H11N2NaO2	274.26	USP, JAN

PHLORIDZIN	60-81-1	C21H24O10	436.42	experimental
PHYSCION	521-61-9	C16H12O5	284.27	experimental
PHYSOSTIGMINE SALICYLATE	57-64-7, 57-47-6	C22H27N3O5	413.48	USP, JAN
PICROPODOPHYLLOTOXIN	477-47-4	C22H22O8	414.42	experimental
PICROTOXININ	17617-45-7	C15H16O6	292.29	experimental
PILOCARPINE NITRATE	148-72-1, 92-13-7 [pilocarpine]	C11H17N3O5	271.28	USP
PIMOZIDE	2062-78-4	C28H29F2N3O	461.56	USP, INN, BAN, JAN
PIMPINELLIN	131-12-4	C13H10O5	246.22	experimental
PINACIDIL	85371-64-8, 60560-33-0	C13H19N5	245.33	USAN, INN
PINDOLOL	13523-86-9	C14H20N2O2	248.33	USP, INN, BAN, JAN
PINOCEMBRIN	36052-37-6	C15H12O4	256.26	experimental
PIOGLITAZONE HYDROCHLORIDE	111025-46-8 (pioglitazone)	C19H21ClN2O3S	392.91	USAN, INN, BAN
PIPERACILLIN SODIUM	59703-84-3, 66258-76-2	C23H26N5NaO7S	539.55	USP, INN, BAN, JAN
PIPERAZINE	110-85-0, 144-29-6	C4H10N2	86.14	USP
PIPERIDOLATE HYDROCHLORIDE	129-77-1, 82-98-4 [piperidolate]	C21H26ClNO2	359.90	USP-XX, INN, BAN, JAN
PIPERINE	94-62-2	C17H19NO3	285.35	USP-VIII
PIRACETAM	7491-74-9	C6H10N2O2	142.16	USAN, INN, BAN
PIRENZEPINE HYDROCHLORIDE	29868-97-1, 28797-61-7	C19H23Cl2N5O2	424.33	USAN, INN, BAN, JAN
PIROMIDIC ACID	19562-30-2	C14H16N4O3	288.31	INN, JAN
PIROXICAM	36322-90-4	C15H13N3O4S	331.35	USP, INN, BAN, JAN
PODOFILOX	518-28-5	C22H22O8	414.42	USAN, BAN
POMIFERIN	572-03-2	C25H24O6	420.47	experimental
POTASSIUM p-AMINOBENZOATE	150-13-0 (acid)	C7H6KNO2	175.23	USP
PRALIDOXIME MESYLATE	154-97-2	C8H12N2O4S	232.26	experimental
PRAMOXINE HYDROCHLORIDE	637-58-1, 140-65-8 [pramoxine]	C17H28ClNO3	329.87	USAN, INN, BAN
PRAVASTATIN SODIUM	81131-70-6	C23H35NaO7	446.52	USAN, INN, BAN, JAN
PRAZIQUANTEL	55268-74-1	C19H24N2O2	312.42	USP, INN, BAN, JAN
PREDNISOLONE	50-24-8 [anhydrous], 52438-85-	C21H28O5	360.45	USP, INN, BAN, JAN
PREDNISOLONE ACETATE	52-21-1	C23H30O6	402.49	USP, JAN
PREDNISONE	53-03-2	C21H26O5	358.44	USP, INN, BAN
PREGABALIN	148553-50-8	C8H17NO2	159.23	USAN, INN
PREGNENOLONE	145-13-1, 4598-67-8	C21H32O2	316.49	INN, BAN
PRIDINOL METHANESULFONATE	511-45-5	C21H29NO4S	391.53	INN, JAN
PRILOCAINE HYDROCHLORIDE	1786-81-8, 721-50-6	C13H21ClN2O	256.78	USAN, INN, BAN
PRIMAQUINE DIPHOSPHATE	63-45-6, 90-34-6 [primaquine]	C15H27N3O9P2	455.34	USP, INN, BAN
PRIMIDONE	125-33-7	C12H14N2O2	218.26	USP, INN, BAN, JAN
PRISTIMERIN	1258-84-0	C30H40O4	464.65	experimental
PROADIFEN HYDROCHLORIDE	78997-40-7	C23H32ClNO2	389.97	USAN, INN
PROBENECID	57-66-9	C13H19NO4S	285.36	USP, INN, BAN, JAN
PROBUCOL	23288-49-5	C31H48O2S2	516.86	USP, INN, BAN, JAN
PROCAINAMIDE HYDROCHLORIDE	614-39-1, 51-06-9	C13H22ClN3O	271.79	USP, INN, BAN, JAN

PROCHLORPERAZINE EDISYLATE	1257-78-9, 84-02-6	C22H30ClN3O6S3	564.15	USP, JAN
PROCYCLIDINE HYDROCHLORIDE	1508-76-5, 77-37-2	C19H30ClNO	323.91	USP, INN, BAN
PROGESTERONE	57-83-0	C21H30O2	314.47	USP, INN, BAN, JAN
PROGLUMIDE	6620-60-6	C18H26N2O4	334.42	USAN, INN, BAN, JAN
PROMAZINE HYDROCHLORIDE	53-60-1, 58-40-2 [promazine]	C17H21ClN2S	320.89	USP, INN, BAN
PROMETHAZINE HYDROCHLORIDE	58-33-3, 60-87-7	C17H21ClN2S	320.89	USP, INN, BAN, JAN
PRONETALOL HYDROCHLORIDE	54-80-8	C15H20ClNO	265.79	INN, BAN
PROPAFENONE HYDROCHLORIDE	34183-22-7, 54063-53-5	C21H28ClNO3	377.92	USP, INN, BAN, JAN
PROPANTHELINE BROMIDE	50-34-0, 298-50-0	C23H30BrNO3	448.40	USP, INN, BAN, JAN
PROPRANOLOL HYDROCHLORIDE (+/-)	318-98-9, 525-66-6	C16H22ClNO2	295.81	USP, INN, BAN, JAN
PROPYLTHIOURACIL	51-52-5	C7H10N2OS	170.23	USP, INN, BAN, JAN
PROTHIONAMIDE	14222-60-7	C9H12N2S	180.27	INN, BAN, JAN
PROTOPORPHYRIN IX	553-12-8	C34H34N4O4	562.67	JAN
PROTOVERATRINE B	124-97-0	C41H63NO15	809.96	INN
PSEUDOEPHEDRINE HYDROCHLORIDE	345-78-8, 90-82-4	C10H16ClNO	201.70	USP, INN, BAN
PUROMYCIN HYDROCHLORIDE	58-58-2, 53-79-2 [puromycin]	C22H31Cl2N7O5	544.44	USAN, INN, BAN
PURPURIN	81-54-9	C14H8O5	256.22	experimental
PYRANTEL PAMOATE	22204-24-6, 15686-83-6	C34H30N2O6S	594.69	USP, INN, BAN, JAN
PYRAZINAMIDE	98-96-4	C5H5N3O	123.12	USP, INN, BAN, JAN
PYRIDOSTIGMINE BROMIDE	101-26-8, 155-97-5	C9H13BrN2O2	261.12	USP, INN, BAN, JAN
PYRILAMINE MALEATE	59-33-6, 91-84-9 [pyrilamine]	C21H27N3O5	401.47	USP, INN, BAN
PYRIMETHAMINE	58-14-0	C12H13ClN4	248.72	USP, INN, BAN, JAN
PYRITHIONE ZINC	13463-41-7	C10H10N2O2S2Zn	319.70	USAN, INN, BAN
PYRITHYLDIONE	77-04-3	C9H13NO2	167.21	INN
PYRVINIUM PAMOATE	3546-41-6	C49H43N3O6	769.91	USP, BAN, JAN
QUASSIN	76-78-8	C22H28O6	388.46	experimental
QUERCETIN	117-39-5	C15H10O7	302.24	experimental
QUERCITRIN	522-12-3	C21H20O11	448.39	experimental
QUINACRINE HYDROCHLORIDE	6151-30-0, 69-05-6	C23H32Cl3N3O	472.89	USP-XXII, INN, BAN
QUINALIZARIN	81-61-8	C14H8O6	272.22	experimental
QUINAPRIL HYDROCHLORIDE	82586-55-8, 85441-61-8	C25H31ClN2O5	474.99	USP, INN, BAN
QUINIDINE GLUCONATE	7054-25-3, 6591-63-5	C26H36N2O9	520.58	USP
QUININE SULFATE	6119-70-6, 804-63-7	C20H26N2O6S	422.50	USP, JAN
QUINOLINIC ACID		C7H5NO4	167.12	experimental
RACEPHEDRINE HYDROCHLORIDE	134-71-4, 90-81-3	C10H16ClNO	201.70	USAN, INN, BAN
RAMIFENAZONE	3615-24-5	C14H20ClN3O	281.79	INN
RANITIDINE	66357-35-5	C13H22N4O3S	314.41	USAN, INN, BAN
RAUWOLSCINE HYDROCHLORIDE		C21H27ClN2O3	390.91	experimental
RESORCINOL	108-46-3	C6H6O2	110.11	USP, JAN
RESORCINOL MONOACETATE	102-29-4	C8H8O3	152.15	USP
RESVERATROL	501-36-0	C14H12O3	228.25	experimental

RETINOL	68-26-8	C20H30O	286.46	INN, BAN
RETINYL ACETATE	127-47-9	C22H32O2	328.50	JAN
RETINYL PALMITATE	79-81-2	C36H60O2	524.88	JAN
RHAPONTIN	155-58-8	C21H24O9	420.42	experimental
RIBOFLAVIN	83-88-5	C17H20N4O6	376.37	USP, INN, BAN, JAN
RIFAMPIN	13292-46-1	C43H58N4O12	822.96	USP, INN, BAN, JAN
RIFAXIMIN	80621-81-4	C43H51N3O11	785.90	USAN, INN
RILUZOLE	1744-22-5	C8H5F3N2OS	234.20	USAN, INN, BAN
RITODRINE HYDROCHLORIDE	23239-51-2, 26652-09-5	C17H22ClNO3	323.82	USAN, INN, BAN
ROFECOXIB	162011-90-7	C17H14O4S	314.36	INN, BAN
RONIDAZOLE	7681-76-7	C6H8N4O4	200.16	USAN, INN, BAN
ROSIGLITAZONE	122320-73-4	C18H19N3O3S	357.43	USAN, INN, BAN
ROSMARINIC ACID	537-15-5	C18H16O8	360.32	experimental
ROSOLIC ACID	603-45-2	C19H14O3	290.32	experimental
ROSUVASTATIN	287714-14-4, 147098-20-2(Ca	C22H28FN3O6S	481.55	USAN, INN, BAN
ROTENONE	83-79-4	C23H22O6	394.43	agricultural use
ROXARSONE	121-19-7	C6H6AsNO6	263.04	USP, INN, BAN
ROXITHROMYCIN	80214-83-1	C41H76N2O15	837.07	USAN, INN, JAN
RUTILANTINONE	21288-61-9	C22H20O9	428.40	experimental
S-(1,2-DICARBOXYETHYL)GLUTATHIONE	1115-52-2	C15H23N3O10S	437.43	experimental
SACCHARIN	81-07-2	C7H5NO3S	183.19	NF
SAFROLE	94-59-7	C10H10O2	162.19	experimental
SALICIN	138-52-3	C13H18O7	286.28	USP-IX
SALICYL ALCOHOL	90-01-7	C7H8O2	124.14	USAN
SALICYLAMIDE	65-45-2	C7H7NO2	137.14	USP, INN, BAN, JAN
SALINOMYCIN, SODIUM	53003-10-4	C42H69NaO11	773.00	INN, BAN
SALSOLINE	89-31-6	C11H15NO2	193.25	experimental
SARAFLOXACIN HYDROCHLORIDE	91296-87-6	C20H18ClF2N3O3	421.83	USAN, INN, BAN
SCOPOLAMINE HYDROBROMIDE	6533-68-2, 114-49-8	C17H22BrNO4	384.27	USP, BAN, JAN
SECNIDAZOLE	3366-95-8	C7H11N3O3	185.18	INN, BAN
SECURININE	5610-40-2	C13H15NO2	217.27	INN
SELAMECTIN	165108-07-6	C43H63NO11	769.98	USAN, INN
SEMUSTINE	13909-09-6	C10H18ClN3O2	247.73	USAN, INN
SENNOSIDE A	81-27-6	C42H38O20	862.76	USP, JAN
SERTRALINE HYDROCHLORIDE	79559-97-0; 79617-96-2(base)	C17H18Cl3N	342.70	USAN, INN, BAN
SIBUTRAMINE HYDROCHLORIDE	84485-00-7; 106650-56-0	C17H27Cl2N	316.32	USAN, INN, BAN
SILDENAFIL	139755-83-2	C22H30N6O4S	474.59	USAN, INN, BAN
SILIBININ	22888-70-6	C25H22O10	482.45	INN
SINOMENINE	115-53-7	C19H23NO4	329.40	experimental
SISOMICIN SULFATE	53179-09-2, 32385-11-8	C19H39N5O11S	545.61	USP, BAN, JAN
S-METHYL-L-THIOCITRULLINE ACETATE	156719-41-4	C7H15N3O2S	205.28	experimental

SNAP (S-NITROSO-N-ACETYLPENICILLAMINE)	79032-48-7	C7H12N2O4S	220.25	experimental
SODIUM beta-NICOTINAMIDE ADENINE DINUCLEOTIDE PHOSPHATE		C21H27N7NaO17P3	765.40	experimental
SODIUM DEHYDROCHOLATE	145-41-5	C24H33NaO5	424.52	USP, INN, BAN, JAN
SPAGLUMIC ACID	4910-46-7	C11H16N2O8	304.26	INN
SPARTEINE HYDROIODIDE		C15H27IN2	362.30	experimental
SPARTEINE SULFATE	6160-12-9, 299-39-8	C15H28N2O4S	332.47	USAN, BIN, JAN
SPECTINOMYCIN HYDROCHLORIDE	22189-32-8, 21736-83-4	C14H26Cl2N2O7	405.28	USP, INN, BAN, JAN
SPERMIDINE TRIHYDROCHLORIDE		C7H22Cl3N3	254.63	experimental
SPIPERONE	749-02-0	C23H26FN3O2	395.48	USAN, INN, BAN, JAN
SPIRAMYCIN	8025-81-8	C43H74N2O14	843.07	USAN, INN, BAN
SPIRONOLACTONE	52-01-7	C24H32O4S	416.58	USP, INN, BAN, JAN
STREPTOMYCIN SULFATE	3810-74-0, 57-92-1	C21H41N7O16S	679.66	USP, INN, BAN, JAN
STREPTOZOSIN	18883-66-4	C8H15N3O7	265.22	USAN, INN
STRYCHNINE	57-24-9	C21H22N2O2	334.42	NF-X
SULCONAZOLE NITRATE	61318-91-0, 61318-90-9	C18H16Cl3N3O3S	460.77	USP, INN, BAN, JAN
SULFABENZAMIDE	127-71-9	C13H12N2O3S	276.32	USP, INN, BAN
SULFACETAMIDE	144-80-9, 127-56-0	C8H10N2O3S	214.24	USP, INN, BAN
SULFACHLORPYRIDAZINE	80-32-0	C10H9ClN4O2S	284.73	USP, INN, BAN
SULFADIAZINE	68-35-9	C10H10N4O2S	250.28	USP, INN, BAN, JAN
SULFADIMETHOXINE	122-11-2	C12H14N4O4S	310.33	USP, INN, BAN, JAN
SULFAGUANIDINE	57-67-0	C7H10N4O2S	214.25	NF-XI, INN, BAN
SULFAMERAZINE	127-79-7	C11H12N4O2S	264.31	USP-XXIII, INN, BAN
SULFAMETER	651-06-9	C11H12N4O3S	280.31	USAN, INN, BAN
SULFAMETHAZINE	57-68-1	C12H14N4O2S	278.33	USP, INN, BAN
SULFAMETHIZOLE	144-82-1	C9H10N4O2S2	270.33	USP, INN, BAN, JAN
SULFAMETHOXAZOLE	723-46-6	C10H11N3O3S	253.28	USP, INN, BAN, JAN
SULFAMETHOXYPYRIDAZINE	80-35-3	C11H12N4O3S	280.31	USP-XVII, INN, BAN
SULFANILAMIDE	63-74-1	C6H8N2O2S	172.21	NF-XI, INN
SULFAPHENAZOLE	526-08-9	C15H14N4O2S	314.37	INN, BAN, JAN
SULFAPYRIDINE	144-83-2	C11H11N3O2S	249.29	USP, INN, BAN
SULFASALAZINE	599-79-1	C18H14N4O5S	398.40	USP, INN, BAN
SULFATHIAZOLE	72-14-0	C9H9N3O2S2	255.32	USP, INN, BAN
SULFINPYRAZONE	57-96-5	C23H20N2O3S	404.49	USP, INN, BAN, JAN
SULFISOXAZOLE	127-69-5	C11H13N3O3S	267.31	USP, INN, BAN, JAN
SULINDAC	38194-50-2	C20H17FO3S	356.42	USP, INN, BAN, JAN
SULOCTIDIL	54063-56-8	C20H35NOS	337.57	USAN, INN, BAN
SULPIRIDE	15676-16-1	C15H23N3O4S	341.43	USAN, INN, BAN, JAN
SUPROFEN	40828-46-4	C14H12O3S	260.31	USP, INN, BAN, JAN
SUPROFEN METHYL ESTER		C15H14O3S	274.34	experimental
SUXIBUZONE	27470-51-5	C24H26N2O6	438.48	INN, BAN, JAN
TAMOXIFEN CITRATE	54965-24-1, 10540-29-1	C32H37NO8	563.65	USP, INN, BAN, JAN

TANNIC ACID	1401-55-4	C76H52O46	1701.23	USP, JAN
TARGININE HYDROCHLORIDE	156706-47-7, 17035-90-	C7H17ClN4O2	224.69	INN, BAN
TEGASEROD MALEATE	189188-57-6	C20H27N5O5	417.47	USAN
TELENZEPINE HYDROCHLORIDE	80880-90-6	C19H23ClN4O2S	406.94	INN
TELITHROMYCIN	191114-48-4	C44H65N5O10	824.04	USAN, INN, BAN
TENIPOSIDE	29767-20-2	C32H32O13S	656.67	USAN, INN, BAN
TENOXICAM	59804-37-4	C13H11N3O4S2	337.38	USAN, INN, BAN, JAN
TERBUTALINE HEMISULFATE	23031-32-5, 23031-25-6	C12H21NO7S	323.37	USP, INN, BAN, JAN
TETRACAINE HYDROCHLORIDE	136-47-0, 94-24-6 [tetracaine]	C15H25ClN2O2	300.83	USP, BAN, JAN
TETRACHLOROISOPHTHALONITRILE		C8Cl4N2	265.91	experimental
TETRACYCLINE HYDROCHLORIDE	64-75-5, 60-54-8 [tetracycline]	C22H25ClN2O8	480.91	USP, INN, BAN, JAN
TETRAHYDROPALMATINE	3520-14-7	C21H25NO4	355.44	experimental
TETRAHYDROZOLINE HYDROCHLORIDE	522-48-5, 84-22-0	C13H17ClN2	236.75	USP, INN, BAN, JAN
TETRANDRINE	518-34-3	C38H42N2O6	622.77	experimental
Tfa-VAL-TYR-VAL-OH	64577-63-5	C21H28F3N3O6	475.47	experimental
THEOBROMINE	83-67-0	C7H8N4O2	180.17	NF-XII, BAN
THEOPHYLLINE	5967-84-0, 58-55-9 [anhydrous]	C7H8N4O2	180.17	USP, BAN, JAN
THIABENDAZOLE	148-79-8	C10H7N3S	201.25	USP, INN, BAN, JAN
THIAMPHENICOL	15318-45-3	C12H15Cl2NO5S	356.23	USAN, INN, BAN, JAN
THIMEROSAL	54-64-8	C9H9HgNaO2S	404.81	USP, INN, BAN, JAN
THIOCTIC ACID	62-46-4	C8H14O2S2	206.33	JAN
THIOGUANINE	154-42-7, 5580-03-0	C5H5N5S	167.19	USP, INN, BAN
THIORIDAZINE HYDROCHLORIDE	130-61-0, 50-52-2 [thioridazine]	C21H27ClN2S2	407.04	USP, INN, BAN
THIOTEPA	52-24-4	C6H12N3PS	189.22	USP, INN, BAN, JAN
THIOTHIXENE	5591-45-7, 3313-26-6 [//Z//]	C23H29N3O2S2	443.63	USP, INN, BAN, JAN
THYROXINE	51-48-9	C15H11I4NO4	776.88	BAN
TIAPRIDE HYDROCHLORIDE	51012-32-9	C15H25ClN2O4S	364.89	USAN, INN, BAN
TIMOLOL MALEATE	26921-17-5, 91524-16-2	C17H28N4O7S	432.50	USP, JAN
TINIDAZOLE	19387-91-8	C8H13N3O4S	247.27	USP, INN, BAN, JAN
TIOXOLONE	4991-65-5	C7H4O3S	168.17	INN, BAN
TODRALAZINE HYDROCHLORIDE	14679-73-3	C11H13ClN4O2	268.70	INN, BAN, JAN
TOLAZAMIDE	1156-19-0	C14H21N3O3S	311.41	USP, INN, BAN, JAN
TOLAZOLINE HYDROCHLORIDE	59-97-2, 59-98-3 [tolazoline]	C10H13ClN2	196.68	USP, INN, BAN, JAN
TOLBUTAMIDE	64-77-7	C12H18N2O3S	270.35	USP, INN, BAN, JAN
TOLFENAMIC ACID	13710-19-5	C14H12ClNO2	261.71	INN, BAN, JAN
TOLMETIN SODIUM	64490-92-2, 26171-23-3	C15H14NNaO3	279.27	USP, JAN
TOLNAFTATE	2398-96-1	C19H17NOS	307.42	USP, INN, BAN, JAN
TOMATINE	86273-92-9	C47H79NO21	994.15	experimental
TOPIRAMATE	97240-79-4	C12H21NO8S	339.37	USAN, INN, BAN
TORSEMIDE	56211-40-6	C16H20N4O3S	348.43	USP, INN, BAN
TRANDOLAPRIL	87679-37-6	C24H34N2O5	430.55	INN, BAN

TRANEXAMIC ACID	1197-18-8	C8H15NO2	157.21	USAN, INN, BAN, JAN
TRANILAST	53902-12-8	C18H17NO5	327.34	USAN, INN, JAN
TRANYLCYPROMINE SULFATE	13492-01-8, 7081-36-9	C9H13NO4S	231.27	USP-XXI, INN, BAN
TRAZODONE HYDROCHLORIDE	25332-39-2, 19794-93-5	C19H23Cl2N5O	408.33	USP, INN, BAN, JAN
TRETINON	302-79-4	C20H28O2	300.44	USP, INN, BAN
TRIACETIN	102-76-1	C9H14O6	218.21	USP, INN, BAN
TRIADIMEFON	43121-43-3	C14H16ClN3O2	293.76	agricultural use
TRIAMCINOLONE	124-94-7	C21H27FO6	394.44	USP, INN, BAN, JAN
TRIAMCINOLONE ACETONIDE	76-25-5	C24H31FO6	434.51	USP, INN, BAN, JAN
TRIAMCINOLONE DIACETATE	67-78-7	C25H31FO8	478.52	USP, JAN
TRIAMTERENE	396-01-0	C12H11N7	253.27	USP, INN, BAN, JAN
TRICHLORMETHIAZIDE	133-67-5	C8H8Cl3N3O4S2	380.66	USP, INN, JAN
TRIFLUOPERAZINE HYDROCHLORIDE	440-17-5, 117-89-5	C21H26Cl2F3N3S	480.43	USP, INN, BAN, JAN
TRIHEXYPHENIDYL HYDROCHLORIDE	52-49-3	C20H32ClNO	337.94	USP, INN, BAN, JAN
TRIMEDLURE	12002-53-8	C12H21ClO2	232.75	agricultural use
TRIMEPRAZINE TARTRATE	4330-99-8, 41375-66-0	C22H28N2O6S	448.54	USP, INN, BAN, JAN
TRIMETHOBENZAMIDE HYDROCHLORIDE	554-92-7, 138-56-7	C21H29ClN2O5	424.93	USP, INN
TRIMETHOPRIM	738-70-5	C14H18N4O3	290.32	USP, INN, BAN, JAN
TRIMIPRAMINE MALEATE	521-78-8, 739-71-9	C24H30N2O4	410.52	USAN, JAN
TRIOXSALEN	3902-71-4	C14H12O3	228.25	USP, INN, JAN
TRIPROLIDINE HYDROCHLORIDE	6138-79-0, 550-70-9	C19H23ClN2	314.86	USP, INN, BAN, JAN
TRISODIUM ETHYLENEDIAMINE TETRACETATE	150-38-9	C10H16N2Na3O8	361.22	USAN
TROLEANDOMYCIN	2751-09-9	C41H67NO15	813.99	USP, INN, BAN, JAN
TROPICAMIDE	1508-75-4	C17H20N2O2	284.36	USP, INN, BAN, JAN
TROXERUTIN	7085-55-4	C33H42O19	742.69	INN, BAN
TRYPTAMINE	61-54-1	C10H12N2	160.22	experimental
TRYPTOPHAN	73-22-3 ['L']	C11H12N2O2	204.23	USP, INN, JAN
TUAMINOHEPTANE SULFATE	6411-75-2, 123-82-0	C7H19NO4S	213.30	USP-XX
TULOBUTEROL	41570-61-0	C12H19Cl2NO	264.20	INN, BAN, JAN
TYLOSIN TARTRATE	1405-54-5, 1401-69-0(base)	C46H77NO17	916.12	USP, INN, BAN
TYROTHRICIN	1404-88-2	C66H85N11O15	1272.48	USP, INN, BAN
URETHANE	51-79-6	C3H7NO2	89.09	INN
URSODIOL	128-13-2	C24H40O4	392.58	USP, INN, BAN, JAN
USNIC ACID	125-46-2	C18H16O7	344.32	experimental
VALDECOXIB	181695-72-7	C16H14N2O3S	314.37	USAN, INN, BAN
VALERYL SALYCILATE	64206-54-8	C12H14O4	222.24	experimental
VALPROATE SODIUM	1069-66-5, 99-66-1 [valproic	C8H15NaO2	166.20	USAN, JAN
VALSARTAN	137862-53-4	C24H29N5O3	435.53	USAN, INN, BAN
VALYLTRYPTOPHAN	24587-37-9	C16H21N3O3	303.36	experimental
VANCOMYCIN HYDROCHLORIDE	1404-93-9, 1404-90-6	C67H77Cl3N8O24	1484.76	USP, INN, BAN, JAN
VENLAFAXINE	99300-78-4, 93413-69-5	C17H27NO2	277.41	USAN, INN, BAN

VERAPAMIL HYDROCHLORIDE	152-11-4, 52-53-9 [verapamil]	C27H39ClN2O4	491.08	USP, INN, BAN, JAN
VERATRIDINE	71-62-5	C37H53NO12	703.83	experimental
VERATRINE SULFATE	62-59-9	C32H51NO13S	689.83	experimental
VESAMICOL HYDROCHLORIDE	120447-62-3	C17H26ClNO	295.86	USAN
VIDARABINE	24356-66-9, 5536-17-4	C10H13N5O4	267.25	USP, INN, BAN, JAN
VINBURNINE	4880-88-0	C19H22N2O	294.40	INN
VINCAMINE	1617-90-9	C21H26N2O3	354.45	INN, BAN
VINPOCETINE	42971-09-5	C22H26N2O2	350.46	USAN, INN, JAN
VULPINIC ACID	521-52-8	C19H14O5	322.32	experimental
XANTHURENIC ACID	59-00-7	C10H7NO4	205.17	experimental
XYLAZINE	23076-35-9, 7361-61-7	C12H16N2S	220.34	USP, INN, BAN
XYLOMETAZOLINE HYDROCHLORIDE	1218-35-5, 526-36-3	C16H25ClN2	280.84	USP, INN, BAN
YOHIMBINE HYDROCHLORIDE	65-19-0	C21H27ClN2O3	390.91	USP
ZAPRINAST	37762-06-4	C13H13N5O2	271.28	INN, BAN
ZIDOVUDINE [AZT]	30516-87-1	C10H13N5O4	267.25	USP, INN, BAN, JAN
ZOLMITRIPTAN	139264-17-8	C16H21N3O2	287.36	USAN, INN, BAN
ZOMEPIRAC SODIUM	64092-49-5, 64092-48-4	C15H14ClNO3	291.74	USAN, INN, BAN
ZOXAZOLAMINE	61-80-3	C7H5ClN2O	168.58	NF-XI, INN, BAN

Table S2. Fascin-pathway enhancers (filagree decreasers) identified in the fascin bioassay.
Each section is arranged in alphabetical order by compound name. Additional abbreviations at bottom of last page.
[1] A: agricultural/aquacultural use; H: human medical use; I: industrial use; V: veterinary medical use;
T: traditional/folk medicine use; [*possible uses, shown in brackets, are based on available data*].
[2] Cytotoxicity: apparent cell death or degeneration.

Activity Class Compound Name	CAS #	Chemical Class	Pharmacological Effects	Therapeutic and other Uses[1]	Therapeutic Class (see Fig. 3D)
High-Potency Fascin-Pathway Enhancers with no cytotoxicity or morphological effects (10)					
5-Nitro-2-(3-phenylpropylamino) benzoic Acid (NPPB)	107254-86-4	Nitrobenzoate	Blocks volume-regulated chloride channels; inhibitor of angiogenesis	[*H: cancer, various*]	Cancer
Carbenoxolone Sodium (CBX)	7421-40-1	Pentacyclic triterpene	Blocks gap junctions & hemi-channels; prostaglandin modulator	[*H: GI ulcers*]	Ulcers
Cyclocreatine	35404-50-3	Imidazole	Anti-proliferation	None	None known
Cyproterone	2098-66-0	Steroid; pregnadiene	Androgen antagonist	[*H: prostate cancer*]	Cancer
Dyphylline	479-18-5	Xanthine	Bronchodilator	H: asthma, emphysema	Pulmonary
Estradiol Propionate	3758-34-7	Steroid, estrogen	Reproductive steroid; Estrogen receptor agonist	[*H: other estrogens used for HRT & OC*}	Endocrine
Mephenesin	59-47-2	Propylene glycol	Muscle relaxation, central-acting	[*H: Spasticity*]	CNS
Palmatine Chloride	10605-02-4	Isoquinoline alkaloid, a/k/a berberine alkaloid	Antibacterial; anti-tumor activity	T: diverse uses as plant extract	Antibacterial, Cancer
Sulfamethazine	57-68-1	Sulfonamide (sulfanilamide)	Antibacterial	V: bacterial infections	Antibacterial
Sulfasalazine	599-79-1	Sulfonamide, sulfapyridine + 5-amino salicylic acid, azo linkage	NSAID; metabolilzed to active 5-aminosalicylic acid	H: ulcerative colitis; rheumatoid arthritis	Anti-inflammatory
High-Potency Fascin-Pathway Enhancers with cytotoxicity[2] at high dose (9)					
Chloroacetoxyquinoline	N/A	Chloroquinoline	unknown	None.	None known
Deguelin (*cis* isomer)	522-17-8	Isoflavonoid	anti-angiogenesis; cancer apoptosis; AKT inhibitor	[*H: cancer prevention or Rx*]	Cancer
Gedunin	2753-30-2	Triterpene	blocks cancer proliferation, gastric acid secretion	[*H: malaria, cancer, peptic ulcer]*	Antiparasitic, Cancer, Ulcers
Juglone	481-39-0	Naphthalene	Inhibits Pin1 isomerase, which regulates neuronal cytoskeleton phosphorylation & promotes tumor growth;	A: food preservative. T: anti-fungal; [*H: neurodegenerative dz; cancer, various*]	Antimicrobial, Cancer, CNS

Table S2. Fascin-pathway enhancers, cont. *(Kraft et al., A cell-based fascin bioassay for multi-purpose compound screening)*

Lasalocid Sodium	25999-20-6	Furan	Calcium ionophore; anti-bacterial, anti-parasitic activity; neurotoxin	A: anti-parasitic, esp. Coccidiosis	Anti-parasitic
N-Formylmethionyl-phenylalanine	22008-60-2	Dipeptide	Neutrophil chemotaxis	None	None known
Pomiferin	572-03-2	Isoflavone	Antioxidant; inhibitor of HDAC & AChE; blocks cancer proliferation	[*H: cardioprotection; cancer, various*]	Cardiovascular, cancer
Pyrvinium Pamoate, a/k/a Povan	3546-41-6	Quinolinium	Kills parasitic worms	H, V: anti-helminthic	Anti-parasitic
Tannic Acid	1401-55-4	Polyphenol, tannin	Antioxidant, astringent	H, V: wound care	Skin
High-Potency Fascin-Pathway Enhancers with morphological effects (5)					
Amlodipine Besylate	111470-99-6	Dihydropyridine	Blocks Ca^{2+} channels; vasodilator	H: hypertension; angina	Cardiovascular
Atorvastatin Calcium	134523-03-8	Pyrrole, statin	HMG-CoA reductase inhibitor	H: Hypercholesterolemia	Cardiovascular
Emetine Dichloride	316-42-7	Isoquinoline alkaloid	Protein synthesis inhibitor (eukaryotic)	H, V: induce emesis or catharsis; amebiasis; nematode infection	Anti-parasitic
Rosolic Acid. a/k/a aurin, corallin	603-45-2	Cyclohexane-carboxylic acid	Colorimetric pH indicator; selective GR modulator	None	None known
Rosuvastatin	287714-14-4	Pyrrole, statin	HMG-CoA reductase inhibitor	H: Hypercholesterolemia	Cardiovascular
Low-potency Fascin-Pathway Enhancers (11)					
Acetylcysteine	616-91-1	Amino acid derivative	Lowers mucus viscosity; blocks HIV effects; increases glutathione levels; antioxidant	H: pulmonary disease, e.g., cystic fibrosis; AIDS; acetaminophen overdose	Pulmonary, Anti-viral, Other
Adiphenine Hydrochloride	50-42-0	Diphenylacetic acid	nAChR blocker	[*Local anesthetic*]	Other
Anisindione	117-37-3	Aromatic Polycyclic Hydrocarbons	Anticoagulant	H: thrombosis and/or embolism	Cardio/Cerebrovascular
Ceftriaxone Disodium	104376-79-6	Cephalosporin	Antibacterial, broad spectrum; neuroprotection	H: numerous bacterial infections, including meningitis [*ALS, stroke*]	Antibacterial, Cerebrovascular, CNS
Estradiol Acetate	4245-41-4	Steroid, reproductive	Estrogen receptor agonist	H: hormone replacement therapy; with progestin for contraception	Endocrine
Geneticin, a/k/a G418	108321-42-2	Aminoglycoside	Antibiotic	[*H,V: parasitic infections*]; experimental	Anti-parasitic
Mechlorethamine	51-75-2	Nitrogen mustard	DNA alkylating agent; toxic to dividing cells	H: Anti-neoplastic, esp. lymphoma	Cancer
Metaraminol Bitartrate	33402-03-8	Phenylpropanolamine	Adrenergic α-agonist; vasoconstriction	H: Hypotension; shock	Cardiovascular

Table S2. Fascin-pathway enhancers, cont. *(Kraft et al., A cell-based fascin bioassay for multi-purpose compound screening)*

Prednisolone	50-24-8	Glucocorticoid	Anti-inflammatory; immunosuppression	H: Arthritis, dermatitis, other -itis; autoimmune dz; allergies/asthma,	Anti-inflammatory, Pulmonary, Skin
Spaglumic Acid (NAAG)	4910-46-7	Dipeptide (endogenous neuropeptide)	Histamine H1-antagonist; glutamate agonist?	H: Allergic rhinitis, conjunctivitis	Other
Tolbutamide	64-77-7	Sulphonylurea	Insulin release; hypoglycemia	H: type 2 diabetes mellitus	Diabetes
Low-potency Fascin-Pathway Enhancers With morphological effects (13)					
Acetylcholine	51-84-3	Biogenic amine	Neurotransmitter	H: OTC homeopathic remedy	Other
Apigenin	520-36-5	Flavone	Cell cycle arrest, apoptosis of tumor cells	[*H: cancer prevention, treatment*]	Cancer
Benzyl Isothiocyanate	622-78-6	Isothiocyanate; dietary phytochemical	Kills soil worms & fungi; apoptosis of cancer cells	A: biofumigant; [*H: cancer prevention*]	Antimicrobial, Cancer
Bithionol	97-18-7	Bithionol	Anti-infective; photosensitizer	V: flatworm infestations	Anti-parasitic
Caffeine	58-08-2	Methylxanthine	CNS stimulant; inhibits phosphodiesterase; blocks adenosine R	H: fatigue; migraine headache; apnea of prematurity	CNS
Cefditorin Pivoxil	117467-28-4	Cephalosporin, 3rd generation	Anti-bacterial	H: bacterial infections, e.g., pneumonia	Antibacterial
Ciclopirox Olamine	41621-49-2	Pyridone	Antifungal, antibacterial	H: skin, nail fungal infections	Antibacterial, Antifungal, Skin
Cloxyquin [fascin blocker @ 10uM]	130-16-5	Chloroquinolinol	Antibacterial, antifungal	[*H: tuberculosis, incl. multidrug resistant*]	Antibacterial, Antifungal
Dyclonine Hydrochloride	536-43-6	Propiophenone	Na+ channel blocker; local anesthetic	H: sore throat	Other
Hydroxytacrine (a/k/a Velnacrine) Maleate,	118909-22-1	Aminoacridine	Cholinesterase inhibitor, centrally acting	[*H: Alzheimer's dz*]	CNS
Oxaprozin	21256-18-8	Phenylpropene	COX inhibitor; NSAID; antipyretic	H: arthritis, osteo- and rheumatioid	Anti-inflammatory
Oxcarbazepine	28721-07-5	Dibenzazepine	Anticonvulsant; Na^+ channel blocker	H: partial seizures (adults & children)	CNS
Thiothixene	5591-45-7	Thioxanthene	Antagonist of dopamine, serotonin, adrenergic, & muscarinic receptors	H: psychosis	CNS

Abbreviations:

AChE, acetylcholinesterase; AIDS, adult immunodeficiency syndrome; a/k/a, also known as; dz, disease; esp., especially; GR, glucocorticoid receptor; HDAC, histone deacetylase; HMG-CoA, hydroxymethylglutaryl-coenzyme A; HRT, hormone replacement therapy; Na^+, sodium ion; nAChR, nicotinic acetylcholine receptor; NMDA, *N*-methyl-D-aspartate; NSAID, nonsteroidal anti-inflammatory drug; OC, oral contraceptive; OTC, over-the-counter; Pin1, peptidylprolyl cis-trans isomerase, NIMA-interacting; R, receptor(s); Rx, treatment

Table S3. Fascin-pathway blockers (filagree increasers) identified in the fascin bioassay.
Each section is arranged in alphabetical order by compound name. Abbreviations on last page.
[1] A: agricultural/aquacultural use; H: human medical use; I: industrial use; V: veterinary medical use; T: traditional/folk medical use; [*possible uses, shown in brackets, are based on available data*].
[2] Cytotoxicity: apparent cell death or neurodegeneration.

Activity Class Compound Name	CAS #	Chemical Class	Pharmacological Effects	Therapeutic and other Uses[1]	Therapeutic Class (see Fig. 3D)
High-Potency Fascin-Pathway Blockers with no cytotoxicity or morphological effects (n = 5)					
Diflunisal	22494-42-4	Salicylate	COX inhibitor; NSAID	H: pain, arthritis	Analgesic, anti-inflammatory
Imipramine HCl	113-52-0	Tricyclic	NE uptake inhibitor	H: depression; enuresis	CNS
Nifedipine	21829-25-4	Dihydropyridine	Blocks Ca^{2+} channels; vasodilation	H: angina, hypertension	Cardiovascular
Spiperone	749-02-0	Buterophenone	Dopamine D2 receptor antagonist	H: psychosis	CNS
Suprofen	40828-46-4	Phenylpropionate	COX inhibitor; NSAID; inhibits pupillary constriction	H: cataract surgery	Analgesic, anti-inflammatory; Other
High-Potency Filagree Increasers with cytotoxicity[2] at high dose (n = 1)					
Broxyquinoline	521-74-4	Hydroxyquinoline	Intestinal antiseptic	H: amoebic dysentery & other diarrheas	Antiparasitic
High-Potency Fascin-Pathway Blockers with morphological effects (n = 6)					
4'-Demethyl-epipodophyllotoxin	N/A	Tetrahydronaphthalene	Blocks IGF1 receptor autophosphorylation	[*H: cancers, various types*]	
Azadirachtin	11141-17-6	Triterpene	Blocks development & reproduction (insects)	A: broad-spectrum insecticide	Other
Cloxyquin	130-16-5	Hydroxyquinoline	Anti-bacterial, anti-fungal	[*H: tuberculosis*]	Antibacterial, Antifungal
Colchiceine, a/k/a demethylcolchicine	477-27-0	Colchicine alkaloid	Blocks MT formation	None known	None known
Colchicine	64-86-8	Colchicine alkaloid	Blocks MT formation, WBC motility, urate crystal deposition	H: gout; Familial Mediterranean Fever	Other; Anti-inflammatory
Picropodophyllotoxin (picropodophyllin)	477-47-4	Tetrahydronaphthalene	Blocks IGF1 receptor autophosphorylation	[*H: cancer, various types*]	Cancer
Low-potency Fascin-Pathway Blockers (n = 17)					
Acetyltryptophan	1218-34-4	Modified aromatic amino acid	Protease inhibitor?	None known	None known
Amantadine HCl	665-66-7	Adamantane	NMDA antagonist; anti-viral activity	H: influenza A; Parkinson's dz; dyskinesia; post- herpetic neuralgia [*H: hepatitis C*]	Anti-viral; CNS

Table S3. Fascin-pathway blockers, cont. *(Kraft et al., A cell-based fascin bioassay for multi-purpose compound screening)*

Aminolevulinic Acid HCl	5451-09-2	Modified amino acid	Photosensitizer	H: actinic keratosis	Skin
Econazol Nitrate	68797-31-9	Imidazole	Anti-fungal agent	H: superficial fungal infections	Anti-fungal
Griseofulvin	126-07-8	Benzofuran	Anti-fungal agent	H: superficial fungal infections	Anti-fungal
Hydroflumethiazide	135-09-1	Sulfonamide	NaCl symporter inhibitor; diuretic	H: hypertension	Cardiovascular
Metoprolol Tartrate	56392-17-7	Phenoxypropanolamine	β1-adrenergic receptor antagonist	H: hypertension, cardiac arrhythmia	Cardiovascular
Naproxen(+)	22204-53-1	Naphthalene	COX inhibitor; NSAID	H: pain, gout, arthritis	Analgesic, anti-inflammatory
Oxybenzone	131-57-7	Benzophenone	Absorbs UV radiation	H: sunscreen	Skin
Propylthiouracil	51-52-5	Thiourea	Inhibits thyroid hormone synthesis	H: Graves dz and other hyperthyroidism	Endocrine
Salicin	138-52-3	Glucoside, benzyl alcohol	COX inhibitor; NSAID	T: inflammation; H: *prev*. rheumatoid arthritis	Anti-inflammatory
Sarafloxacin HCl	91296-87-6	Fluoroquinolone	Anti-bacterial, broad spectrum	A: bacterial infections	Antibacterial
S-Nitroso-*N*-Acetyl-penicillamine (SNAP)	79032-48-7	S-Nitrosothiol	Spontaneous NO donor, vasodilator; cysteine protease inhibitor	None known; research reagent	None known
Sulfamethoxazole	723-46-6	Sulfonamide (sulfanilamine)	Blocks folic acid synthesis	H: bacterial infection, various	Antibacterial
Telenzepine HCl	80880-90-6	Benzodiazepine	M1 mAChR antagonist; parasympatholytic	[*H: peptic ulcer; weight loss*]	Ulcer
Triadimefon	43121-43-3	Triazole	Anti-fungal; blocks cell wall synthesis	I, A: fungicide; teratogenic in vertebrate animals	Anti-fungal
Vinburnine	4880-88-0	Indole alkaloid (Vinca)	Vasodilation	[*H: stroke*]	Cerebrovascular
Low-potency Fascin-Pathway Blockers with morphological effects (n = 5)					
Baclofen	1134-47-0	Butyric acid	GABA agonist	H: spasticity	CNS
Citrinin	518-75-2	Benzopyran	Mitochondrial dysfunction	None known; associated with fungal contaminated food	None known
Iopanoic Acid	96-83-3	Iodobenzene	Blocks deiodinase activity & thyroid hormone release	H: oral contrast agent, thyrotoxicosis	Endocrine
Nateglinide	105816-04-4	Cyclohexane	Stimulates insulin release	H: type 2 diabetes mellitus	Diabetes
Paclitaxel	33069-62-4	Taxoid cyclodecane	Tubulin stabilizer; anti-mitotic agent	H: cancer, various	Cancer

Abbreviations:
COX, cyclooxygenase; dz, disease; GABA, gamma amino butyric acid; HCl, hydrochloride; IGF1, insulin-like growth factor; mAChR, muscarinic acetylcholine receptor; MT, microtubule; NaCl, sodium chloride; NE, norepinephrine; NMDA, *N*-methyl-D-aspartic acid; NO, nitric oxide; NSAID; non-steroidal anti-inflammatory drug; prev., previously; UV, ultraviolet; WBC, white blood cell(s)