Developmental disorders: microRNA helps fragile X protein control stem cells

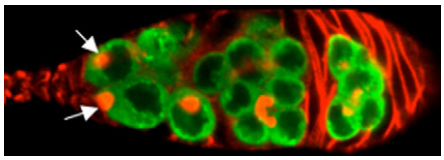

Image reproduced from *PloS Genet*. (Yang et al., 2009).

Fragile X syndrome is the most common inherited form of mental retardation. Trinucleotide repeat expansions in the fragile X mental retardation (*FMR1*) gene cause a loss of functional fragile X mental retardation protein (FMRP). This protein selectively binds to mRNAs to regulate translation. It was shown previously that the Drosophila ortholog of *FMR1*, *dFmr1*, helps maintain germline stem cells in the Drosophila ovary. A new study by Yang et al. shows that several microRNAs interact physically with FMRP in the Drosophila ovary. They also demonstrate that interaction between *dFmr1* and the bantam microRNA, a microRNA known to promote tissue growth, controls germline stem cell fate in the fly. This work suggests that FMRP uses microRNAs to regulate mRNA transcription.

Yang, Y., Xu, S., Xia, L., Wang, J., Wen, S., Jin, P. and Chen, D. (2009). The bantam microRNA is associated with Drosophila fragile X mental retardation protein and regulates the fate of germline stem cells. *PLoS Genet*. **5**, e1000444.

Neuroscience: HD protein clearance via acetylation

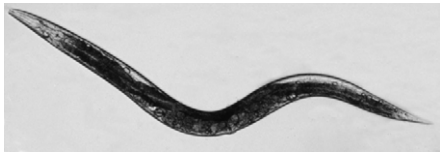

Image reproduced from Andersen et al. (2006). *Development* **133**, 2695-2704.

Huntington's disease (HD) is an incurable illness that causes a progressive loss of coordination and cognitive ability. Patients also develop choreaic (spastic and uncoordinated) movements. HD is one of many neurodegenerative diseases in which a mutant protein accumulates and aggregates in the brain. In the case of HD, the huntingtin protein accumulates in the nucleus and cytoplasm of neurons, thus, one suggested therapeutic strategy is to promote clearance and degradation of this protein. Using primary rat neuron cultures and a transgenic *C. elegans* model of HD, Jeong et al. demonstrate that acetylation of mutant huntingtin has a neuroprotective effect against toxicity and neurodegeneration. This acetylation improves huntingtin clearance by targeting it for autophagic degradation, thus suggesting a strategy for removing mutant protein in HD.

Jeong, H., Then, F., Melia, T. J., Jr, Mazzulli, J. R., Cui, L., Savas, J. N., Voisine, C., Paganetti, P., Tanese, N., Hart, A. C. et al. (2009). Acetylation targets mutant huntingtin to autophagosomes for degradation. *Cell* **137**, 60-72.

Stem cells: G proteins promote marrow engraftment

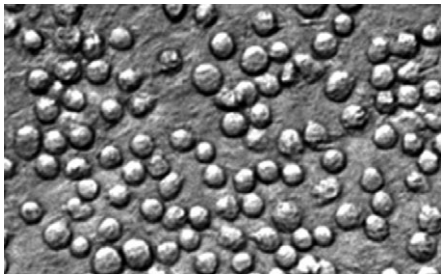

Image reproduced from Taoudi et al. (2005). *Development* **132**, 4179-4191.

Cancer and leukemia patients can benefit from hematopoietic stem cell transplants to replace damaged or diseased bone marrow. One key determinant of a successful transplant is the correct localization of stem cells following transfusion into the patient. Thus, a major area of investigation is aimed at improving the honing and engraftment of hematopoietic stem and progenitor cells (HSPCs) into the bone marrow. A recent study by Adams et al. uses knockout mice to demonstrate that G protein-mediated signaling facilitates cell engraftment into bone marrow. HSPCs from mice lacking $G\alpha_s$ do not localize or engraft in bone marrow. Alternatively, pharmacological enhancement of $G\alpha_s$ activation improves HSPC localization, suggesting that activation of this pathway has the potential to improve transplantation efficiency in the clinic.

Adams, G. B., Alley, I. R., Chung, U. I., Chabner, K. T., Jeanson, N. T., Celso, C. L., Marsters, E. S., Chen, M., Weinstein, L. S., Lin, C. P. et al. (2009). Haematopoietic stem cells depend on Gα(s)-mediated signalling to engraft bone marrow. *Nature* Mar 25 [Epub ahead of print] [doi:10.1038/nature07859].

Infectious disease: deadly flu strains manipulate the immune response

Image reproduced from Colvin et al. (2001). *Development* **128**, 2095-2106.

The number of seasonal influenza deaths is highest in the very young or very old. However, certain influenza epidemics and pandemics, such as the 1918 'Spanish flu', disproportionately kill otherwise healthy individuals. It is thought that highly pathogenic (HP) influenza strains stimulate a stronger immune response than seasonal strains, causing severe vascular leakage and lung edema, and eventual death. Aldridge et al. studied mouse immune cell responses following exposure to mouse-adapted influenza viruses that mimic either a seasonal flu or a HP flu strain. Compared with a sublethal strain, the HP strain recruited large numbers of TNF-α/inducible nitric oxide synthase-producing dendritic cells (tipDCs) to the lung. Whereas complete elimination of tipDCs results in lethality, limiting the tipDC response with pioglitazone, a peroxisome proliferator-activated receptor (PPAR)-γ agonist used to treat type II diabetes, improved viral tolerance in mice. Pioglitazone administration decreased mortality and improved recovery from HP strains of influenza, suggesting potential for its use as a therapeutic defense against pandemic forms of influenza.

Aldridge, J. R., Jr, Moseley, C. E., Boltz, D. A., Negovetich, N. J., Reynolds, C., Franks, J., Brown, S. A., Doherty, P. C., Webster, R. G. and Thomas, P. G. (2009). TNF/iNOS-producing dendritic cells are the necessary evil of lethal influenza virus infection. *Proc. Natl. Acad. Sci. USA* **106**, 5306-5311.