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CELL SURFACE GLYCOCONJUGATES AND CARBOHYDRATE-BINDING PROTEINS: POSSIBLE RECOGNITION SIGNALS IN SENSORY NEURONE DEVELOPMENT

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SUMMARY

Dorsal root ganglion (DRG) neurones transmit cutaneous sensory information from the periphery to the dorsal horn of the spinal cord. Subpopulations of DRG neurones that subserve distinct sensory modalities project to discrete regions in the dorsal horn. The formation of specific sensory connections during development may involve cell-surface interactions with spinal cord cells. Molecules that are expressed on the surface of functional subpopulations of DRG and dorsal horn neurones have therefore been identified.

Distinct subsets of DRG neurones express globo- or lactoseries carbohydrate differentiation antigens. The expression of defined carbohydrate structures correlates with the embryonic lineage, peptide phenotype and the central termination site of DRG neurones. Similar or identical glycoconjugates have been implicated in cellular interactions that contribute to preimplantation embryonic development.

Small-diameter DRG neurones that project to the superficial dorsal horn express *N*-acetyllactosamine backbone structures that are potential ligands for β-galactoside-specific binding proteins (lectins). Two lectins have been identified that are expressed early in development in the superficial dorsal horn. These complementary molecules may contribute to the development of sensory afferent projections in the spinal cord.

INTRODUCTION

Primary sensory neurones in the dorsal root ganglion (DRG) transmit peripheral sensory information from cutaneous and muscle receptors to second-order neurones in the spinal cord. Analysis of the receptive properties and specialized terminal morphology of peripheral sensory endings has delineated more than a dozen classes of DRG neurones (Iggo, 1973, 1976; Willis & Coggeshall, 1978). The central integration of sensory information is achieved, in part, by the projection of functional classes of DRG neurones to discrete regions of the spinal cord (Brown, 1981; Light

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& Perl, 1984). Individual sets of cutaneous sensory afferents project to segregated domains of the dorsal horn (Brown, 1981) that coincide with the laminar divisions originally defined on the basis of spinal cord neuronal cytoarchitecture (Rexed, 1952). The central terminals of most nociceptive cutaneous afferents project to the superficial dorsal horn (laminae I and II) (Rethelyi, 1977; Light & Perl, 1979; Ribiero da Silva & Coimbra, 1982), whereas the majority of low threshold mechanoreceptive afferents terminate within laminae III and IV of the dorsal horn (Brown, Rose & Snow, 1977; Semba *et al.* 1983; Ralston, Light, Ralston & Perl, 1984).

Some of the developmental interactions that underlie the specificity of sensory projection patterns in the mature spinal cord are now clear. The initial outgrowth of afferent fibres from sensory neurones in the rat DRG occurs soon after the differentiation of sensory neuroblasts into post-mitotic neurones (Altman & Bayer, 1984). The first post-mitotic neuroblasts give rise to large-diameter neurones, probably muscle afferents, that send processes into the dorsal root entrance zone (DREZ) on embryonic days (E) 12–13. The processes of later differentiating, small-diameter neurones that convey cutaneous sensory information reach the spinal cord shortly after. Although sensory neurones of different functional classes are intermingled within the DRG, a mediolateral segregation of large and small sensory axons can be detected by the time afferent fibres reach the spinal cord (Altman & Bayer, 1984; Yamada, 1985). Upon arrival in the DREZ, sensory axons bifurcate and, for a period of 24–36 h, extend ascending and descending processes that form fibre tracts overlying the dorsal horn without giving off collaterals into the grey matter (Smith, 1983; Altman & Bayer, 1984).

Specificity in the central projections of different classes of primary afferents is apparent from the time that afferent fibres first enter the embryonic rat dorsal grey matter (Smith, 1983; Yamada, 1985). Large-diameter fibres enter the dorsal horn from the medial compartment of the DREZ and maintain a position that is medial to smaller diameter axons (Altman & Bayer, 1984). Histological and horseradish peroxidase (HRP)-labelling studies indicate that the first collaterals to enter the spinal cord fasciculate in the medial aspect of the dorsal horn, and navigate a direct path to the motoneurone pool (Altman & Bayer, 1984; Yamada, 1985). Cutaneous afferent fibres enter the spinal grey matter more laterally and project almost exclusively to the dorsal horn.

The temporal sequence of sensory neurone differentiation and central axon outgrowth may contribute to the segregation of afferent fibres during their projection along the dorsal root. The resulting mediolateral compartmentation of fibre classes in the DREZ may, in turn, influence the initial trajectory of sensory axons within the spinal cord. Analysis of the projections of HRP-filled afferents, however, indicates that the central branches of distinct classes of DRG neurone migrate towards appropriate targets over a narrow and superimposed period of embryonic development (Smith, 1983; Yamada, 1985). Additional guidance mechanisms may therefore exist that operate independently of any temporal and positional constraints on axonal outgrowth. The existence of specific targeting mechanisms is supported by anatomical and functional studies on cutaneous sensory afferents that make initial errors in their

central projections and enter the spinal cord *via* the ventral roots. Ventral root afferents reach the spinal cord about 120° displaced from their normal site of entry, yet appear to project to appropriate regions of the dorsal horn *via* what must represent highly aberrant spinal pathways (Coggeshall, Emery, Ito & Maynard, 1977; Clifton, Coggeshall, Vance & Willis, 1976; Chung, Lee, Endo & Coggeshall, 1983; Light & Metz, 1978).

One component of a specific guidance system could involve the interaction of molecules that act as recognition signals on sensory axons and developing spinal cord cells. At present, the existence and nature of such molecules has not been established. In order to address this problem we have begun to characterize cell-surface molecules that are selectively expressed by functionally distinct populations of sensory neurones and spinal cord cells. The identification of neurone-specific surface molecules will provide markers with which to analyse, in greater detail, early sensory neurone development. Some of these molecules may also contribute to recognition between primary afferents and dorsal horn cells. The studies outlined in this chapter provide evidence that cell-surface oligosaccharide structures and complementary carbohydrate-binding proteins are expressed in a temporally and positionally restricted manner on subsets of DRG and dorsal horn neurones during development. These molecules constitute one recognition system that may be involved in guiding sensory axons to spinal cord targets.

NEURONE-SPECIFIC SURFACE OLIGOSACCHARIDES

Initial studies have focused on the localization of two families of oligosaccharides, the globoseries and lactoseries carbohydrates (Dodd, Solter & Jessell, 1984; Dodd & Jessell, 1985; Jessell & Dodd, 1985). The globoseries carbohydrates are characterized by the backbone oligosaccharide sequence Gal*N*Acβ1-3Galα1-4Galβ1-R (Kannagi *et al.* 1983*b*) and the lactoseries oligosaccharides are derived from lacto-*N*-biose I (Galβ1-3Glc*N*Ac-R) (Type 1) or *N*-acetyllactosamine (Galβ1-4Glc*N*Ac-R) (Type 2) backbone structures (Feizi, 1985) (Table 1). The pattern of expression of individual members of these oligosaccharide families during spinal sensory development can be divided into three categories: (1) molecules expressed exclusively by subsets of DRG neurones, (2) molecules expressed transiently on subsets of spinal cord cells and (3) molecules that are expressed coincidentally with the differentiation of DRG and spinal cord neurones.

DRG-specific oligosaccharides

The expression of oligosaccharides by DRG neurones has been studied in adult animals in order to correlate the distribution of neurones bearing particular saccharide structures with the established morphology and projection sites of identified subsets of DRG neurones. More than 80% of adult DRG neurones can be labelled with monoclonal antibodies (MAbs) directed against globo- and lactoseries determinants. These two classes of carbohydrate structure are expressed selectively in the cytoplasm of non-overlapping subsets of rat DRG neurones and on the surfaces of

separate populations of cultured neonatal DRG neurones (Dodd & Jessell, 1985; Jessell & Dodd, 1985).

Globoseries glycoconjugates, recognized by the MAbs anti-SSEA-3 and anti-SSEA-4 (Table 1), are associated with overlapping populations constituting approximately 10–15% of DRG neurones that are of small and large diameter. DRG neurones that express globoseries structures do not contain neuropeptides or other cytochemical markers that delineate subpopulations of small-diameter DRG neurones.

The central terminals of SSEA-3/4$^+$ DRG neurones are concentrated in lamina III and the medial part of lamina IV, with a sparse projection to laminae I and V, of the dorsal horn (Fig. 1C) (Dodd *et al.* 1984). Immunoreactive fibres are also found in the gracile and cuneate fasciculi and in the gracile and external cuneate nuclei. The distribution of afferent fibres that express these globoseries antigens suggests that globoseries determinants are restricted to myelinated primary afferents conveying low-threshold cutaneous information to deeper laminae and high-threshold mechanoreceptive or thermoreceptive information to lamina I (Brown *et al.* 1977; Rethelyi, 1977; Gobel, Falls & Humphrey, 1981; Nagy & Hunt, 1983; Perl, 1983).

Approximately 50% of adult DRG neurones express the type 2 backbone lactoseries structure recognized by MAb A5 (Table 1). This antigen appears during embryonic development and is present in approximately 10% of neurones in E 18 DRG. During the first postnatal week the proportion of neurones expressing this structure increases to 50%. The A5-reactive *N*-acetyllactosamine structure is expressed in the cytoplasm and on the surface of small- and intermediate-diameter DRG neurones (Fig. 1A) and on the central terminals of these neurones in laminae I and II of the dorsal horn (Fig. 1B). The A5$^+$ population of DRG neurones contain substance P (SP), somatostatin (SOM) and the sensory neurone-specific acid phosphatase, FRAP (Dodd & Jessell, 1985; Jessell & Dodd, 1985).

The expression of α-galactose-extended type 2 lactoseries structures is associated with more restricted subsets of small-diameter DRG neurones (Dodd & Jessell,

Table 1. *Carbohydrate epitopes recognized by monoclonal antibodies*

MAb	Carbohydrate structure	Reference
α-SSEA-3	Gal*N*Acβ1-3Galα1-4Galβ1-R	Shevinsky, Knowles, Damjanov & Solter, 1982
α-SSEA-4	Neu Acα2-3Galβ1-3Gal*N*Ac-R	Kannagi *et al.* 1983*a*
A5	Galβ1-4Glc*N*Ac	Fenderson, Hahnel & Eddy, 1983
LD2*	Galα1-3Galβ1-4Glc*N*Ac-R′	Dodd & Jessell, 1985
LA4*	Galα1-3Galβ1-4Glc*N*Ac-R″	Dodd & Jessell, 1985
AC4*	Galβ1-4(Fucα1-3)Glc*N*Ac-R‴	J. Dodd & T. M. Jessell, unpublished
α-SSEA-1*	Galβ1-4(Fucα1-3)Glc*N*Ac-R	Gooi *et al.* 1981
HNK-1	GlcUA(SO_4)β1-3Galβ1-4Glc*N*Ac-R	Chou *et al.* 1985
α-B	Galα1-3(Fucα1-2)Galβ1-4Glc*N*Ac-R	Chembiomed Ltd

*MAbs LA4 and LD2, and AC4 and SSEA-1 recognize closely related but distinct epitopes. Clarification of the structural differences between these epitopes, here designated R′, R″ and R‴, R, require further investigation.

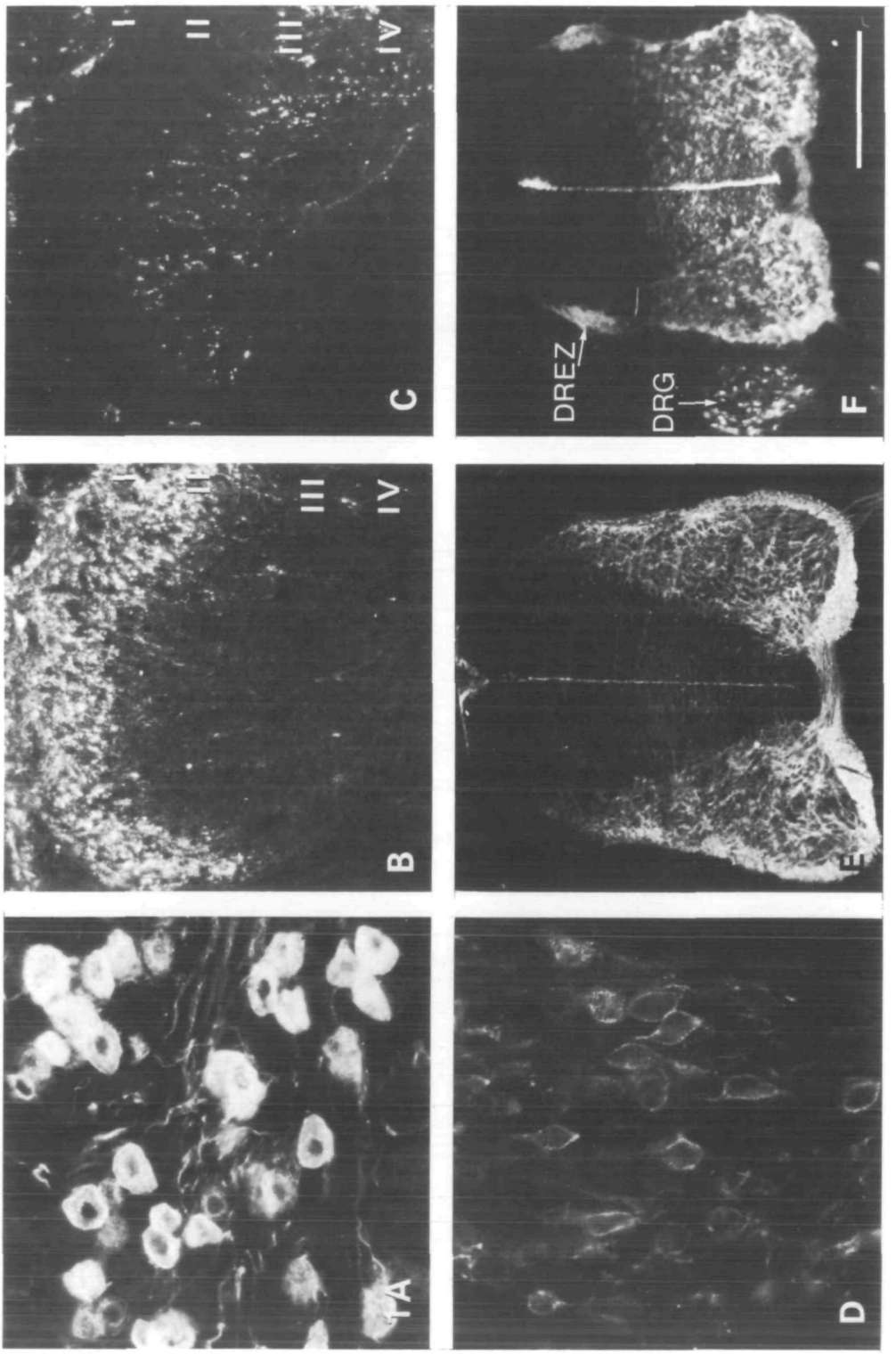
1985; Jessell & Dodd, 1985). The complex type 2 lactoseries structure identified by MAb LD2 (Table 1), is expressed by a subpopulation of small DRG neurones that projects to the dorsal region of lamina II. The LD2-reactive lactoseries oligosaccharide co-segregates with the peptide phenotype of small-diameter sensory neurones, in that it is expressed by all SOM^+ but by no SP^+ DRG neurones. A related galactose-extended lactoseries structure, recognized by MAb LA4 (Table 1), is found on a separate population of small- and intermediate-diameter DRG neurones (constituting 40–50 % of total DRG neurones) that project predominantly to the ventral part of lamina II (Dodd & Jessell, 1985; Jessell & Dodd, 1985). Nearly all FRAP-containing DRG neurones express the LA4-reactive oligosaccharide. Other complex type 1 and type 2 lactoseries oligosaccharides delineate further subsets of small-diameter DRG neurones (Dodd & Jessell, 1985). The distribution of afferent terminals expressing lactoseries determinants suggests that they represent C fibres and also some Aδ fibres (Gobel *et al.* 1981; Rethelyi, 1977). Galactose-extended complex lactoseries structures can be detected on the surface of subsets of DRG neurones in explants of E 13 DRG (T. M. Jessell & J. Dodd, unpublished results).

Spinal cord-specific oligosaccharides

A fucosylated lactoseries structure that includes the lactofucopentaose III trisaccharide (Table 1) is expressed selectively in embryonic spinal cord (J. Dodd & T. M. Jessell, unpublished). This antigen, identified by MAb AC4, is first detected on cells in the ventricular zone and on differentiated cells in more lateral regions of the dorsal spinal cord at E 13–14. The dorsal expression of this molecule does not correlate with the known state of differentiation of spinal cord cells at this stage. Moreover, the appearance of the AC4 antigen in dorsal spinal cord is transient, reaching a peak at E 14·5–15. By E 15·5, the antigen is almost undetectable. At later stages of embryonic development a distinct, fucosylated lactoseries structure that is recognized by MAb anti-SSEA-1, is expressed in other regions of the spinal cord, and by birth the SSEA-1 antigen is distributed throughout the spinal cord. This distribution is maintained in adult animals. The AC4 and anti-SSEA-1-reactive antigens are essentially absent from embryonic or adult DRG neurones *in situ*.

Differentiation-dependent oligosaccharide antigens

The expression of two additional complex lactoseries oligosaccharides is regulated according to the state of differentiation of DRG and spinal cord neurones. The structures detected by MAbs HNK-1 and anti-B (Table 1) are present on embryonic DRG neurones by E 12·5. Initially, the HNK-1 and B determinants are expressed by a low percentage of DRG neurones (Fig. 1D,F). During embryonic development, however, there is a marked increase in the number of neurones that express these antigens. By postnatal day (P) 0, all DRG neurones are, and continue to be, B^+ whereas there is a substantial postnatal decrease in the expression of HNK-1, from about 50 % of neurones at P 0 to approximately 10–15 % in the mature ganglion.


A
B
I
II
III
IV
C
I
II
III
IV
D
E
F
DREZ
DRG

In developing spinal cord, the HNK-1 and B structures show similar, but not identical, patterns of expression. At E 12–14 both molecules are expressed on ventral spinal cord cells in the region of differentiating motoneurones (Fig. 1E,F). At subsequent stages of embryonic development, these molecules appear on spinal cord neurones as they differentiate. By P 0 the HNK-1 and B determinants are present in all regions of the dorsal and ventral horn.

LACTOSERIES OLIGOSACCHARIDES IMPLICATED IN CELL ADHESION

The cell-surface globo- and lactoseries oligosaccharides that exhibit temporal- and regional-specific patterns of expression in developing sensory systems have been identified on early embryonic cells and have been implicated in the adhesive events associated with the compaction of pre-implantation stage embryos (Solter & Knowles, 1978; Fenderson, Zehavi & Hakomori, 1984; Stern, 1984; Rastan *et al.* 1985). The onset of expression of the lactoseries oligosaccharide recognized by MAb anti-SSEA-1 immediately precedes the compaction of 8-cell-stage embryos (Solter & Knowles, 1978). Synthetic oligosaccharide haptens or multivalent glycoconjugates containing fucosylated *N*-acetyllactosamine structures induce the decompaction of 8-cell morulae and inhibit subsequent blastocyst formation (Bird & Kimber, 1984; Fenderson *et al.* 1984). In addition, enzymatic cleavage of internal β-galactoside linkages on embryonic cell-surface polylactosamine structures delays the recompaction of dissociated 8-cell-stage embryos (Rastan *et al.* 1985). These findings raise the possibility that lactoseries oligosaccharides on DRG neurones and spinal cord cells mediate adhesion between neurones during spinal cord development.

Cellular interactions mediated by cell-surface oligosaccharides are likely to involve complementary receptors that function as carbohydrate-binding proteins (Barondes, 1970). A wide variety of membrane-bound (Ashwell & Harford, 1982) and soluble (Barondes, 1984) carbohydrate-binding proteins have been isolated from vertebrate tissues. Several of these proteins recognize β-galactoside linkages contained within the lactoseries structures described above. β-Galactoside-binding proteins have been detected in embryonic brain and spinal cord (DeWaard, Hickman & Kornfeld, 1976; Kobiler & Barondes, 1977; Kobiler, Beyer & Barondes, 1978; Eisenbarth, Ruffolo,

Fig. 1. Developmental expression of oligosaccharide structures in dorsal root ganglion (DRG) and spinal cord. (A) A subpopulation of small- and intermediate-diameter adult DRG neurones are $A5^+$. (B),(C) Comparison of central terminal projection sites of adult DRG neurones expressing lactoseries (B) and globoseries (C) oligosaccharides. (B) $A5^+$ terminals occupy laminae I and II. (C) Terminals labelled with anti-SSEA-3 are restricted to laminae III and IV. (D),(E),(F) Differentiation-dependent oligosaccharide expression. (D) NHK-1 is present on a subset of neurones in E 14 DRG. (E) HNK-1 is expressed by differentiated cells in the ventral horn of E 14 spinal cord. (F) Anti-B labels a subpopulation of E 14 DRG neurones and their axons in the dorsal root entrance zone (DREZ). Within the spinal cord, B^+ cells are present in ventral regions. Differentiated cells are most strongly labelled. The distribution of this antigen is complementary to that revealed by MAb AC4 (not shown). All plates in Figs 1 and 2 show 10 μm cryostat sections of paraformaldehyde-fixed tissue, stained by indirect immunofluorescence techniques. Calibration bar represents (A) 100 μm; (B),(C) 300 μm; (D) 50 μm; (E) 400 μm; (F) 500 μm.

Walsh & Nirenberg, 1978; Childs & Feizi, 1979). This class of carbohydrate-binding protein exists in neural tissue in soluble form and appears to have multiple carbohydrate binding sites (Barondes, 1984). There is increasing evidence for the release of these lectin-like molecules from the cells that synthesize them (Beyer & Barondes, 1982; Cerra, Haywood-Reid & Barondes, 1984; Bols *et al.* 1986). Multivalent carbohydrate-binding proteins (lectins), therefore, represent ligands that might mediate interactions between lactoseries structures on DRG neurones and spinal cord cells. In initial attempts to identify carbohydrate-binding proteins that may be involved in spinal sensory development, the expression of β-galactoside-binding lectins has been examined in DRG and spinal cord.

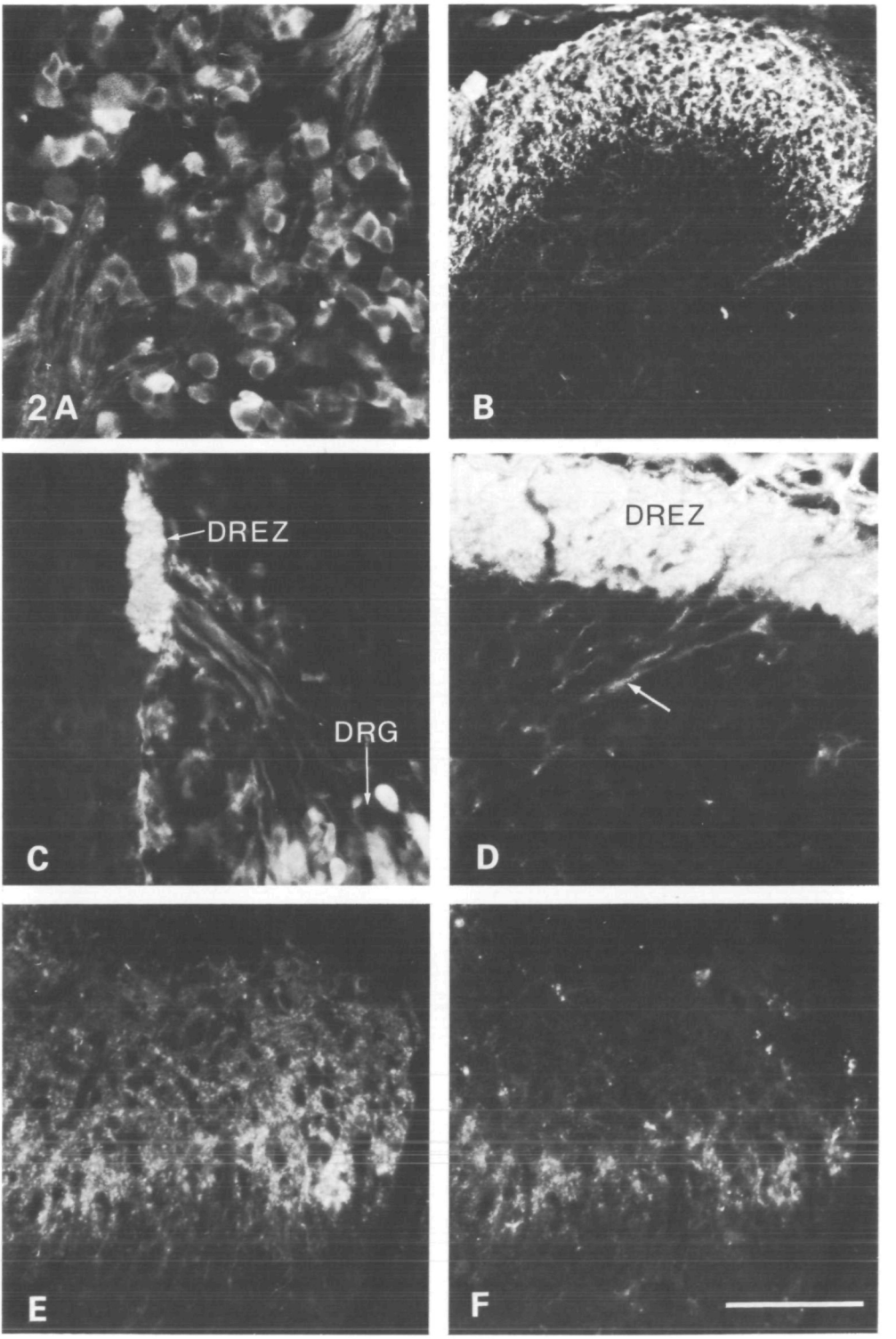
β-GALACTOSIDE-BINDING PROTEINS IN DEVELOPING SENSORY SYSTEMS

Antibodies raised against rat β-galactoside binding lectins originally isolated from lung (Cerra, Gitt & Barondes, 1985) have been used to identify two related or identical proteins in DRG and spinal cord (Regan, Dodd, Barondes & Jessell, 1986). These two lectins, termed RL 14·5 and RL 29, have subunit M_r values of 14 500 and 29 000, respectively, and are present in a subset of DRG neurones and in their central terminals in the superficial dorsal horn (Fig. 2A,B). Dual-fluorochrome immunofluorescence experiments have established that both lectins are synthesized almost exclusively in the population of DRG neurones that expresses cell surface lactoseries glycoconjugates (Regan *et al.* 1986). Dorsal horn neurones that express lactoseries structures do not appear to synthesize these two β-galactoside-binding proteins.

RL 14·5 is first detectable in DRG neurones and sensory axons in the DREZ at E 13–14 (Fig. 2C), whereas RL 29 cannot be detected before E 15. From E 16 both lectins are present in sensory afferent fibres as they enter the spinal cord (Fig. 2D). Afferent fibres that terminate in superficial dorsal horn express these proteins (Regan *et al.* 1986) (Fig. 2B,E,F).

β-Galactoside-binding lectins similar to those identified in DRG neurones are known to be released from cells and can interact with membrane-bound or extracellular glycoconjugates on adjacent cells (Barondes & Hayward-Reid, 1981; Beyer & Barondes, 1982). In preliminary studies, it has been possible to detect the release of RL 14·5 and RL 29 from neonatal rat DRG neurones maintained in dissociated cell culture (L. Regan, J. Dodd, S. H. Barondes & T. M. Jessell, unpublished results).

Fig. 2. Developmental expression of β-galactoside-binding proteins in dorsal root ganglion (DRG) and spinal cord. (A),(B) RL 29 is synthesized by a subpopulation of neurones in E 19 DRG (A), the central terminals of which are restricted to laminae I and II (B). (C) RL 14·5 is present in a subset of DRG neurones at E 14. The axons of RL $14{\cdot}5^+$ DRG neurones project to the dorsal root entrance zone (DREZ) prior to penetrating the dorsal grey matter. (D) RL 14·5-immunoreactive afferents (arrow) begin to penetrate the dorsal grey matter from the DREZ by E 16. (D),(E),(F) Comparison of the central terminal fields of DRG neurones containing β-galactoside-binding proteins and complex lactoseries oligosaccharides. (E) The distribution of RL 29 in laminae I and II. (F) $LA4^+$ terminals are restricted to the ventral region of laminae II, within the region occupied by RL 29^+ terminals. Calibration bar represents: (A) 75 μm; (B) 140 μm; (C)–(F) 100 μm.


2A
B
DREZ
DRG
C
DREZ
D
E
F

Moreover, affinity-purified RL 14·5 and RL 29 bind to the surface of subpopulations of dissociated DRG and dorsal horn neurones in dissociated cell culture (J. Dodd & T. M. Jessell, unpublished). These experiments suggest that the RL 14·5 and RL 29 may be localized extracellularly in the embryonic dorsal horn.

β-Galactoside-binding proteins isolated from non-neural tissues bind with differing affinities to lactoseries glycoconjugates modified by different saccharide side-chain substitutions (Sarkar *et al.* 1979). The relative affinities of RL 14·5 and RL 29 for the variety of complex lactoseries carbohydrates expressed by populations of DRG neurones and dorsal horn cells has not yet been determined.

MOLECULAR DETERMINANTS OF AXON GUIDANCE AND NEURONAL CONNECTIVITY

Anatomical studies have revealed that DRG neurones arborize in a stereotyped and directed manner in developing spinal cord (Smith, 1983; Yamada, 1985). These observations suggest that there may be specific cues that enable sensory axons to find their appropriate spinal targets (Vaughn & Grieshaber, 1973; Singer, Nordlander & Egar, 1979; Altman & Bayer, 1984). Analysis of the development of axonal projections in several invertebrate and vertebrate neural systems has recently provided evidence that the establishment of specific connections with appropriate post-synaptic targets involves a series of progressively more selective axon–target interactions (Goodman *et al.* 1985; Taghert & Lichtman, 1986). The initial projections of axons to the general vicinity of target neurones may result from guidance by cues that influence the choice of early pathways taken by incoming axons. After axons have reached an appropriate target area, there appears to be a refinement of axonal arbors and the establishment of precise synaptic connectivity.

In some vertebrate systems axonal arbors are initially diffuse, with transient projections to broad target regions (Cowan *et al.* 1985; Shatz & Sretavan, 1986). However, in other systems, notably the amphibian retino-tectal pathway, axons appear to home in a precise manner to appropriate targets under the influence of specific guidance mechanisms (Holt & Harris, 1983; Sakaguchi & Murphey, 1985; Harris, 1986). Moreover, retinal axons have been shown to navigate to their central targets in the absence of impulse activity (Harris, 1984) and independently of the temporal sequence of axon outgrowth (Holt, 1984). *In vitro* analyses of the nature of guidance cues in the retino-tectal system have not, so far, demonstrated the existence of chemotactic signals (Harris, Holt, Smith & Gallenson, 1985). There is, however, increasing evidence in support of the idea (Sperry, 1963) that retinal axon-target interactions are mediated by cell-surface recognition molecules (Marchase, 1977; Trisler, Schneider & Nirenberg, 1981; Bonhoeffer & Huf, 1982; Thanos, Bonhoeffer & Rutishauser, 1984).

Studies discussed in this chapter raise the possibility that the targeting of sensory axons in developing spinal cord involves the recognition of cell-surface oligosaccharides by complementary carbohydrate-binding proteins. These two molecular classes exhibit cell-type and positional specificity at appropriate stages of spinal cord

development. Moreover, there is direct evidence that the same oligosaccharides are involved in the process of cell adhesion in preimplantation embryos. At present, the role of these molecules in sensory neurone development has not been established. However, several possible modes of interaction can be envisaged. For example, the transient expression of lactoseries structures on embryonic dorsal horn neurones, combined with the onset of synthesis of β-galactoside-binding lectins could provide a signalling mechanism that both initiates the ingrowth and restricts the dorsoventral projection of sensory axons that express lactoseries oligosaccharides. Attempts to perturb sensory projections with antibodies or multivalent oligosaccharide ligands that block saccharide–carbohydrate-binding protein interaction may provide more direct evidence about the role of these molecules.

Other mechanisms of cell adhesion may also contribute to sensory axon guidance and synaptic connectivity. Neural cell adhesion molecules (CAMs) such as N-CAM and L1 are expressed on sensory neurones early in development (Edelman, Hoffman, Chuong & Cunningham, 1985; M. Schachner, personal communication). The widespread distribution of neural CAMs over the period during which selective sensory connections are established, however, suggests that N-CAM and L1 may be involved in more general neural adhesive interactions. Recent studies have suggested that there may be some degree of overlap in recognition and adhesion systems mediated by lactoseries oligosaccharides and neural CAMs. The HNK-1 lactoseries oligosaccharide structure (Chou *et al.* 1985) is expressed on a subset ofN-CAM, L1 and J1 adhesion molecules (Kruse *et al.* 1984, 1985). Other lactoseries oligosaccharides expressed by subsets of sensory and spinal cord neurones may also be associated with neural CAMs and these saccharide groups may play an active role in specifying neuronal interactions at certain stages of development.The molecular probes now available should permit a more detailed analysis of the different recognition and adhesion systems involved in specifying sensory projections in developing spinal cord.

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