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Original Article

The expression of *XIF3* in undifferentiated anterior neuroectoderm, but not in primary neurons, is induced by the neuralizing agent noggin

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ABSTRACT The gene *XIF3* encodes a neural-specific type-III intermediate filament protein whose expression in the embryo precedes that of the neurofilaments by several hours. We now show, by *in situ* hybridization, that it is expressed at the neurula stage in primary neurons and, to a lesser extent, in undifferentiated anterior neuroectoderm. At the swimming tadpole stage, strong expression is restricted to the midbrain-hindbrain boundary, even-numbered rhombomeres of the hindbrain and the Vth and VIIth cranial ganglia. *XIF3* gene expression can be induced in ectodermal cells (animal caps) derived from blastula when grown to the neurula stage in the presence of the neuralizing agent noggin. In agreement with the proposed ability of noggin to neuralize, but not to promote neuronal differentiation, we find that the pattern of noggin-inducible *XIF3* expression in animal caps is consistent with expression in undifferentiated anterior neuroectoderm but not in primary neurons.

KEY WORDS: *Xenopus, intermediate filament, XIF3, primary neurons, noggin*

Introduction

The dynamic organization of the cell is maintained by a cytoskeleton consisting of microtubules, actin filaments and intermediate filaments (IFs). All the IF proteins share a conserved central alpha-helical rod domain that is important for protein dimerization and aggregation into higher order structures culminating in 8-10 nm filaments. The intermediate filaments have been subdivided into a number of classes according to sequence similarity (Steinert and Roop, 1988). Included in the type III IFs are vimentin, glial fibrillary acidic protein (GFAP) and desmin. Vimentin is expressed in neural cells at an early stage of development and widely within cells of mesenchymal origin where it has been attributed a range of functions (Evans, 1998). In contrast, the expression of GFAP in glial cells and desmin in muscle is normally restricted to a single cell type. The expression of the three type IV IFs is also restricted, in this case to neurons and consequently the type IV IFs are known collectively as the neurofilaments though it is clear that neurons often express other classes of IF proteins in addition to the neurofilaments.

The gene *XIF3* encodes a type III intermediate filament protein found predominantly in neural tissue (Sharpe *et al.*, 1989). It is closely related in sequence to mouse peripherin, a gene which is expressed widely in the peripheral nervous system and induced in PC12 cells in response to nerve growth factor (NGF) promoted neuronal differentiation (reviewed in Greene, 1989). In *Xenopus*, *XIF3* mRNA is first found at a low level in animal cap cells and then accumulates rapidly in the neurectoderm. *XIF3* therefore represents a gene encoding a type III intermediate filament protein whose expression becomes neural specific. *XIF3* gene expression in the neurula embryo precedes that of the type IV neurofilaments which in *Xenopus* are expressed first at the early tailbud stage (Sharpe, 1988).

During *Xenopus* development, the dorsal part of the animal cap becomes the neuroectoderm which will form the neural tube. Probably as an adaptation to a free swimming larval lifestyle, a small number of neurons rapidly differentiate to control the earliest movements of the newly hatched larva (Roberts and Clarke, 1982). These are the primary neurons, defined by their large size, precocious commitment to a neuronal fate and early axonal extension (Lamborghini, 1980; Hartenstein, 1989; Hartenstein, 1993). Within the neuroectoderm the primary neurons arise in restricted domains, marked at an early stage by the expression of *neurogenin*, a homolog of the fly proneural genes (Ma *et al.*, 1996). Within these regions, some cells are selected to become primary neurons by lateral inhibition, a process mediated by Delta-Notch signaling (Chitnis *et al.*, 1995). Selected cells then begin to differentiate and by the mid-neurula stage express a neuron-specific type-II β-

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