

Introduction: preface to the Hedgehog family of proteins review volume

P. W. Ingham and M. Placzek

University of Sheffield, The Krebs Institute, Developmental Genetics Programme, Firth Court, Western Bank, Sheffield S10 2TN (United Kingdom), Fax +44 114 222 27 88, e-mail: P.W.Ingham@sheffield.ac.uk

Over the past 6 years, members of the Hedgehog family of secreted proteins have come to be recognised as key players in a wide variety of vertebrate developmental processes, from the control of cartilage differentiation or the regulation of hair follicle development to the patterning of the limb or the specification of different neuronal cell types. In addition, the aberrant activation of the Hedgehog pathway has been identified as the likely cause of a number of tumours in humans, including basal cell carcinomas and primitive neuroectodermal tumours. Understanding the mechanisms by which Hedgehog signals are regulated and transduced will thus have widespread implications for our understanding of both normal development and disease.

Although now widely recognised for these various and important roles in vertebrate development, Hh signalling was originally described in *Drosophila*. In contrast to vertebrates, where multiple Hh-family members have been identified, flies have only a single *hh* gene, but as in vertebrates Hh signalling controls a number of key developmental processes in these animals. A major function of *hh* in the *Drosophila* embryo is in the patterning of the larval body segments. Animals lacking hh

function die at the end of embryogenesis and secrete a larval cuticle that is covered in spiky processes called denticles, giving the animal an appearance of the eponymous hedgehog. This phenotype is shared by mutations of several other genes, collectively termed the segment polarity genes, and it is through the genetic analysis of such mutations that most of what is currently known about the transduction of the hh signal has been adduced.

One intriguing feature of the Hh family is the finding that the active signalling form of the protein is covalently coupled to cholesterol, a modification that appears to influence the range of its signalling activity. This discovery has given new insights into the effects of some well-known teratogens and has led to new approaches to the analysis of the Hh pathway.

For this special issue, we have commissioned five articles to reflect the breadth and depth of our current understanding of Hh proteins and their multifarious roles. We hope that this will prove a stimulating introduction to the uninitiated as well as providing a useful resource for those already engaged in the analysis of these fascinating signalling molecules.