

Prof F Beck - Genetic regulation of mammalian development

The development of multicellular animals is dependent upon the expression of a hierarchy of genes, which sequentially provide increasingly detailed positional information. Many of these genes contain a conserved "homeobox" sequence coding for a DNA binding homeodomain. Homeobox genes are found in species as diverse as worms and humans. Their level of evolutionary conservation is consistent with their demonstrated function of controlling the establishment of basic anatomical relationships.

Our particular interest is in a homeobox gene called *Cdx2*, a homologue of the *Caudal* gene found in *Drosophila*. *Cdx2* is expressed from the earliest stages of embryonic development and throughout adult life in mammals. We have "knocked out" the *Cdx2* gene by homologous recombination, and found it to be crucial in many areas of development, including implantation of the embryo, placental patterning and function, skeletal development, and gut morphogenesis. It appears to be a fundamental regulatory factor in the specification of colonic tissue, and has been linked to bowel cancer in humans.

We wish to investigate further the role of *Cdx2* and of other homeobox genes, during gut and placental development. Use of conditional gene inactivation technology, based on the Cre-Lox system, will delineate the important time periods for *Cdx2* action during development. The creation of transgenic animals that express *Cdx2* at ectopic sites in the gut will provide insight into its possible role as a master gene in the specification of intestinal tissue. The role of *Cdx2* in blastocyst implantation and placental development will focus on studies of the relevant extracellular matrix using a variety of in vitro techniques.

References

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