PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Preface to Epithelial cell growth and differentiation. The proceedings of a Discussion Meeting held at the Royal Society of London.

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Preface

This issue contains a series of related articles derived from a Discussion Meeting on the important topic of the control of growth and differentiation in epithelial cells. Epithelial cells themselves cover our body surfaces, line our intestines and lungs, and have important functions in protection, secretion and absorption. Equally importantly, numerically speaking, they give rise to most of the important cancers which afflict us—colon, lung, breast, skin and stomach. This collection of articles gives a thorough account of the current state of our knowledge in several of the most important areas.

The issues of epithelial stem cells, and the control of their proliferation and number, are central to the maintenance of tissue homeostasis: studies in the gut (Potten) indicate that these cells form a small subpopulation in the base of intestinal crypts, possibly only 6–8 in number, out of a total proliferative cellularity of about 120, divide slowly, and have a mechanism for preventing accumulation of stem cell genomic damage by apoptotic cell death after, for example, irradiation. As in the human gut, stem cells are multipotential, giving rise to all cell lineages in the crypt (Wright). Similarly, in the epidermis, stem cells form a subpopulation which supply transit amplifying cells and maintain their own number (Watt); recent evidence suggests that expression of integrins of the β1 family can be used to identify this subpopulation. Cells in the hair follicle, when targeted with mutant *ras* frequently undergo malignant transformation, unlike cells in the epidermis, indicating that the target cell for the initiating event (possibly a stem cell population), is a major determinant of malignant capacity (Balmain). The liver seems to have developed not one, but two stem cell systems (Alison)—the hepatocytes, which are involved in regeneration in circumstances where only liver cell mass is lost, and the 'oval cell' originating from the biliary tree, and active when, for any reason, hepatocytes are unable to divide. The control of cell proliferation in epithelia is a burgeoning topic, with growth factors such as EGF and TGFα, cytokines and peptides all contributing (Burgess), while their motility is controlled partially by a family of peptides, the trefoil proteins, secreted by mucous cells in the gut and elsewhere (Wright).

Stroma and stromal cell populations have important effects on epithelial cells in development and differentiation: laminin, a component of basal lamina, influences epithelial polarity, possibly through an effect on *hox* gene regulation (Kedinger). Using sucrase–isomaltase as a model system, Traber delineates the control of gene expression in the intestine: further insights in to the role of genes such as *cdx*-1 and *cdx*-2 are given in this respect. Studies in three-dimensional culture have shown that the extracellular matrix largely defines organotypic differentiation, despite significant genetic defects in the epithelial cells (Bissell).

The close study of the *Min* mouse, which carries a mutation in the same gene involved in the genesis of polyposis coli in humans, has given researchers a great deal of insight into the role of this gene in the production of colorectal cancer, its modification by other loci, and the seemingly revolutionary concept that early colorectal adenomas are polyclonal (Dove). In what is possibly the best understood tumour from the viewpoint of genetic pathogenesis, Hamilton reviews the very rapid developments in the molecular pathology of colorectal cancer, pointing to several genes involved in the process, whose functions are still ill-defined.

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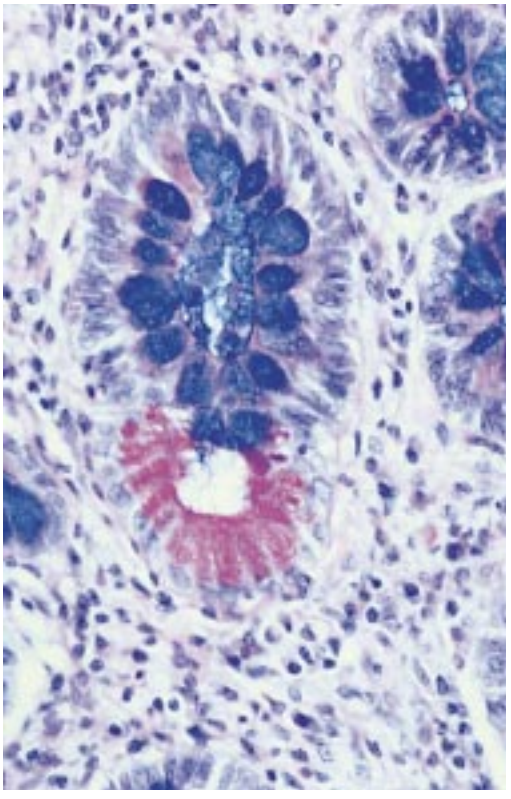

Figure 1. A bud of the developing ulcer-associated cell lineage, taking its origin from the stem-cell zone in the human small intestine, in a case of Crohn's disease with ulceration. Stained with periodic acid-Schiff and Alcian Blue, the magenta colour of the bud reflects its content of neutral mucin, different from the blue-staining acid sialomucin in the goblet cells of the parent crypt. This bud will develop into a new gland, make contact with the lumen and secrete a number of peptides active in the mucosal healing (see Wright, this issue).

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