

Stem cells: patterning and differentiation.

[I. Mackenzie](#)

University of Wales College of Medicine, Cardiff, Wales, GB

INTRODUCTION: In an appropriate environment, adult somatic stem cells can be induced to participate in the formation of a range of tissues. An aim of tissue engineering is to be able to direct new patterns of differentiation and tissue morphology. With this in mind, we have been working to determine the extent to which particular stem cell behaviours are intrinsic, i.e. arise from properties of the stem cells themselves, or are dependent on interactions with their environment.

Characteristic properties of epithelial stem cells are their high capacity for self renewal and their generation of cascades of amplifying cells that augment the differentiating population. In vitro growth and clonal analysis indicates that the generation of a stem and amplifying pattern is an intrinsic stem cell property. In vivo, individual stem cells give rise to clonal clusters of cells associated with small units of structure. Lineage marking shows that these patterns are readily re-formed by cells transplanted to in vivo sites after amplification in vitro. However, the normal regional distribution of stem cells in larger epithelial structures, such as rete, is not re-established after reconstruction. Other work shows that adult epithelial stem cells are normally stably committed to produce cells differentiating in particular regionally determined lineages but that alternative lineages can be generated by appropriate mesenchymal signals. It is concluded that the ability of epithelial stem cells to set up clonal cell hierarchies is an intrinsic property but that re-differentiation and development of complex structure occurs only in response to environmental signals.

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