

An integrative Computational Model of Colorectal Carcinogenesis

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Abstract:

As part of the Integrative Biology project, we have formulated a multi-scale model to describe the processes involved in normal intestinal tissue renewal and colorectal cancer (CRC) development. At the subcellular level, deterministic continuum models characterise the behaviour of fundamental biochemical networks (i.e. cell-cycle control and Wnt signalling) in response to intra- and extra-cellular cues. The outcome of these models determines the regulation and co-ordination of cellular events (i.e. proliferation, differentiation, apoptosis, migration and adhesion) within the intestinal epithelium. Under aberrant conditions, loss of control can cause increased cell division and/or decreased cell differentiation and death. This can have serious implications for the maintenance of the integrity of the crypt, as the resulting proliferative excess and biomechanical stress can lead to crypt deformation, fission and eventual polyp formation. Our multi-scale approach enables us to investigate the impact of mutations commonly detected in CRCs, combine highly disparate data-sets, explore possible interactions between phenomena occurring at different levels of organisation and, in the future, test anti-cancer drugs on the system as a whole.

Venue:Seminar Room, Hamilton Institute, Rye Hall, NUI MaynoothTime:2.00 - 3.00pm (followed by tea/coffee)Travel directions are available at www.hamilton.ie

