Wnt Signalling: The Subcellular and Cellular Consequences

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Abstract

Wnt signalling plays a key regulatory role in many biological processes including cell proliferation, migration and cell fate specification. It is active during development and also during adulthood when it assists in the maintenance of homeostasis. Dysregulation of the Wnt signalling pathway is a hallmark of several developmental disorders, a number of degenerative diseases and a variety of different cancers. As such, it is an obvious target for therapeutic intervention. However, its complexity and cross talk with other subcellular and cellular processes make it difficult to understand the consequences of abnormal Wnt signalling and to predict (and compare) the impact of different therapeutic approaches.

Motivated in part by these considerations, a variety of mathematical models of the Wnt signalling pathway have now been developed. The models are typically formulated as systems of ordinary differential equations that describe how the subcellular concentrations of proteins such as β-catenin, APC and Axin change over time and in response to Wnt stimulation. Recent models account for the localisation of these Wnt proteins in different subcellular compartments (e.g. the cytoplasm, nucleus and membrane), their transport between the various pools and, to a limited extent, their cross talk with the Delta-Notch and ERK signalling pathways.

In this talk I will review existing subcellular and multiscale models of Wnt signalling, with particular focus on the intestinal crypt.