

Identifying targets for anti-cancer treatment by a mathematical model for the Wnt signaling pathway

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Aberrant activation of the Wnt/beta-catenin signaling pathway, which controls stem-cell fate decision, is common in different types of cancer. Many of the genes in the Wnt pathway, which were first discovered to function transiently in development, turned out to act as oncogenes and tumour suppressors when deregulated in human cancer. Presently, much effort is invested worldwide in developing anti-cancer therapeutic agents, which function by controlling the Wnt pathway.

In order to identify improved targets for therapeutic intervention we have developed a mathematical model for the binding of Wnt to its receptors, the effect of secreted Frizzled Receptor Proteins (sFRP) and **Dickkopf** (DKK) on Wnt binding and β -catenin accumulation. The binding system of Wnt, Dkk, sFRP and frizzled (Fzd) and lipoprotein-receptor-related protein (LRP) receptors is described by a system of ordinary differential equations. Model parameters have been evaluated from direct measurements reported in the literature .

The model has been validated by comparing its predictions to independent published data. Model predictions will be used for identifying improved targets for Wnt signaling inhibition and cancer treatment.