Notch control of cell architecture: Potential implications for future cancer therapy

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Dissecting the mechanisms implicated in cell architecture should provide new insights for understanding development and tissue morphogenesis in general. An European study focused on the role of the Notch signalling pathway in regulating cell architecture.

The Notch pathway is a cell communication pathway conserved throughout the animal kingdom and is implicated in various developmental processes as well as linked to many diseases including cancer. Apart from its role in cell fate control, the Notch pathway is believed to regulate the cytoskeleton and cell morphology. However, the precise mechanism by which Notch exerts its effects on these processes remains elusive.

The 'Understanding Notch function in cell architecture regulation' (NOTCH AND CELL ARCH) proposal therefore aimed to identify and analyse new Notch target genes involved in cell architecture regulation.

By performing a genome-wide analysis of Notch-regulated genes, it was possible to identify genes coding for key proteins involved in cell morphology. These were categorised according to whether they presented changes in expression or they were located in proximity to a genomic region occupied by the transcription factor Su(H) which is known to mediate Notch responses. This led to the identification of 30 potential Notch targets with function related to cell behaviour regulation.

The function of these targets was tested using assays based on cell migration and differentiation during oogenesis, myogenesis and formation of the Drosophila wing disc. Using the technology of RNA interference (RNAi) to knock down gene expression, scientists identified nine genes whose depletion induced phenotypes associated with muscle formation defects, and two others (Moesin and Chickadee) that were required for the proper organisation of the wing disc.

The role of Notch in controlling the expression of cytoskeletal and cell behaviour regulators was also evaluated. Genomic analysis of three candidate genes (Reck, Rhea/Talin and Trio) for Su(H) and Twist binding positions is expected to provide important information regarding the implication of Notch in their transcription regulation.

Overall, the outcomes of the NOTCH AND CELL ARCH project offered new knowledge on the role of the Notch signalling pathway in cell architecture. Given the importance of Notch signalling and cell organisation integrity in many cancers, these new identified factors might have important implications for future therapy.

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