Role of DNA methylation and nucleosome occupancy in aberrant splicing of the WNT co-receptor LRP5

Elham Barazeghi

WNT/β-catenin signaling pathway directs cell fate and proliferation during embryonic development and adult homeostasis. De-regulation of this signaling pathway in the cell has been linked to different types of cancer. For example, it has been shown that in hyper-parathyroid tumors and breast cancer, the WNT co-receptor LRP5, named LRP5Δ, consists of an in-frame deletion of 142 amino acids. This deletion in the mRNA of LRP5Δ causes abnormal activation of the WNT/β-catenin signaling pathway that leads to cancer.

The reason behind this deletion in LRP5Δ is not known but preliminary results indicated that the genomic DNA sequence contains no deletion or other abnormalities. Therefore, it could be the epigenetic alterations responsible for this deletion in LRP5Δ mRNA because epigenetic mechanisms regulate gene expression and function without alteration in DNA sequence.

In this study, we wanted to investigate possible epigenetic mechanisms like DNA methylation, and nucleosome positioning behind expression of LRP5Δ in parathyroid tumors.

Degree project in Biology, Master of Science (2 years), 2013

Examensarbete i biologi 45 hp till magisterexamen, Uppsala universitet, 2013

Biology Education Center and Department of Surgical Sciences,

Supervisor: *Professor Gunnar Westin and Dr. Cihan Cetinkaya*