

# The Wnt Pathway as in silico disease model for neuro-oncology

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## Motivation

Rational drug design requires a profound understanding of the events taking place at the biomolecular level in the cell. Signaling and metabolic pathways are thus becoming increasingly important for the drug discovery process. This in-silico analysis of gene and protein interaction networks can be helpful in many ways for example to bring together and structure the present status of scientific knowledge. Specifically the Wnt pathway is relevant within neuro-oncology diseases like gliomas and medulloblastomas as well as in Alzheimers disease. Wnt signaling pathway plays a key role in essential cancer relevant processes.

## Methods

We created a Wnt pathway mainly by using a combination of tools and sources that allowed the creation of a pathway map; this map was built using the LION Bioscience Pathway editor which contains database derived annotations as well as manually inserted annotations such as literature references and literature summaries. The platform supports the direct linking to relevant information (UniProt, ENSEMBL, OMIM, PDB, MedLine etc.) and is furthermore linked to experimental data and results from in-house information coming from wet lab (quantitative RTPCR experiments), 2D-gel, MS/MS and in-silico analysis. The problem of overlapping and connecting pathways was handled by incorporating links between them and embedding them into presented pathway.

## Results

At SienaBiotech S.p.A. we constructed a Wnt pathway to support target identification as part of the drug discovery process. It has impacted projects covering brain cancer and Alzheimer's disease, delivering an overview of the proteins and available information. The pathway is used as a storage, visualization and communication tool to support the interdisciplinary work involving biologists, neurobiologists, oncologists and bioinformaticians. This leads to a better understanding of the disease mechanisms in CNS, and can help to unravel unknown mechanisms involved in the Wnt signaling pathway.

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