The Amyloid-beta toxicity core pathway

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Motivation

Pathway models or protein-protein interaction networks are excellent tools for the drug discovery process. They can be used to identify and select relevant targets to test a disease hypothesis. Combining information from diverse sources (in house experiments as well as literature) potentially transforms protein-protein interaction networks into detailed descriptions of cellular pathways. Interactive diagrams allow the linking of data directly onto the pathway and in this way can be used to integrate all relevant data regarding a protein or pathway entry into one framework. This not only leads to a better understanding of the biological mechanisms of normal and disease processes but also enable scientists to compare data from diverse experimental areas.

Methods

We used a combination of expert knowledge (hand curation) and text mining tools. Due to the fact that the analysis was and is an iterative process (Analysis-Representation-Construction-Review/Assessment-Analysis-…), the documentation of all investigated proteins (even those not included in the pathway) was crucial. Associations between proteins were visualized employing the LTE Pathway Editor module, which allows connection to other data sources and identification of potential cross-talk between pathways.

Results

At Sienabiotech, we started to build an Amyloid-beta toxicity pathway to support our target identification and validation activities. The initial focus was to describe how Amyloid-beta leads to cell death and to identify (if possible) specific molecular interactions. This “pathopathway” of relevance for AD will be a crucial part in an EU Framework VI project (ADIT). The pathway diagrams will also be used as communication tools, particularly for the interdisciplinary project teams, since they ensure a common understanding and facilitate critical assessment of disease hypotheses or mode-of-actions.

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