

Translocatome: a Novel Tool for Drug Target Discovery, Based on the Systematic Analysis of Protein Translocation

Spatial and temporal localization of the proteins has a key role in their regulation and biological function. In eukaryotic cells subcellular organelles are well separated compartments providing different microenvironments and containing many different molecular interactions. Translocation of proteins between subcellular organelles has a key role in the regulation of cellular processes.

One common example is the translocation of proteins from the cytoplasm to the mitochondria resulting in apoptosis of the cell (e.g. P53), another is, when transcription factors translocate from the cytoplasm to the nucleus enabling their control of gene expression (e.g. IGF2BP2 inducing angiogenesis). Perturbations of these translocation-based biological processes can lead to the transformation of a healthy cell into a cancer cell, highlighting the essential need of a deeper and more systematic understanding of this phenomenon. Despite the fact that possible subcellular localizations and the interactome of the proteins are well known, a compendium of translocating proteins and the systematic analysis of their role in signaling networks is still missing.

Our aim was to build a model that fills this gap: a novel database and modeling environment of translocating proteins called the Translocatome. Our database is based on the integration of (i) predicted proteins likely translocating, filtered from our ComPPI (comppi.linkgroup.hu) database (over 1600 proteins), (ii) a heavily manually curated data core (over 50 proteins) with a strong focus on the structural aspects of translocation regulation, and (iii) metadata gathered from different source databases, such as DisProt or LocSigDB. The database contains each protein's signaling network as well, with a main focus on cancer-related signaling.

After data collection, our aim is to perform systems-scale analysis on the network using AI-guided network dynamics simulations performed by our in-house developed software (www.turbine.ai) in order to analyze the effect of certain translocations between the compartments. With the help of our database and modelling environment new cancer regulators and potential drug targets can be determined.

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