



ABSTRACT BOOK



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Using AI-driven Protein Interaction Prediction to Investigate the Connection Between Arylsulfatase B and the Canonical Wnt/ β -catenin Pathway

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Introduction

Previous studies have shown the potential involvement of arylsulfatase B (ARSB) in the pathogenesis of malignant tumours, such as colorectal and prostate cancer. The Wnt/ β -catenin signalling pathway has been identified as one of the primary molecular mechanisms driving tumourigenesis, for example, in colorectal cancer. In silico prediction of protein-protein interactions using deep-learning technology provides a cost-effective and intuitive solution, which can guide experimental research.

Aim of the study

The aim of our research was to investigate the potential link between ARSB and the canonical Wnt/ β -catenin pathway using artificial intelligence-based protein interaction predictions.

Materials and methods

The interaction network of ARSB was analysed to identify potential interactions with members of the Wnt/ β -catenin pathway using the STRING bioinformatic database. The confidence threshold for interaction strength was set to the recommended value of 0.400. The PEPPI tool was used to predict the likelihood of interaction between individual proteins based on their amino acid sequences. The AlphaFold Server was employed to further analyse the most optimal interaction sites between the examined proteins based on their tertiary structures.

Results

The STRING database indicated that the strongest interaction pathway between ARSB and members of the Wnt/ β -catenin pathway involves GUSB (0.778) and HSP90AB1 (0.626). HSP90AB1 was predicted to interact with three proteins involved in the Wnt/ β -catenin pathway: CTNNB1, TLE3, and GSK3B, with confidence scores of 0.759, 0.625, and 0.920, respectively. The PEPPI tool predicted the likelihood of interaction of these proteins with HSP90AB1 as follows: CTNNB1 ($\log(\text{LR}) = -2.326$), TLE3 ($\log(\text{LR}) = -2.475$), and GSK3B ($\log(\text{LR}) = 1.212$). The AlphaFold Server predicted the following template modelling (pTM) scores: 0.43 (CTNNB1), 0.41 (TLE3), and 0.47 (GSK3B).

Conclusions

The most probable interaction pathway linking ARSB to proteins of the Wnt/ β -catenin pathway appears to involve GUSB and HSP90AB1. GSK3B is the most likely candidate for interaction with HSP90AB1. This protein is a central element of the Wnt/ β -catenin pathway, which forms a multimeric complex with APC, AXIN1, and CTNNB1. The interaction between HSP90AB1 and GSK3B has been previously validated using co-immunoprecipitation and mass spectrometry assays. This computational approach holds promise for future biomedical research, providing potential candidates for experimental validation.

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