Targeting the DBHS family of proteins to treat telomerase-active cancers

Approximately 80-90% of all human cancers utilise the telomerase pathway to elongate the telomeric caps of chromosomes in cancerous cells. This allows the cancer to proliferate uncontrollably without inevitably resulting in replicative senescence.

NONO, a homodimeric protein that is one of three members of the DBHS family of proteins, has been identified to have a role in the telomerase pathway. Specifically, it is implicated in the assembly of active telomerase by aiding in the transit of matured human telomerase RNA (hTR) out of Cajal bodies to associate with telomerase reverse transcriptase (hTERT).

This project involves developing potent inhibitors of the NONO homodimer for treatment in telomerase-active cancers. Three different approaches – Fragment-Based Drug Discovery (FBDD), Random Non-Standard Peptide Integrated Discovery (RaPID), and rational design – are taken to develop an inhibitor that is both potent and exhibits desirable biological properties. The hope is to develop a selective, bioactive, potent inhibitor capable of inhibiting NONO in cancerous cells, thereby depriving the cancer of this pathway to inconsequentially proliferate.