Analysis of the role of Hop/STIP1 in anchorage-independent growth in cancer cell

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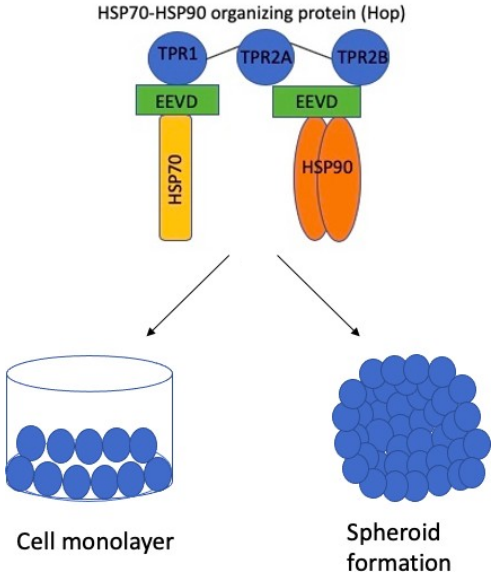

Figure 1: The potential role of Hop in the regulation of cancer cell growth under anchorage-dependent and independent conditions

Introduction: Heat shock proteins (HSPs) are a large, highly conserved protein family, several members of which are molecular chaperones that have a vital role for cell survival and development. This project focuses on the HSP70 and HSP90 chaperone complexes. The HSP70-HSP90 organizing protein (Hop) also known as stress- inducible protein 1 (STI1/STIP1) is a 60-kDa ubiquitous protein characterized by its ability to bind two chaperones, HSP70 and HSP90. Hop contributes to cancer proliferation, migration, and drug resistance. The evidence of Hop as a biomarker for tumours and cancer suggest its importance as a target for therapeutic strategies. However, to date all *in vitro* studies on Hop function have used two-dimensional (2D) cell culture. Three-dimensional (3D) cell culture systems are emerging as a more appropriate tool for drug discovery and tissue engineering as they offer greater physiological insight and similarity to *in vivo* testing compared with 2D culture systems. While representing amenable models for fundamental research, 2D culture systems do not fully recapitulate the *in vivo* scenario where cells grow in a 3D environment.

Methodology: To determine whether Hop is essential for cancer cell growth under 3D conditions and to begin to understand the mechanism, a range of anchorage-independent growth techniques were conducted using cell line models expressing or lacking Hop. Comparison of the growth phenotype and morphology of Hop knockout cell lines with wild type equivalents were conducted in soft agar, tumoursphere and hanging drop 3D assays.

Results: Comparison of the growth phenotype and morphology of Hop knockout cell lines with wild type equivalents in soft agar, tumoursphere and hanging drop 3D assays revealed differences across all three cell lines. In the soft agar analysis, HCT116 cell lines lacking Hop had reduced colony formation compared to the wildtype.

Discussion and Conclusion: Mechanistic analysis of phenotypic and morphological differences observed by western blot and immunofluorescence microscopy suggested that changes in cell adhesion proteins may regulate the biology of all three cell lines. Taken together, these data support a role for Hop in cancer cell growth and identify Hop as a potential drug target.

References:

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