The role of different Hsp70-Hsp90 Organising Protein (HOP) isoforms in cancer biology

K. Schwarz[1]*, S.A. Mattison[1], A.L. Edkins[1]

[1]Biomedical Biotechnology Research Unit (BioBRU), Department of Microbiology and Biochemistry, Rhodes University, Makhanda, South Africa
*E-mail: g14s0683@campus.ru.ac.za

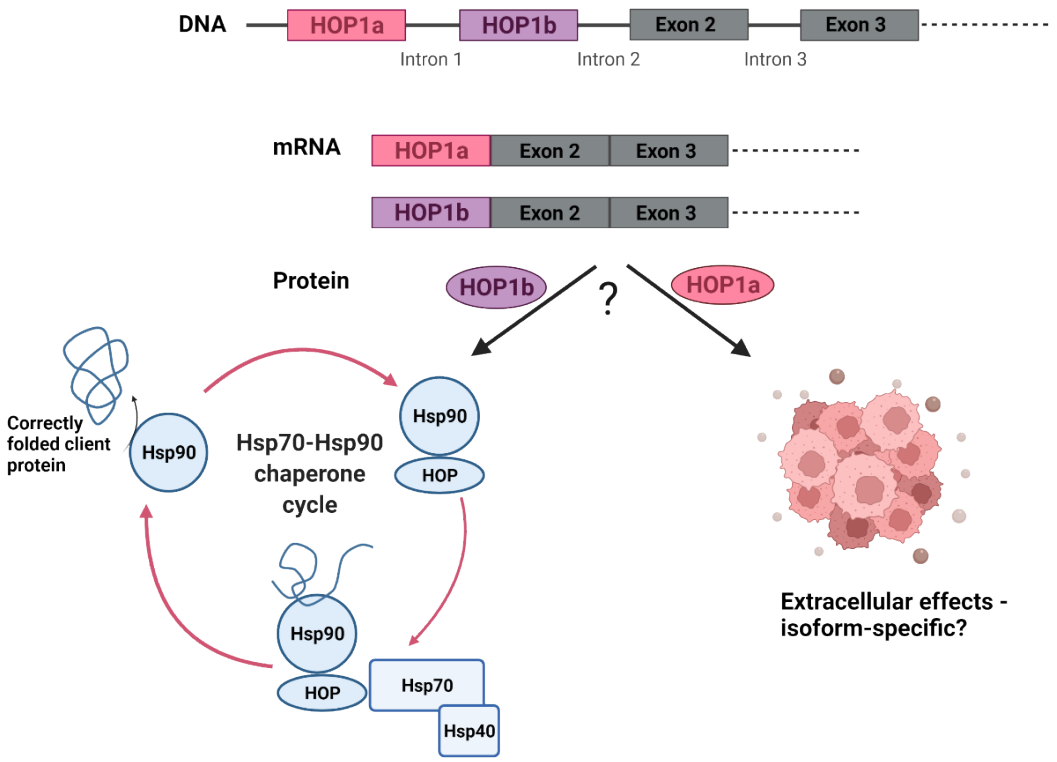

Figure 1: HOP isoforms may perform specific cellular functions, some of which may be disease related.
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Introduction: The Hsp70-Hsp90 Organising Protein (HOP) performs an extracellular role that is distinct from its canonical function as a co-chaperone of the Hsp90 chaperone system. We have identified a novel isoform of HOP (designated HOP1a) that incorporates a 47 amino acid extension at the N-terminus of the canonical full length human HOP (designated HOP1b). The additional amino acid sequence of HOP1a is a possible Golgi targeting sequence and may indicate how this HOP isoform is directed to the extracellular environment.

Results: Biochemical analysis and confocal microscopy indicated that HOP1a associates with the Golgi membrane in a Type I topology, while analysis of the cell biological effects of HOP1a and HOP1b showed evidence of isoform-specific effects on cell migration and proliferation. Western Blot analysis of cancer cell lines across different cancer types revealed evidence of HOP at sizes other than those predicted for HOP1a and HOP1b.

Discussion and conclusion: While we detected evidence of cancer-specific post-translational modification of HOP1a, it is also possible that the additional HOP bands may represent the product of a different HOP transcript or an alternatively spliced variant to both HOP1a and HOP1b. The ENSEMBL database describes four alternate transcripts of HOP1b that putatively encode protein, including HOP1a.This raises the question of whether additional alternative isoforms of the HOP gene exist, the levels and functions of which are temporally and spatially regulated in cells to fulfil distinct roles, some of which may be disease related. Our study is currently unravelling this question.

References:

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