

**P021** Interaction of SUMO-1 and RanGAP1 with Hepatoma derived growth factor

**Ketan Thakar<sup>1</sup>, Rainer Niedenthal<sup>2</sup> and Frank Dietz<sup>1</sup>**

*1. Centre for Biomolecular Interactions Bremen, University of Bremen*

*2. Department for Biochemistry, Hannover Medical School*

Hepatoma-derived growth factor (HDGF) is a ubiquitously expressed nuclear targeted mitogen first isolated as a secreted protein from supernatant of transformed liver cells. Extracellular HDGF undergoes receptor mediated internalization after which it is targeted to the nucleus via a bipartite nuclear localization signal (NLS) present in its C-terminal region. The regulatory signal(s) controlling the possible exchanges between the nuclear and cytoplasmic pools of HDGF are yet unknown. Recent study has shown that HDGF is SUMOylated at a non-consensus motif in its N-terminal region. RanGAP1, the GTPase-activating protein for Ran, is involved in regulating nucleocytoplasmic transport. RanGAP was the first protein identified to be SUMO-1 modified. Unmodified RanGAP1 is present in the cytoplasm and SUMO-1–modified RanGAP1 is associated with the cytoplasmic fibers of NPCs. SUMO-1 modification is emerging as a major mechanism that can influence the specificity, function, cellular distribution and stability of proteins.

In this study we show that upon overexpression of HDGF, SUMO-1 and RanGAP1, free unbound SUMO-1 and unSUMOylated RanGAP are able to co-precipitate with HDGF. This interaction occurs in the cytoplasm of the cell confirmed by co-precipitation for HDGF-NLS mutant (cytoplasmic) but not for HDGF wild-type protein (nuclear). By using C-terminally truncated HDGF variants we can narrow down a putative SUMO-1 binding motif (SBM) in HDGF where these protein interactions and possible interplay might be taking place.