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Discovery of small molecule inhibitors of protein-protein interactions using DNA-encoded chemical libraries

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Abstract

Discovery of small molecule inhibitors of protein-protein interactions (PPIs) has been limited due to technological hurdles. Here we present the discovery of small molecule (MW< 500 Da) inhibitors of PPIs with IC50 in the µM range from a 2 million compound DNA-encoded chemical library. The screening of the library was performed using a recently developed homogenous binding assay. This format avoids protein target denaturation and matrix binding artifacts associated with conventional heterogeneous binding assays. The screening process relies on target binding only and not on functionality i.e. inhibition of PPI. However, interestingly, the majority of binders discovered are inhibitors of the PPI. Could this indicate that most binders are homing to the so called protein hotspots when the protein target is in native confirmations?

Biography

Dr. Nils Hansen is the CEO and founder of Vipergen ApS. He is the principal inventor of the enabling YoctoReactor® and Binder Trap Enrichment® drug discovery technology platforms. He previously worked for Praecis Pharmaceuticals Inc., Waltham, MA, USA (now GSK) and Symphogen A/S, Copenhagen, Denmark. Dr. Hansen earned his Ph.D. in immunology from the University of Copenhagen, Denmark in 2000 and his M.Sc. in Chemistry and Biotechnology from the University of Aarhus, Denmark in 1996.