Targeting Sam-Sam interactions mediated by EphA2 receptor: design and evaluation of peptide inhibitors

Sam (Sterile alpha Motif) domains represent small protein binding modules provided with a helical fold and playing different functions in diverse cellular processes [1]. The Eph family of tyrosine kinase receptors contains at the C-terminus a Sam domain; the Sam domain from EphA2 (EphA2-Sam) has received the largest attention [2]. EphA2 is well known for its controversial role in cancer; indeed, this receptor is over-expressed in several tumors and upon stimulation with an ephrin ligand, undergoes endocytosis and consequent degradation, a process that could be exploited to lower tumor malignancy. EphA2-Sam represents the site where protein modulators of receptor endocytosis and stability (like the lipid phosphatase Ship2 and the adaptor protein Odin) are engaged by means of heterotypic Sam-Sam interactions [2].

Ship2 acts as an inhibitor of receptor endocytosis and its binding to EphA2-Sam is expected to primarily induce pro-oncogenic outcomes in cell. During the last few years, in an attempt to discover novel potential anticancer therapeutics, we designed and evaluated peptide inhibitors of EphA2-Sam mediated interactions through different strategies and a multidisciplinary approach based on extensive use of solution NMR (Nuclear Magnetic Resonance) techniques, molecular modeling, MST (MicroScale Thermophoresis) and in vitro cell-based assays [3-4].


Keywords: ONCOLOGY; STRUCTURAL BIOLOGY; NMR

Contacts: Marilisa Leone; marilisa.leone@cnr.it
Website(s): http://www.ibb.cnr.it/?command=viewu&id=418

Other: