Selective Protein Kinase Inhibitors Targeting EPHA2

Reference No: B76157

CHALLENGE
Protein kinases are important players of cellular signalling pathways and are crucial for regulating key processes like proliferation and migration. Dysregulation of protein kinases can lead to severe disorders and pathological conditions evoking inflammation or cancer. During the last two decades protein kinases therefore evolved as promising therapeutic targets. The Ephrin receptor EPHA2 has been identified as a valuable therapeutic target being implicated in several cancer-related processes. However, the lack of designated EPHA2 inhibitors still hampers the development of therapeutical strategies.

INNOVATION
Here, novel EPHA2 kinase inhibitors have been developed. The inhibitors borrow the chemical scaffold of the drug Dasatinib that was approved for treatment of chronic myelogenous leukemia, on which chemical moieties tailored to specifically bind EPHA2 are grafted.

Advantage of the novel inhibitors:
- higher selectivity compared to the existing non-designated alternatives
- less likely to be accompanied by side effects arising from off-target inhibition

Figure: The novel small molecule kinase inhibitor engages the ATP binding site of kinases. It displays higher affinity to EPHA2 with improved selectivity as compared to its lead compound Dasatinib (left figure). The viability of EPHA2-dependent SF-268 cells is significantly decreased upon treatment with the novel EPHA2 inhibitor, matching the cellular potency of Dasatinib (right figure).

COMMERCIAL OPPORTUNITIES
The novel inhibitors with their high selectivity for EPHA2 are promising candidates for the therapy of kinase-dependent diseases (cancer, autoimmune diseases etc.), including resistant tumors. This offers enormous potential in the emerging field of targeted therapies.

DEVELOPMENT STATUS
Proof of concept in vitro.

REFERENCES:
SF-268 cells were kindly provided by NCI.