28AB-ISMS21 Fast Identification of Novel HGK Inhibitors via Click Chemistry

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Hepatocyte progenitor kinase-like kinase (HGK) is a serine/threonine kinase that belongs to MAPK family. HGK is overexpressed in many types of cancers and plays important roles in cell migration and invasiveness of cancer cells. Therefore, HGK is considered a potential drug target for treating cancers.

To identify novel HGK inhibitors, high-throughput screening against recombinant HGK was conducted, and a hit compound having triazole structure was identified (IC_{50} = 0.92 μM). Subsequent optimization using click chemistry, led to two regio-isomeric potent HGK inhibitors having similar IC_{50} values. It was noteworthy that 1,5-substituted triazole analog showed high kinase selectivity while 1,4-substitued regio-isomer was a promiscuous inhibitor. We will present a detailed SAR of triazole analogs synthesized with shift of kinase selectivity profiles.