KIT Kinase

Kinase mutant panel performed with ^{33}PanQinase™ assay technology.

KIT Kinase $_{T544\text{-}V976}$ Mutant Panel

v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog

Synonyms: CD117, PBT, SCFR, c-Kit

KIT is a key controlling receptor for several cell types, including hematopoietic stem cells, mast cells, melanocytes and germ cells. Gain-of-function mutations in c-Kit have been described in a number of human cancers, including testicular germinomas, acute myeloid leukemia and gastrointestinal stromal tumors[1]. Imatinib (Glivec) acts as potent inhibitor of wild type KIT and has been approved for the treatment of gastrointestinal stromal tumors (GIST)[2].

Wild type KIT as well as nine pathophysiologically relevant KIT mutants are available as recombinant human active protein kinases and for compound testing services (Figure 1).

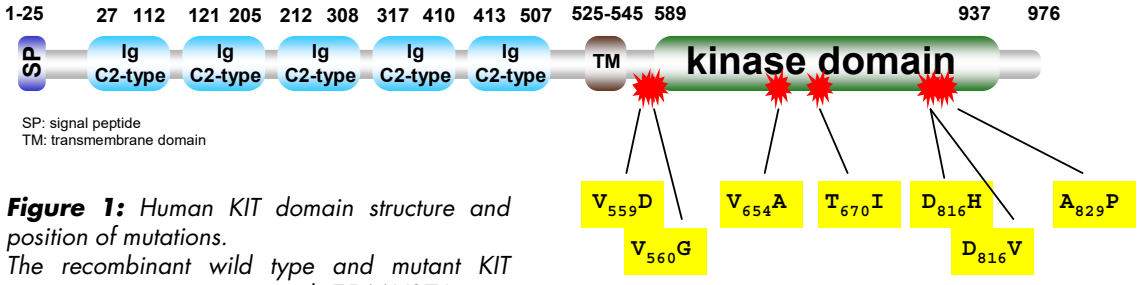

Figure 1: *Human KIT domain structure and position of mutations.*
The recombinant wild type and mutant KIT proteins comprise amino acids T544-V976.

Side-by-side comparison of wild type KIT and KIT mutants

Wild type KIT and nine different KIT mutants were compared side-by-side with respect to inhibition by reference inhibitors Staurosporine, Imatinib (Gleevec) and Nilotinib (Tasigna) (Figure 2). IC50 determinations of the three inhibitors were performed at corresponding app. ATP-Km (see Table 1) using our radiometric 33PanQinase Assay™.

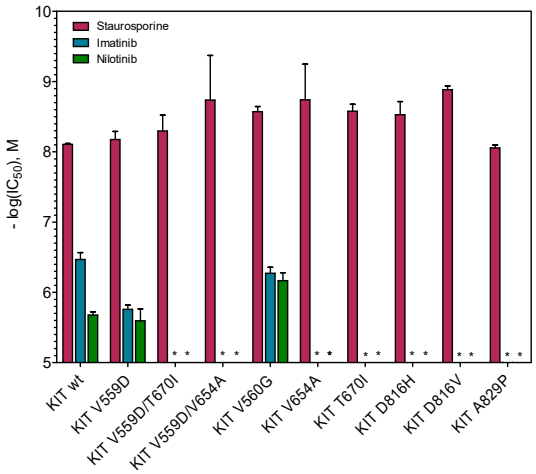

Figure 2:
*Differential inhibition of 10 KIT variants by the inhibitors Staurosporine, Imatinib (Gleevec) and Nilotinib (Tasigna) at app. ATP Km (n= 2-3). *IC50 > 10 µM*

References
[1] Signal transduction via the stem cell factor receptor/c-Kit: L. Rönnstrand, Cell. Mol. Life Sci. 61, 2535–2548 (2004)
[2] Inhibition of c-kit receptor tyrosine kinase activity by STI 571, a selective kinase inhibitor, M. C. Heinrich et al., Blood 96, 925-932 (2000)

TARGET-SPECIFIC ASSAY SERVICES