KIT Kinase

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

➢ KIT Kinase $_{T544-V976}$ 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 tumors1. 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; see also reverse side).

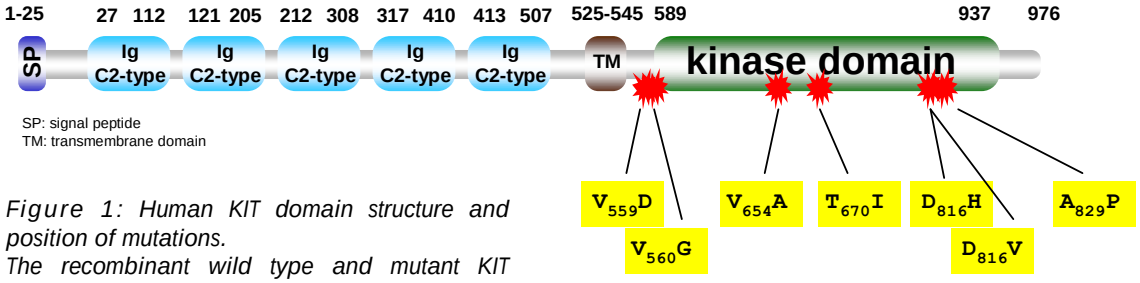

Figure 1: Human KIT domain structure and position of mutations.
The recombinant wild type and mutant KIT proteins comprise amino acids T544-V976.

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™.

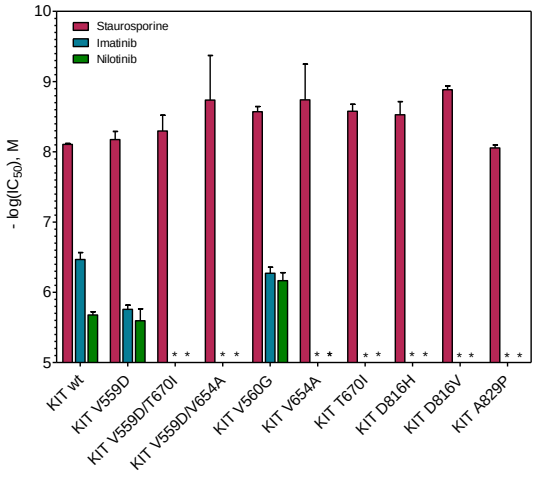

Figure 2:
*Differential inhibition of 10 KIT variants by the inhibitors Staurosporine, Imatinib (Gleevec) and Nilotinib (Tasigna) at app. ATP Km (n= 2-3). *IC50 > 10 µM*

TARGET-SPECIFIC ASSAY SERVICES

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)