MET Kinase

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

➢ MET Kinase $_{K956\text{-}S1390}$ Mutant Panel

met proto-oncogene

Synonyms: c-MET, HGFR

MET plays a pivotal role in tumor growth, metastasis and angiogenesis. Many pathophysiological and oncogenic MET mutants have been described. Furthermore, several MET mutations confer resistance against therapeutical MET kinase inhibitors1,2.

MET wildtype (wt) and nine pathophysiologically relevant MET mutants are available as recombinant human active protein kinases and for compound testing services (Figure 1; see also reverse side).

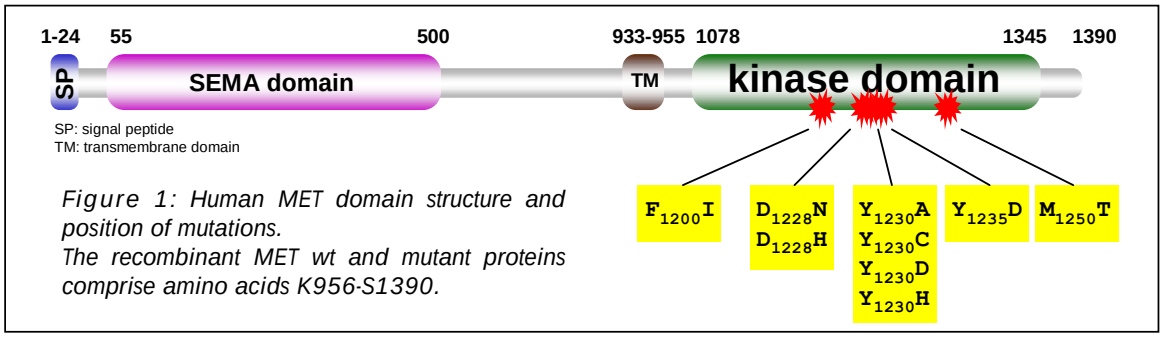

Figure 1: Human MET domain structure and position of mutations.
The recombinant MET wt and mutant proteins comprise amino acids K956-S1390.

Side-by-side Comparision of MET wt and MET Mutants

All MET variants were compared side-by-side with respect to inhibition by reference inhibitor PHA665752 (Figure 2). IC50 determinations of PHA665752 were performed at corresponding app. ATP Km of each MET variant (see Table 1) in our radiometric ^{33}PanQinase™ Assay.

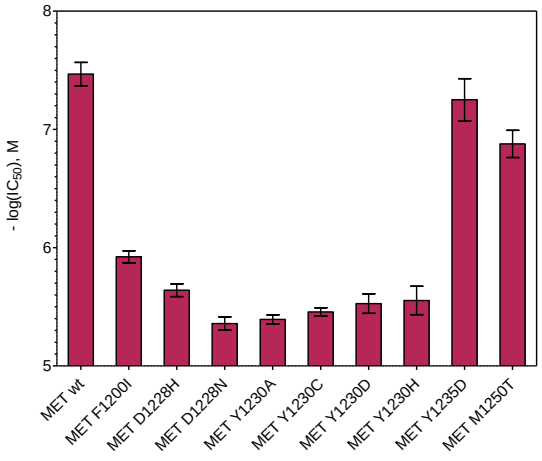

Figure 2:
Differential inhibition of 10 MET variants by MET inhibitor PHA665752 at app. ATP Km (n=2).

References

[1] c-Met Inhibitors with Novel Binding Mode Show Activity against Several Hereditary Papillary Renal Cell Carcinoma-related Mutations: Steven F. Bellon et al.; JBC 283, 2675-2683 (2008)

[2] The Met kinase inhibitor SU11274 exhibits a selective inhibition pattern toward different receptor mutated variants: Sylvie Berthou et al., Oncogene 23, 5387-5393 (2004)

TARGET-SPECIFIC ASSAY SERVICES