

# MET Kinase $K_{956}$ - $S_{1390}$ <sup>\*</sup>

met proto-oncogene (hepatocyte growth factor receptor)

## Wildtype and Mutant Panel

Synonyms: c-MET, HGFR

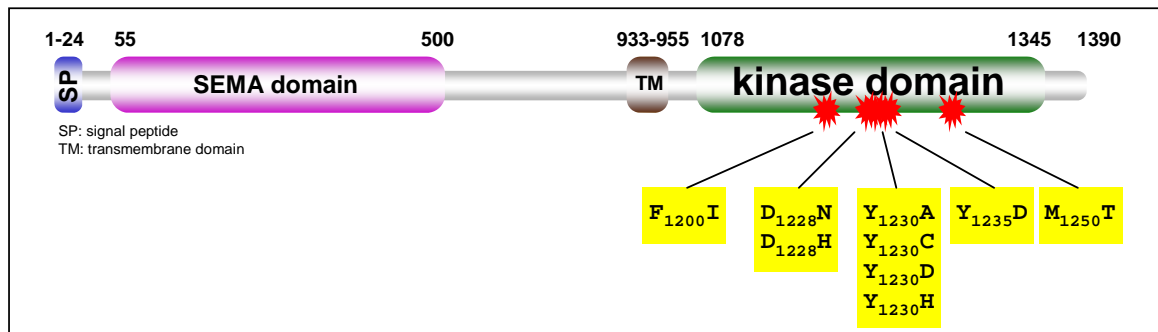
MET plays a pivotal role in tumor growth, metastasis and angiogenesis. Many pathophysiological and oncogenic MET mutants have been described. Furthermore, several MET mutations confer resistance against therapeutical MET kinase inhibitors<sup>1</sup>.

### References

<sup>1</sup>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)

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

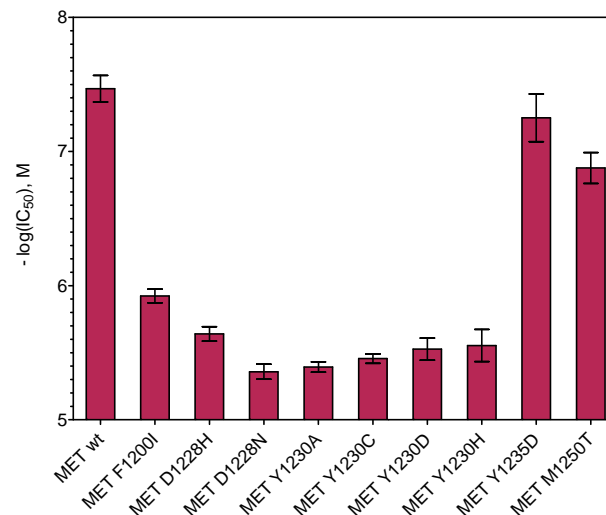
**MET wildtype (wt) and nine pathophysiological relevant MET mutants are available at ProQinase as recombinant human active protein kinases and for compound testing services (Figure 1; see also reverse side).**



**Figure 1:** Human MET domain structure and position of mutations. ProQinase recombinant MET wt and mutant proteins comprise amino acids  $K_{956}$ - $S_{1390}$ .

### Side-by-side Comparison of MET wt and MET Mutants

All MET variants were compared side-by-side with respect to inhibition by reference inhibitor PHA665752 (Figure 2). IC<sub>50</sub> determinations of PHA665752 were performed at corresponding app. ATP Km of each MET variant (see Table 1) in our radiometric <sup>33</sup>PanQinase Assay™.



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

## Available MET products and services

### Human active recombinant MET proteins

- Individual MET mutants and wild type, respectively
  - All proteins are available separately from 10 µg up to mg amounts, each.
- MET Mutant KinaseSampler
  - Includes 10 µg of nine MET mutants and of wildtype MET
- MET Mutant KinaseSampler<sup>Plus</sup>
  - Equals the MET Mutant KinaseSampler but includes substrates

All ProQinase MET proteins (Table 1) comprise amino acids K<sub>956</sub>-S<sub>1390</sub> and are expressed with identical tag and linker sequences as N-terminal GST-HIS<sub>6</sub> fusion proteins with a 3C cleavage site in Baculovirus infected Sf9 cells. Proteins are purified by identical GST-affinity chromatography procedure and identity is confirmed by mass spectroscopy.

Product	Product #	App. ATP Km [µM]
MET Mutant KinaseSampler	7000-0103-1	
MET Mutant KinaseSampler <sup>Plus</sup>	7000-0103-2	
MET wt*	0171-0000-1	3.1
MET F1200I (F1218I)	0978-0000-1	1.0
MET D1228H (D1246H)	0995-0000-1	1.9
MET D1228N (D1246N)	0994-0000-1	1.4
MET Y1230A (Y1248A)	0944-0000-1	1.9
MET Y1230C (Y1248C)	0980-0000-1	3.4
MET Y1230D (Y1248D)	0981-0000-1	5.2
MET Y1230H (Y1248H)	0976-0000-1	2.5
MET Y1235D (Y1253D)	0993-0000-1	25
MET M1250T (M1268T)	0982-0000-1	1.4

\* Two distinct Met amino acid sequences have been published that differ in residue numbering by 18 amino acids<sup>1</sup>. The nomenclature in this Fact Sheet corresponds to the -18 amino acids numbering<sup>1</sup>, whereas the nomenclature in other publications, e.g. Berthou et al.<sup>2</sup>, corresponds to the +18 amino acids numbering. Where appropriate, we have added the +18 amino acid nomenclature in parentheses within this Fact Sheet.

### Available Screening Services including MET Mutants

#### MET MutantProfiler

In our MET MutantProfiler your compound(s) will be tested at 10 different concentrations (standard range: 3x10<sup>-10</sup>M–1x10<sup>-5</sup>M; semilog dilutions) against wild type MET and nine MET mutants and IC50 values will be calculated. IC50 values of MET reference inhibitor PHA665752 will be determined side-by-side. All assays will be performed at the corresponding app. ATP Km of each protein kinase, using our radiometric <sup>33</sup>PanQinase Assay<sup>TM</sup>.

#### FreeChoice Kinase Assay Services

ProQinase offers completely flexible biochemical kinase assay services (FreeChoice). For each project you may freely choose the number of test compounds, the kinase panel and the number of data points for each test compound (i.e. concentrations and number of replicates). Assay technology: Radiometric <sup>33</sup>PanQinase<sup>TM</sup> assay. Test mode: Single concentration measurement or IC50 Profiling (10 conc. in semi-log steps)

#### ProQinase's WholePanelProfiler and WholePanelProfiler<sup>Plus</sup>

ProQinase's WholePanelProfiler comprises more than 350 active protein kinases, whereas our WholePanelProfiler<sup>Plus</sup> includes in addition seven lipid kinases. Both profilers allow broad selectivity profiling of your compounds.

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