RET Kinase

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

RET Kinase $_{H658-S1114}$ Mutant Panel

Ret proto-oncogene

Synonyms: CDHF12, CDHR16, HSCR1, MEN2A, MEN2B, MTC1, PTC, RET51, RET-ELE1

RET is a receptor tyrosine kinase which is the catalytically active part of the signaling complex for the glial cell line-derived neurotrophic factor family of ligands. Gain-of-function mutations in RET are implicated in human cancers[1]. Several physiological RET mutations have been described, RET and its mutants seem to be promising oncological targets for small molecule kinase inhibitor-based therapies[2].

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

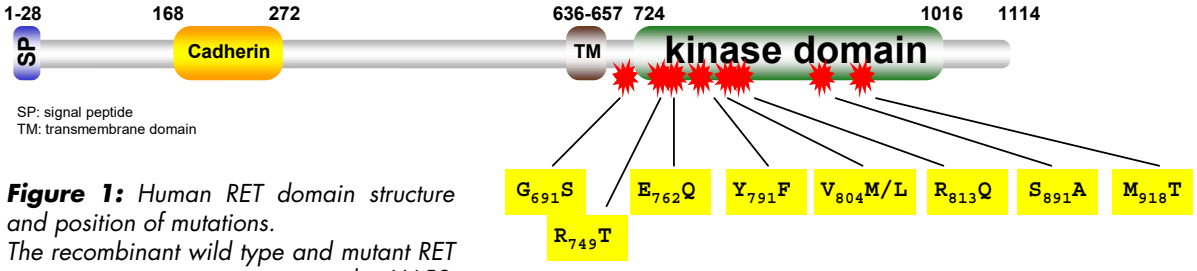

Figure 1: *Human RET domain structure and position of mutations. The recombinant wild type and mutant RET proteins comprise amino acids H658-S1114.*

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

Wild type RET and nine different RET mutants were compared side-by-side with respect to inhibition by the reference inhibitor BIBF1120 (Vargatef) (Figure 2). IC50 determinations of BIBF1120 (Vargatef) were performed at corresponding app. ATP-Km (see Table 1) using our radiometric ^{33}PanQinase Assay™.

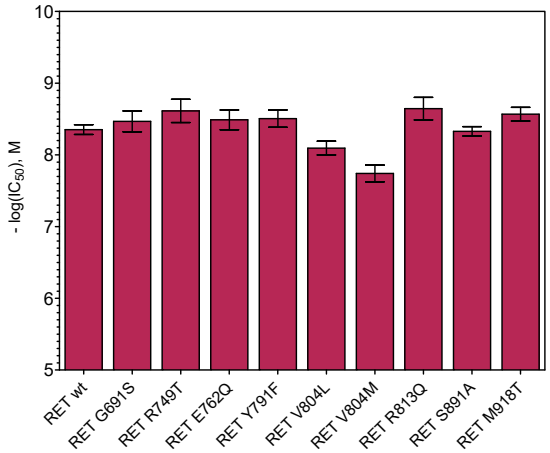

Figure 2:
Differential inhibition of 10 RET variants by the inhibitor BIBF1120 (Vargatef) at app. ATP Km (n= 2).

TARGET-SPECIFIC ASSAY SERVICES

References

[1] Structure and chemical inhibition of the RET tyrosine kinase domain: P. P. Knowles et al., J. Biol. Chem. 281, 33577-33587 (2006)

[2] Disease associated mutations at valine 804 in the RET receptor tyrosine kinase confer resistance to selective kinase inhibitors, F. Carlomagno et al., Oncogene 23, 6056–6063 (2004)