TARGET-SPECIFIC ASSAY SERVICES

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

➢ ABL1 Kinase P_{118}-S_{525} Mutant Panel

v-abl Abelson murine leukemia viral oncogene homolog 1

Synonyms: c-Abl, JTK7, p150

ABL1 is a therapeutical target in chronic myeloid leukaemia (CML), in which the chimeric BCR-ABL protein incorporates an active ABL kinase domain, initiating CML. Imatinib (Gleevec®) was the first approved ABL inhibitor, directed against ABL in CML[1]. Many pathophysiological and oncogenic ABL1 mutants have been described. Furthermore, several ABL1 mutations confer resistance against the therapeutically used ABL1 kinase inhibitor Imatinib[2].

ABL1 wildtype (wt) and eight pathophysiologically relevant ABL1 mutants are available as recombinant human active protein kinases and for compound testing services (Figure 1; see also reverse side).

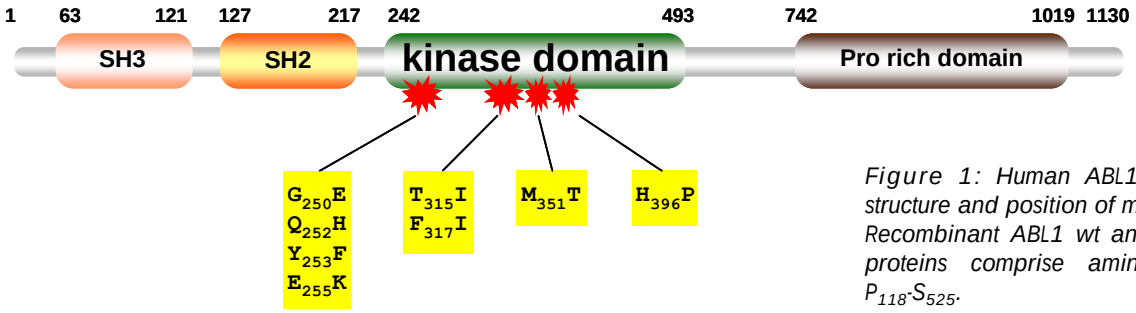

Figure 1: Human ABL1 domain structure and position of mutations. Recombinant ABL1 wt and mutant proteins comprise amino acids P_{118}-S_{525}.

Side-by-side Comparison of ABL1 wt and ABL1 Mutants

All ABL1 variants were compared side-by-side with respect to inhibition by reference inhibitor Imatinib (Gleevec®) (Figure 2). IC_{50} determinations of Imatinib were performed at corresponding app. ATP Km of each ABL1 variant (see Table 1) in our radiometric ^{33}PanQinase Assay™.

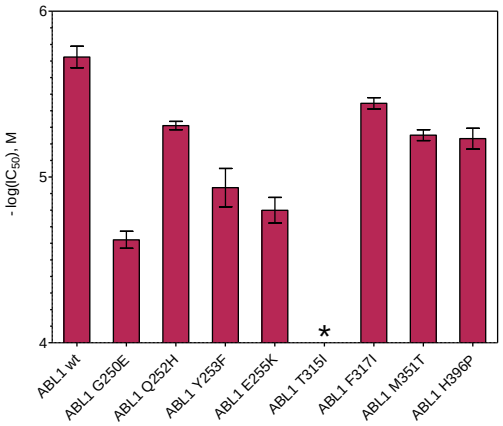

Figure 2:
*Differential inhibition of 9 ABL1 variants by ABL1 inhibitor Imatinib (Gleevec®) at app. ATP Km (n=2). *IC50 > 100 µM.*

References

[1] Mechanisms of BCR-ABL in the pathogenesis of chronic myelogenous leukaemia: Ruibao Ren et al., Nature Reviews Cancer 5, 172-183 (2005)

[2] Advances in the structural biology, design and clinical development of Bcr-Abl kinase inhibitors for the treatment of chronic myeloid leukaemia: Paul W. Manley et al., Biochim. et Biophys. Acta 1754, 3-13 (2005)