

# ABL1 Kinase P<sub>118</sub>-S<sub>525</sub>

v-abl Abelson murine leukemia viral oncogene homolog 1

## Wildtype and Mutant Panel

Synonyms: c-Abl, JTK7, p150

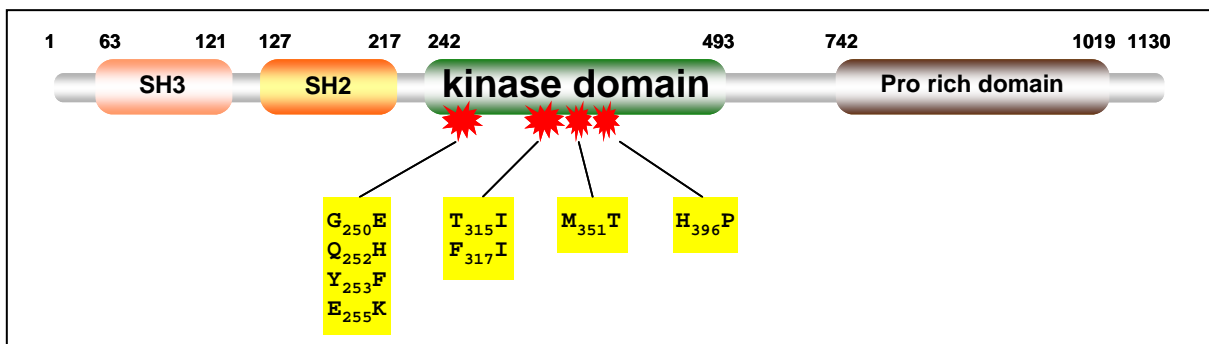
ABL1 is a therapeutic target in chronic myeloid leukaemia (CML), in which the chimeric BCR-ABL protein incorporates an active ABL kinase domain, initiating CML. Imatinib (Gleevec®) was the first approved ABL inhibitor, directed against ABL in CML<sup>1</sup>. Many pathophysiological and oncogenic ABL1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

### References

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

<sup>2</sup> 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)

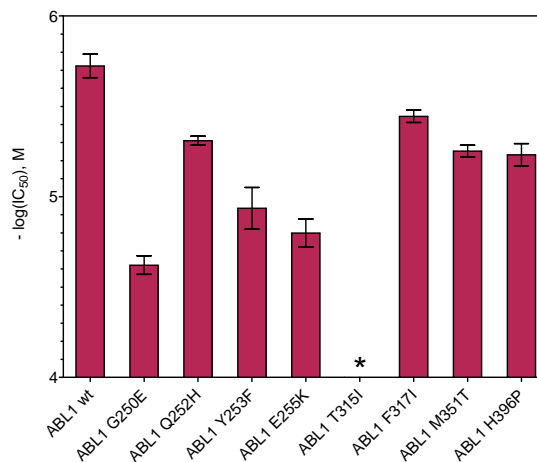
**ABL1 wildtype (wt) and eight pathophysiological relevant ABL1 mutants are available at ProQinase as recombinant human active protein kinases and for compound testing services (Figure 1; see also reverse side).**



**Figure 1:** Human ABL1 domain structure and position of mutations. ProQinase recombinant ABL1 wt and mutant proteins comprise amino acids P<sub>118</sub>-S<sub>525</sub>.

### 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<sub>50</sub> determinations of Imatinib were performed at corresponding app. ATP Km of each ABL1 variant (see Table 1) in our radiometric <sup>33</sup>PanQinase Assay™.



**Figure 2:** Differential inhibition of 9 ABL1 variants by ABL1 inhibitor Imatinib (Gleevec®) at app. ATP Km (n=2). \*IC<sub>50</sub> > 100 μM

## Available ABL1 products and services

### Human active recombinant ABL1 proteins

- Individual ABL1 mutants and wild type, respectively
  - All proteins are available separately from 10 µg up to mg amounts, each.
- ABL1 Mutant KinaseSampler
  - Includes 10 µg of eight ABL1 mutants and of wild type ABL1
- ABL1 Mutant KinaseSampler<sup>Plus</sup>
  - Equals the ABL1 Mutant KinaseSampler but includes substrates

All ProQinase ABL1 proteins (Table 1) comprise amino acids P<sub>118</sub>-S<sub>525</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]
ABL1 Mutant KinaseSampler	7000-0101-1	
ABL1 Mutant KinaseSampler <sup>Plus</sup>	7000-0101-2	
ABL1 wt	0992-0000-1	0.3
ABL1 G250E	0925-0000-1	0.3
ABL1 Q252H	0926-0000-1	0.5
ABL1 Y253F	0927-0000-1	0.4
ABL1 E255K	0924-0000-1	0.4
ABL1 T315I	0757-0000-1	0.2
ABL1 F317I	0989-0000-1	0.3
ABL1 M351T	0990-0000-1	0.3
ABL1 H396P	0991-0000-1	0.4

### Available Screening Services including ABL1 Mutants

#### ABL1 MutantProfiler

In our ABL1 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 ABL1 and eight ABL1 mutants and IC50 values will be calculated. IC50 values of ABL1 reference inhibitor Imatinib (Gleevec®) 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™.

#### 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™ 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.

This product is for in vitro research use only, not for use in humans or animals. ProQinase disclaims any warranty explicitly or implied that the use of the product or parts of the product is free from third party intellectual property claims unless this is explicitly stated.