

Kinase mutant panel performed with ³³PanQinase™ assay technology.

ALK Kinase L1066-S1437 Mutant Panel

anaplastic lymphoma kinase (Ki-1)

ALK is a receptor tyrosine kinase which is driving transformation in lymphomas through many molecular mechanisms. Several physiological ALK mutations have been described and due to chromosomal translocation, Nucleophosmin-ALK fusionproteins, called NPM1 ALK, are generated in several lymphomas¹. The potential of ALK and its mutants as a specific target for the therapy of anaplastic large cell lymphoma and other cancers is discussed for small molecule kinase inhibitor-based therapies².

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

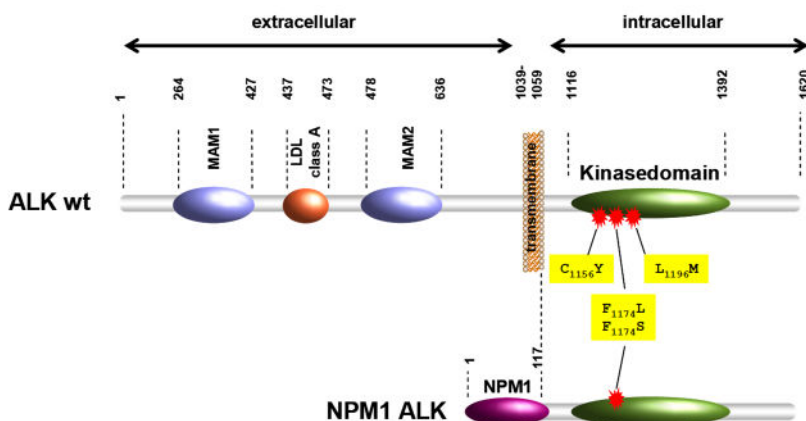


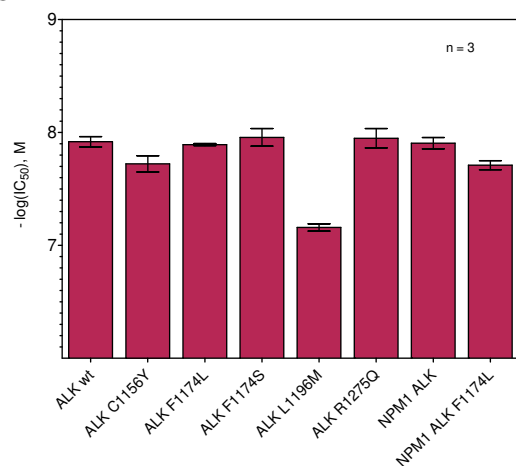
Figure 1: Human ALK domain structure and position of mutations..

The recombinant wild type and mutant ALK proteins comprise amino acids L1066-S1437.

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

Wild type ALK and seven different ALK mutants were compared side-by-side with respect to inhibition by the reference inhibitor Crizotinib (Xalkori) (Figure 2). IC₅₀ determinations of Crizotinib (Xalkori) were performed at corresponding app. ATP-K_m (see Table 1) using our radiometric ³³PanQinase Assay™.

Figure 2: Differential inhibition of 8 ALK variants by the inhibitor Crizotinib (Xalkori) at app. ATP K_m (n= 3).



References

- ¹ Mechanistic insight into ALK receptor tyrosine kinase in human cancer biology, Bengt Hallberg and Ruth H. Palmer, Nature Reviews Cancer 13, 685–700 (2013)
- ² The anaplastic lymphoma kinase in the pathogenesis of cancer, Roberto Chiarle et al., Nature Reviews Cancer 8, 11-23 (2008)