EGF-R Kinase

REACTION BIOLOGY

TARGET-SPECIFIC ASSAY SERVICES

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

➢ EGF-R Kinase $_{H672-A1210}$ Mutant Panel

Epidermal growth factor receptor

Synonyms: ERBB, ERBB1

EGF-R plays a pivotal role in tumor growth, metastasis and angiogenesis, and in addition in tumor resistance to chemotherapy and radiotherapy. EGF-R is therefore a therapeutical target in many human cancer indications1. Many pathophysiological and oncogenic somatic EGF-R mutants have been described, in particular in non-small cell lung cancer2. Furthermore, some EGF-R mutations confer resistance against the therapeutically used EGF-R kinase inhibitor Gefitinib (Iressa)3.

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

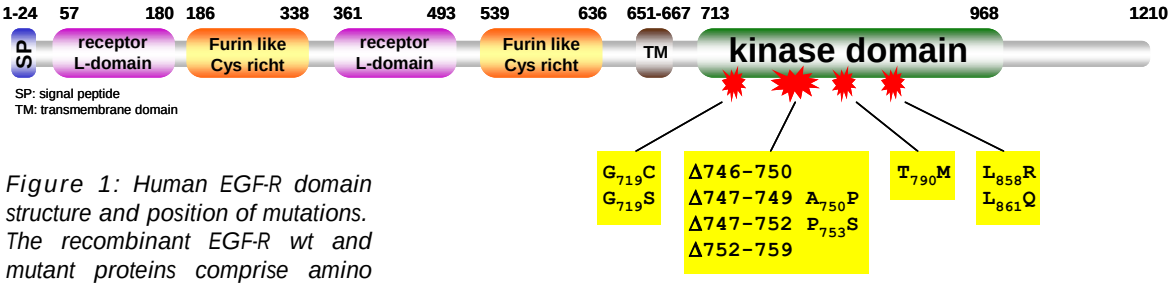

Figure 1: Human EGF-R domain structure and position of mutations. The recombinant EGF-R wt and mutant proteins comprise amino acids H672-A1210.

Side-by-side Comparison of EGF-R wt and EGF-R Mutants

All EGF-R variants were compared side-by-side with respect to inhibition by reference inhibitor Gefitinib (Iressa) (Figure 2). IC50 determinations of Gefitinib (Iressa) were performed at corresponding app. ATP Km of each EGF-R variant (see Table 1) in our radiometric 33PanQinase Assay™.

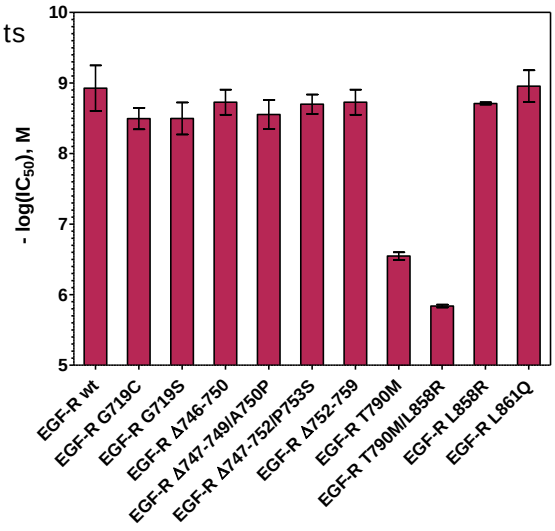

Figure 2: Differential inhibition of 11 EGF-R variants by EGF-R inhibitor Gefitinib (Iressa) at app. ATP Km (n=2).

References

[1] ZD1839 (Iressa): An Orally Active Inhibitor of Epidermal Growth Factor Signaling with Potential for Cancer Therapy: Alan E. Wakeling et al.; Cancer Research 62, 5749–5754 (2002)

[2] The EGFR mutation and its correlation with response of gefitinib in previously treated Chinese patients with advanced non-small-cell lung cancer: X. T. Zhang; Annals of Oncology 16, 1334-1342 (2005)

[3] Rational, biologically based treatment of EGFR mutant non-small-cell lung cancer: William Pao and Juliann Chmielecki; Nature Reviews Cancer 10, 760-774 (2010)