# EGFR Mutational Analysis

**See Technical Bulletin- EGFR Assay**

Mutation analysis of the EGFR gene (exons 18-21) is performed at CPAL. Using Scorpions and ARMS technologies, the EGFR real time PCR assay is highly sensitive (typically able to detect mutations present in samples at a level of 1-5%) and is capable of detection of 29 somatic mutations in the EGFR oncogene. **Mutation List**

If a deletion or insertion mutation is detected by the PCR assay, the sample is further subjected to DNA sequence analysis and the specific characterization of the mutation is reported. See Interpretive Comments

EGFR or epidermal growth factor receptor is a protein found on the surface of cells to which epidermal growth factor (EGF) binds. When EGF attaches to EGFR, it activates the enzyme tyrosine kinase thus triggering reactions that cause the cells to grow and multiply. The EGFR molecule has 3 regions, one projects outside the cell and contains the site for binding EGF, the second is embedded in the cell membrane and the third projects into the cytoplasm of the cell's interior. Receptor tyrosine kinases, like EGFR, have been shown not only to be key regulators of normal cellular processes but also have a critical role in the development and progression of many types of cancer.

EGFR dimerization stimulates its intrinsic intracellular protein, tyrosine kinase activity. As a result, autophosphorylation of several tyrosine residues in the C-terminal domain of EGFR occurs. This elicits downstream activation and signaling by several other proteins that associate with the phosphorylated tyrosines through their own phosphotyrosine-binding SH2 domains. These downstream signaling proteins initiate several signal transduction cascades, principally the MAPK, AKT and JNK pathways, leading to DNA synthesis and cell proliferation. Mutations that lead to EGFR overexpression have been associated with a number of cancers as these mutations could lead to the constant activation of EGFR which could result in uncontrolled cell division.

**The MAP-Kinase (MAPK) signaling pathway**

The identification of EGFR as an oncogene has led to the development of anticancer therapeutics directed against EGFR including gefitinib and erlotinib for lung cancer and cetuximab for colon cancer. Cetuximab is an example of a monoclonal antibody inhibitor (IgG I type). Monoclonal antibodies block the extracellular ligand binding domain, and with the binding site blocked, signal molecules can no longer attach there and activate the tyrosine kinase.

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