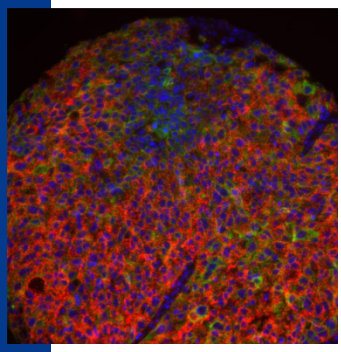
New Receptor Tyrosine Kinase Assay for Patient Treatment Selection Based on Protein-Protein Binding



This technology is a biomarker for predicting response to tyrosine kinase inhibitors by quantifying signaling associated protein complexes. A mature assay for Epidermal Growth Factor Receptor (EGFR) complexes has been created and validated. A percentage of lung cancers have active EGFR but test negative for mutant EGFR by current methods; these tumors with active EGFR may be due to rare mutations, overexpression, or excess EGF. These patients with active EGFR are currently not receiving EGFR inhibitors that might benefit them. Our assay can determine which patients have an activated EGFR tyrosine kinase pathway for any molecular reason, allowing physicians to determine effective care using a single assay.

COMMERCIAL OPPORTUNITY

- Lung cancer was diagnosed in over 220,000 Americans in 2010 and over half of those tumors would be of advanced stage to qualify them to be tested as candidates for EGFR inhibitor therapy.
- EGFR small molecule inhibitor therapies for lung cancer, erlotinib and gefitinib, are only prescribed for patients whose tumors harbor mutations in the EGFR gene that are thought to activate EGFR signaling of cell growth. Currently, EGFR mutation testing is recommended for greater than 110,000 lung cancer patients per year.
- EGFR mutation testing costs anywhere from $150-300 per tumor sample. Because our test can detect receptor tyrosine kinase activation, regardless of protein mutation status or expression level, the potential market size for our test would be all patients eligible for mutation testing, or the remaining 80% that test negative for mutations.
- Our test might also eventually be useful in other markets such as the metastatic colorectal or head & neck cancer patients who are currently prescribed the EGFR antibody inhibitor cetuximab.
- Additionally, prototype assays for other receptor tyrosine kinases, including MET, FGFR, and ALK have been developed; all of these are active targets for pharmaceutical therapeutics.

TECHNOLOGY

This technology is a novel use of a proximity ligation assay (PLA) for the selection of patients for treatment based on measurements of functional signaling associated protein complexes. Growth factor receptor binding protein 2 (GRB2) binding to EGFR is a critical component of EGFR activity and cell growth signaling. Our assay can be used on standard formalin-fixed paraffin embedded tissue samples to detect this interaction between EGFR and GRB2 *in situ* as a direct biomarker of EGFR activity. In multiple cohorts of lung cancer patient tissue samples, this assay detected active EGFR-GRB2 complexes in patients with and without activating EGFR mutations. In patient-derived xenograft mouse models of multiple tumor types, EGFR-GRB2 PLA was associated with cetuximab response ($p=0.006$). In a retrospective mixed-histololgy cohort of 91 patients that were treated with EGFR tyrosine kinase inhibitors, high EGFR-GRB2 PLA signal intensity was statistically significantly associated with improved overall survival ($p=0.045$) and a doubling in median overall survival time (10 vs. 20 months).

PUBLICATION/PATENT

- PCT application filed on 9/27/2012 for Dr. Eric Haura

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LICENSING OPPORTUNITY

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