Notes on EGFR and ALK

Bradley Hintze

October 4, 2016

1 Epidermal Growth Factor Receptor (EGFR)

Overview:

Epidermal Growth Factor Receptor (EGFR) is a cell surface receptor that is activated when it binds its ligand causing homodimerization [1]. This dimerization causes activation if the inner-cellular C-terminal kinase activity causing autophosphorylation of C-terminal tyrosines Y992, Y1045, Y1068, Y1148 and Y1173 [2]. This phosphorylation acts as a siglnal to mainy pathways involved in cell migration, adhesion, and proliferation [3].

Implications in NSCLC:

Mutations in EGFR have been linked to squamous-cell carcinoma [4]. The drug gefitinib has been shown to be a stong inhibitor of L858R mutant of EGFR [5]. Bradley needs to do more research!

Questions Pending

- Read this [6].
- Are there published guidlines for using gefitinib or erlotinib?
- What mutations are (and are not) sensative to gefitinib and erlotinib?
- Paez et al. showed that mutations in EGFR to be more common in japanese (asians?) compared to european decendants and women compared to men [5]. Can we show frequency of mutation vs. race/sex?

- Is targeted treatment bing misused, i.e. is gefitinib being used on patients lacking the EGFR L858R mutant? If so, are survival rates as expected – lower than the group having the L858R mutant?

2 Anaplastic Lymphoma Kinase (ALK)

Bradley needs to do research!

References

[1] Yosef Yarden and Joseph Schlessinger. Epidermal growth factor induces rapid, reversible aggregation of the purified epidermal growth factor receptor. *Biochemistry*, 26(5):1443–1451, mar 1987.

[2] J. Downward, P. Parker, and M. D. Waterfield. Autophosphorylation sites on the epidermal growth factor receptor. *Nature*, 311(5985):483–485, oct 1984.

[3] Kanae Oda, Yukiko Matsuoka, Akira Funahashi, and Hiroaki Kitano. A comprehensive pathway map of epidermal growth factor receptor signaling. *Mol Syst Biol*, 1(1):E1–E17, may 2005.

[4] Francine Walker, Laurent Abramowitz, Dalila Benabderrahmane, Xavier Duval, Véronique Descatoire, Dominique Hénin, Thérèse Lehy, and Thomas Aparicio. Growth factor receptor expression in anal squamous lesions: modifications associated with oncogenic human papillomavirus and human immunodeficiency virus. *Human Pathology*, 40(11):1517–1527, nov 2009.

[5] J. G. Paez. EGFR mutations in lung cancer: Correlation with clinical response to gefitinib therapy. *Science*, 304(5676):1497–1500, jun 2004.

[6] Rafael Rosell, Teresa Moran, Cristina Queralt, Rut Porta, Felipe Cardenal, Carlos Camps, Margarita Majem, Guillermo Lopez-Vivanco, Dolores Isla, Mariano Provencio, Amelia Insa, Bartomeu Massuti, Jose Luis Gonzalez-Larriba, Luis Paz-Ares, Isabel Bover, Rosario Garcia-Campelo, Miguel Angel Moreno, Silvia Catot, Christian Rolfo, Noemi Reguart, Ramon Palmero, José Miguel Sánchez, Roman Bastus, Clara Mayo, Jordi Bertran-Alamillo, Miguel Angel Molina, Jose Javier Sanchez, and Miquel Taron. Screening for epidermal growth factor receptor mutations in lung cancer. *New England Journal of Medicine*, 361(10):958–967, sep 2009.