The Negative Regulators of EGFR

Popular science version

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In multi-cellular organisms, cells communicate with each other using signals. Cells get these signals from their surrounding via receptor proteins. *Epidermal Growth Factor Receptor* (EGFR) is a sub-family of *Receptor Tyrosine Kinases* (RTKs) which belong to *Enzyme-Linked Receptor* super family. These are trans-membrane receptors and binding of a ligand to the outside of the cell to these receptors causes enzymatic activity on the inside of the cell. EGFR is frequently expressed in epithelial tumors.

When EGF as a ligand binds to the extra-cellular part of the EGFR, it promotes receptor dimerization, which stimulates the intracellular processes. This leads to a lot of cellular and developmental programs including proliferation, survival, migration and so on. Therefore it is quite important to study EGFR and its putative negative regulators in cancer treatment.

In this study, some putative negative regulators of EGFR have been selected. Then by producing viruses carrying small hairpin RNA, which are used for silencing of genes of interest, we were able to knock-down these putative negative regulators of EGFR. After that primary mammary gland cells of mice were infected by the viral constructs. So we could establish stable cell lines which have lack of the genes of putative negative regulators of EGFR. In these established cell lines, the protein level and activation level of EGFR have been studied. Also the cells were monitored while keeping in culture to control the differentiation and possible morphological changes.

This project is at an early stage but we have got some interesting findings already. We established new cell lines knocking-down some putative negative regulators of EGFR. By now, we have some indication that some of these putative negative regulators have more effects in regulation of EGFR activation than others. Also the data may suggest that knock down cells can display a different result in differentiation study when they are kept in culture for longer times.

For the future we will investigate epithelial stem cell maintenance and cell differentiation in 3D cultures in order to avoid the limitations of 2D culture. Then we are going to use selected lentiviruses to infect primary mammary epithelial cells from mice and transplant them back into cleared mammary fat pads to study these genes *in vivo*.

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