Inhibiting the mTOR Pathway as an Anti-Cancer Strategy

There’s a class of drugs that are being studied in fighting cancer, known as mTOR inhibitors. mTOR stands for mammalian target of rapamycin, which is an immunosuppressant drug that also has anti-fungal activity, but which was also found to have anti-proliferative activity (keeping cells from growing and dividing), which suggested that it could have useful anti-cancer activities. The entire class of drugs that block the rapamycin target are now the subject of study in fighting cancer, and one called temsirolimus has been approved against kidney cancer. The target is shown in this figure that illustrates that mTOR is downstream as part of a path that starts with growth factor receptors we’ve met before, such as the epidermal growth factor receptor (EGFR) and insulin-like growth factor receptor (IGF-1R):
There is certainly preclinical (lab-based) research that suggests that mTOR is important in human cancer. One study looked at various lung cancers at different stages and found higher...
levels of expression of a downstream marker of mTOR activity called phospho-s6 (\textit{phosphorylation}, or adding a phosphate chemical group to a protein, is a common way to to activate a protein) in higher stage cancers, and that inhibiting mTOR could reduce cancer growth in mice with genetic mutations that lead to induction of cancers (abstract here). And there’s evidence that it may be particularly relevant for lung tumors that carry EGFR or KRAS mutations, because levels of the mTOR activation marker phospho-s6 were more likely to be high in these patients than others (abstract here). Although we still need to learn much more about the interactions of mTOR with lung cancer in general and our current treatments, there are some experts who believe that mTOR may be a key mediator of resistance to EGFR inhibition.

For those of you who aren’t interested in biochemistry, all you need to know is that there is a relatively new class of anticancer drugs called mTOR inhibitors that act downstream of some of the same pathways shared by our other molecularly targeted therapies. mTOR inhibitors have been shown to have some activity as single agents in a few kinds of cancer, including kidney cancer as well as lung cancer (although very limited single agent activity in lung cancer). There are several mTOR inhibitors being studied, but all are in pretty early stages for lung cancer research. We'll cover some of the angles for study in both SCLC and NSCLC very soon.