Aurora Kinase Inhibitors as a Novel Anti-Cancer Approach

One emerging class of targeted therapy for cancer that is just entering clinical trials is a group of agents called aurora kinases. A kinase is a protein that modifies the structure and function of other proteins by adding a phosphate group to it, which is like flipping an on/off switch. Aurora was discovered by Dr. David Glover and colleagues at the University of Cambridge, who found that the protein is involved in the normal process of mitosis (cell division after duplication of the DNA), and that mutated forms of the proteins led to disruption of normal cell division. Because it is involved in the polar regions of the cell, it was named Aurora after the aurora borealis, or northern lights:

Aurora was later found to exist in three different forms in humans (A, B, & C), all involved in parts of the cycle of cell division, including how chromosomes move around in the dividing cell. Because cancer cells tend to divide faster than normal cells of the body, proteins that disrupt the process can preferentially harm cancer cells before non-cancer cells in the body.

There are some hints that aurora kinases may be relevant for lung cancer. Heighway and colleagues found that these proteins were strongly overexpressed in more than 40 NSCLC tumors tested (abstract here). In another study, by Smith and colleagues, overexpression of an aurora kinase protein in lung tumors was associated with worse survival (abstract here):

There are several aurora kinases that have been developed and are now in or about to enter clinical trials. The ones furthest along in testing are MK-0457 (Merck), AZD1152 (AstraZeneca), and PHA-739385 (Nerviano). They are all intravenous drugs that share grade 3 neutropenia, a significant drop in the white blood cell count, as the leading side effect that limits the dose to be used. These studies are just getting the first sense of activity of these drugs, which have not yet demonstrated an effect of significant tumor shrinkage but have led to prolonged stable disease. In addition to these three agents, several others are in development through several companies (oral and IV) and should be entering into clinical trials in the near future.
For now, these agents provide another very new way to potentially treat cancers in a targeted way, but we'll need to see whether they actually have significant activity in lung cancer. We'll learn more as the trials become available and reported.