Shining the Light on Aurora-A Kinase as a Drug Target in Pancreatic Cancer

David J. Bearss

Commentary on:

We were honored to learn that our article, “The mitotic serine threonine kinase, Aurora-2, is a potential target for drug development in human pancreatic cancer” was selected as one of “The Best of MCT-10 Years.” The work presented in this paper has led to many studies examining the role of Aurora kinases in cancer and additional translational studies taking new drugs forward into the clinic. For many years, my research group has had an interest in identifying new potential targets for drug discovery and development in adenocarcinomas of the pancreas. Our earlier work from genomic and gene expression studies using pancreatic cancer cell lines and tumor samples taken directly from patients, identified Aurora-2 (also known as Aurora-A), as a gene that was amplified and significantly up-regulated at the mRNA and protein level in pancreatic cancers (1). At the time of publication of our gene expression work, there were only a handful of reports linking Aurora kinases to cancer. Our group was among the first to use genetic tools to validate that inhibiting Aurora kinases in cancer cells led to specific phenotypes in the cell cycle and induction of cell death. Since this work was published in 2004, there have been more than 750 publications reporting the targeting of Aurora kinases with inhibitors and several Aurora kinase inhibitors have been moved forward into clinical trials. Indeed, my group discovered and filed an investigational new drug application with the U.S. Food and Drug Administration for a very selective Aurora-A compound recently. It has been incredibly rewarding and exciting to take our initial observations, that Aurora-A was a potential drug target, and see this translated into the clinic. Pancreatic cancer remains a key target for the clinical development of several of the Aurora kinase inhibitors that are progressing in clinical development. As compounds have moved into the clinic, we have learned a great deal about the activity and on-target toxicity of Aurora kinase inhibitors. One major finding is that treatment with compounds with strong Aurora-B inhibitory activity leads to neutropenia in patients, complicating the development of these agents. Currently, Aurora-A selective compounds are thought to be more active and less toxic and have the potential as new therapeutics in several tumor types. As we learn how to best dose and schedule these compounds in the clinic, we hope to see Aurora kinase inhibitors continue to be important tools for the treatment of pancreatic, and other cancers.

Disclosure of Potential Conflicts of Interest

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