Editorial

Molecular Cancer Therapeutics: From Bench to Bedside

The American Association for Cancer Research is pleased to offer researchers an important new tool in the fight against cancer—the new AACR journal *Molecular Cancer Therapeutics* (*MCT*). This new journal is dedicated to accelerating the exchange of important information in the development of new therapeutic and preventive agents.

The inaugural issue of *MCT* presents studies of many targets. He *et al.* utilize epothilone-resistant cell lines to study sites in class I β-tubulin that are critical for the regulation of microtubule stability. Notably, they found one epothilone-resistant cell line that is actually hypersensitive to microtubule-destabilizing agents such as vinblastine.

Gamcsik *et al.* report important findings on the interactions of 7-peptidyl derivatives of camptothecin and topoisomerase I. Their results indicate that these derivatives represent an important new class of camptothecin analogues that give remarkably stable topoisomerase I-DNA cleavage complexes.

The work by Cai *et al.* certainly teaches us that when we think we know the mechanism for something, we probably do not. They found that O^6-benzylguanine enhances the cytotoxicity and decreases the mutagenicity of nitrogen mustard through a mechanism that is independent of the activity of O^6-alkylguanine-DNA alkyltransferase. They found that O^6-benzylguanine actually causes cells to arrest in the G_1 phase of the cell cycle. This new finding offers the potential for new clinical trial strategies with the agent.

A number of antisense molecules are in clinical trials. Ross *et al.* review *Kirsten-ras* as a target of great interest. They note that the use of an antisense oligonucleotide that inhibits *Ki-ras* expression in a colorectal cancer cell line (SW480) gives very surprising results indeed. They found that inhibitors of *Ki-ras* had little effect on cell numbers but did significantly affect the secretion of vascular endothelial growth factor, and the expression of other genes involved in invasion and metastasis.

In the category of new agents, Yin *et al.* report on the isocoumarin NM-3. The antitumor activity of NM-3 has been thought to be through its effect on tumor vascular endothelial cells. The study found that at higher concentrations NM-3 can also inhibit growth of human cancer cells via generation of reactive oxygen species and by activation of the *p53* tumor suppressor gene.

In the area of adenovirus-mediated *p53* gene therapy, Carroll *et al.* show one additional possible explanation for the frequently seen bystander effect of gene therapy (in which tumor cells that do not receive the therapeutic gene, but are near those tumor cells that do receive the gene, are also eliminated). They found that natural killer cells in nude mice play a role in the bystander effect seen in adenovirus-*p53* gene therapy of experimental ovarian cancer.

Toyooka *et al.* report an important study on DNA methylation patterns in non-small cell lung cancers and neuroendocrine lung tumors (small-cell type cancer and bronchial carcinoids). They note that these methylation patterns in the neuroendocrine tumors are very different from the non-small cell lung carcinomas. They also note that, in comparison to lung tumors taken directly from patients, in general, tumor cell lines appear to be appropriate models to study aberrant DNA methylation. These studies define new targets for both treatment and prevention (or for the treatment of very early cancer).

Finally, Shain and Dalton treat us to a review that brings us up to date on how contact between a cancer cell and its extracellular matrix can yield *de novo* multidrug resistance. The review presents several new ideas for targeting this important clinical problem.

In summary, *MCT* spans a broad area of interests. Our editorial team hopes that you will find the studies in this inaugural issue of interest and useful in your work in finding new ways of preventing and curing cancer.

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