PEOPLE

Douglas Hanahan, PhD, director of the Swiss Institute for Experimental Cancer Research in Lausanne, received the American Association for Cancer Research (AACR) Award for Lifetime Achievement in Cancer Research in April at the organization's Annual Meeting in San Diego, CA. The award honors his pioneering and lasting contributions to the cancer research community, such as the development of one of the first transgenic mouse models of cancer. In addition, Hanahan has made groundbreaking contributions to the understanding of autoimmunity and tumor microenvironment, and helped establish the field of tumor angiogenesis.

Webster K. Cavenee, PhD, director of the Ludwig Institute for Cancer Research in San Diego and distinguished professor at the University of California, San Diego, received the AACR Margaret Foti Award for Leadership and Extraordinary Achievements in Cancer Research. Cavenee's pioneering work in retinoblastoma provided indisputable evidence for the existence of tumor suppressor genes in humans. He has also made key contributions to understanding the biology of glioblastoma multiforme, illuminating the molecular mechanisms that drive the growth, migration, and survival of tumor cells and identifying potential new therapies for the disease.

University of Alabama Birmingham

Boris Pasche, MD, PhD, began his new position as director of the Comprehensive Cancer Center at Wake Forest Baptist Medical Center in Winston-Salem, NC, on March 1. Prior to joining Wake Forest, he was a professor of medicine and served as director of the division of hematology/oncology at the University of Alabama Birmingham. As a researcher, he has focused on the role of the TGF-β pathway in cancer development and progression.

Technique Helps Target microRNA

Researchers at The Scripps Research Institute's (TSRI) Jupiter, FL, campus have successfully used a drug-discovery technique based on human sequence data to identify a lead drug compound that selectively targets RNA associated with cancer.

"For the first time, we've been able to take the products of genetic material and, in a rational way, design small molecules that precisely target a cancer-associated microRNA," says Matthew Disney, PhD, associate professor at TSRI and lead author of the study, reported online in February (Nat Chem Biol 2014;10:291–7).

Disney's team developed a technique, dubbed Inforna, to identify therapeutic small molecules based on RNA sequence information. Then, in the current study, they screened millions of potential precursor microRNA–drug interactions and designed 27 compounds that target disease-associated microRNAs.

The most active interaction was between the compound benzimidazole, which has antiparasitic and antifungal properties, and microRNA-96, which represses the forkhead family transcription factor FOXO1, inhibits apoptosis, and is associated with metastatic breast cancer, Disney says. Benzimidazole upregulated FOXO1 in cancer cells and induced apoptosis.

"The selectivity of the small molecule was very surprising to us," says Disney. "Known chemotherapy drugs like cisplatin [Platinol-AQ; Bristol-Myers Squibb] and chlorambucil [Leukeran; Aspen Global] often act indiscriminately on healthy and diseased cells and don't target biomolecules specific to cancer, whereas this molecule appeared to be very selective for a microRNA that is contributing to cancer."

The next step for researchers is testing the efficacy of microRNA-targeting compounds in animal models, Disney says.

The current method of targeting microRNAs is to use oligonucleotides, which generally are not cell permeable and may cause nonspecific immune effects, says Disney. The Inforna technique may allow identification of small-molecule lead compounds that specifically target disease-associated RNAs without the disadvantages of oligonucleotides.

The Inforna technique has far-reaching implications, Disney says, and could lead to new drugs targeting any disease-associated RNA molecule.

"In the case of a hepatitis or human immunodeficiency virus that's resistant to chemotherapeutics, potentially you could use Inforna to design small molecules that specifically target and modulate mutated viral RNAs to be a potential therapy," he explains.

"We're trying to broadly use this as a technological platform where one could target any RNA from sequence," he continues. "That could allow us to make a chemical probe to help study the function of these RNAs." ■

Researchers Identify Stem Cell Origin of AML

For most patients with acute myeloid leukemia (AML), the disease seems to arise suddenly, with no previous indication, raising questions about its origin and evolution. Researchers have now identified ancestral pre-leukemic hematopoietic stem cells (HSC) that may give rise to the disease.

These ancestral stem cells are present at diagnosis, can survive chemotherapy, and persist in the bone marrow, potentially leading to disease recurrence, according to a report published in February (Nature 2014;506:328–33). These observations may lead to the identification of pre-leukemic HSCs in healthy individuals, and the HSCs may be viable targets for intervention.

John E. Dick, PhD, a researcher at the Princess Margaret Cancer Centre in Toronto and the University of Toronto in Canada, and his colleagues sequenced 103 commonly mutated leukemia genes in 83 patients. In roughly 25% of the samples, they identified mutations in the *DNMT3A* gene in the AML cells. The researchers found another well-known leukemia mutation in *NPM1c*, which occurred in 88% of the samples that carried mutations in *DNMT3A*.

However, the analysis turned up an unexpected surprise: T cells in 15 patients also contained the *DNMT3A*