Scientist helps revisit 'Hallmarks of Cancer'

March 16 2011, by Nicole Giese

Renowned cancer researchers Robert Weinberg, a Founding Member of Whitehead Institute, and Douglas Hanahan, Director of the Swiss Institute for Experimental Cancer Research (ISREC) have updated their seminal review, "Hallmarks of Cancer," which has influenced the study of cancer and the development of therapeutics for more than a decade.

Published in January 2000, their original work, which codified the traits that all cancers have in common, would go on to become the most-cited article ever to appear in the journal Cell. Their new paper, "Hallmarks of Cancer: The Next Generation," incorporates information gleaned from the past eleven years of cancer research. This latest review, found in a recent edition of Cell, is expected to have a similarly profound impact on the study of cancer and the quest for approaches to treat it.

Cancer is a large class of very different diseases, all of which grow uncontrollably and have the ability to spread, or metastasize, throughout the body. Thousands of studies annually try to decipher these diseases and produce immense datasets that are not necessarily applicable across the constellation of cancers. To help researchers develop a functional framework for cancer as a whole, the first article distilled all of the existing research to describe six fundamental characteristics of cancer.

"In this way, the original review has been highly influential to a generation of scientists both in and outside of the cancer field," says Robert Kruger, Deputy Editor of Cell. " It is indeed rare to go to a scientific meeting on cancer and not see the figures from the review presented in the introductory slides of researchers' talks."

"The six organizing principles we proposed in the year 2000 have found, I would say, rather wide acceptance," says Weinberg, who is also a professor of biology at Massachusetts Institute of Technology. "Having gone back and critically examined them, we were most reassured that they still seemed to be robust; we had converged on fundamental principles that to this day seem to be essential to the process of creating cancer."

The original six hallmarks are: self-sufficiency in growth signals, insensitivity to anti-growth signals, tissue invasion and metastasis, limitless replicative potential, sustained angiogenesis (blood vessel growth), and evasion of apoptosis (cell death). In the updated version, the authors refined these hallmarks using information from transgenic animals and biochemical assays that did not exist a decade ago.

Hanahan and Weinberg also added two categories in the update: "enabling characteristics" and "emerging hallmarks.". The two enabling characteristics of cancer-- tumor-promoting inflammation and gene instability and mutation--do not necessarily cause cancer but assist cells in a transition from normal to oncogenic.

Although common characteristics of many cancers, the two emerging hallmarks (reprogramming of energy metabolism and evasion of the immune system) have not been integrated into the canonical six because Hanahan and Weinberg remain unsure whether they are pervasive in all cancers.

In addition to providing a solid basis for cancer research, the hallmarks have served to identify certain cell functions that have become therapeutic targets. However, the utility of such attempts has been limited because tumor cells have demonstrated an ability to develop resistance to drugs that disrupt a single pathway. This adaptability of cancer cells suggests to Hanahan and Weinberg that simultaneous

targeting of two or more hallmark pathways may be a more effective approach to therapy.

"Hallmarks of Cancer: The Next Generation" is the culmination of more than five years of work, so Hanahan says he'd like it to become as useful as the original.

"The hope is that this new iteration will continue that tradition of communicating some of this essence of trying to grapple with the daunting complexity of cancer and to think about it somewhat in a rational way," says Hanahan, who is also a professor at the Swiss Federal Institute of Technology Lausanne (École Polytechnique Fédérale de Lausanne; EPFL). "So I would hope that we would add new concepts and new insights into the foundation that we set in 2000."

More information: "Hallmarks of Cancer: The Next Generation" *Cell*, March 4, 2011.

Provided by Whitehead Institute for Biomedical Research