In search of cancer's common ground: A next-generation view

March 3 2011

Researchers have synthesized the vast literature on cancer to produce a next-generation view of the features that are shared amongst all cancer cells. These hallmarks of the disease provide a comprehensive and cohesive foundation for the field that will influence biomedical researchers in their quest for new cancer treatments.

The review article by Douglas Hanahan of École Polytechnique Fédérale in Switzerland and Robert Weinberg of the Whitehead Institute for Biomedical Research appears in the March 4th issue of *Cell*, a Cell Press publication. The new article updates and expands on the authors' classic review, "Hallmarks of Cancer," the most cited *Cell* article of all time.

"To our knowledge there has been no such synthesis for another disease," Hanahan said. "What was special for cancer was the explosion of knowledge, daunting in its scope and detail, but sufficient in terms of mechanistic pieces of a puzzle, to allow such a formulation."

"Cancer is special because it is, conservatively, more than 100 distinct diseases," Weinberg added. "The question is whether one can find commonalities shared by this motley crew."

The approach, as Hanahan and Weinberg explain it, was to stand back and attempt to produce some overarching conceptual scaffold, imposing some order on the vast and seeming unmanageable flood of observations and conceptual models that had poured out of the cancer field since the discovery of the first oncogene in the 1970s. The original "hallmarks" or

functional abilities that characterize cancer include: 1) self-sufficiency in growth signals, 2) insensitivity to anti-growth signals, 3) tissue invasion and metastasis, 4) limitless replicative potential, 5) sustained blood vessel growth (angiogenesis), and 6) resistance to cell death.

As the new work details, much has been revealed in the last decade about the molecular and genetic underpinnings of these six original hallmarks. The authors also introduce two enabling hallmarks -- genomic instability and inflammation – and two emerging hallmarks – evasion of the immune system and reprogrammed energy metabolism.

Enabling characteristics set the stage for cancer, Hanahan explained. Genomic instability results in rare mutations that contribute to the regulation or functional mechanics of cancer's acquired capabilities. Inflammation of tumors mistaken for wounds by the immune system brings in wound-healing cells that inadvertently encourage proliferation, angiogenesis, and invasion.

Emerging hallmarks, on the other hand, are features that are beginning to appear as though they may be core features in nearly all cancers based on recent evidence. "While not yet clearly documented to be widespread or ubiquitous in cancers, they may well become so over the coming years," Weinberg said.

Understanding these principles has implications for cancer treatment.

"Drugs targeting each discrete hallmark or enabling characteristic are either clinically approved or are in clinical development, but virtually all show limited benefit due to the development of resistance," Hanahan said. "We pose the reasonable - but far from certain - hypothesis, that by co-targeting multiple hallmarks, drug resistance may be more difficult for a cancer to achieve, thereby producing more enduring clinical benefits for cancer patients."

Ultimately, though, it all comes down to one simple notion: "As before, we believe that there is much to be gained from stepping back and understanding the basic principles of cancer biology rather than burrowing deeply into its myriad details," Weinberg said.

Provided by Cell Press