HALLMARKS OF CANCER: FROM CONCEPTS TO APPLICATIONS

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The hallmarks of cancer constitute an organizing concept that may provide a rational basis for distilling the diversity and complexity of human cancers so as to better understand mechanisms of the disease and its manifestations (Hanahan and Weinberg, 2011). The conceptualization involves eight acquired capabilities – the hallmarks of cancer - and two generic characteristics of neoplastic disease that facilitate their acquisition during the multistage process of neoplastic development and malignant progression. The distinctive and quasi-independent hallmark capabilities consist of sustaining proliferative signaling, evading growth suppressors, resisting cell death, enabling replicative immortality, inducing angiogenesis, activating invasion and metastasis, deregulating cellular energetics and metabolism, and avoiding immune destruction. The principal facilitators of their acquisition are genome instability with consequent gene mutation, and tumor-promoting immune inflammation. The integration of these hallmark capabilities in symptomatic disease involves multiple cell types populating the tumor microenvironment, including heterogeneous populations of cancer cells, in particular cancer stem cells, and three prominent classes of stromal support cells – angiogenic vascular cells, cancer associated fibroblasts, and infiltrating immune cells. Notably, these stromal cells populating the tumor microenvironment have the demonstrated capacity to contribute to seven of the eight hallmark capabilities (Hanahan and Coussens, 2012). Thus, while the functional contributions of stromal cells and their pathologic importance will likely vary between different cancers and indeed at different stages of tumorigenesis and tumor progression, the evidence is clear that a sole focus on the transformed cancer cell (and its genome) cannot fully inform us about mechanism of the disease. One premise, to be discussed in this keynote lecture, is that the hallmarks of cancer may prove to be a useful heuristic tool for designing innovative new mechanism-guided (hallmark-targeting) therapeutic approaches for cancer treatment. A second premise to be considered in depth throughout this conference, is that the ability to image the hallmarks of cancer will likely prove to be instrumental in assessing the prominence of particular hallmarks in different types and subtypes of human cancer, and to monitor hallmark changes in response to therapy, to reveal both efficacy and direct/indirect forms of adaptive resistance.

References: 1) Hanahan, D., & Weinberg, R.A. (2011). Hallmarks of cancer: the next generation. Cell 144: 346-674. 2) Hanahan, D. & Coussens, L.M. (2012). Accessories to the crime: functions of cells recruited to the tumor microenvironment. Cancer Cell. 2012 Mar 20;21(3):309-22.