

Cancer rearranges the rules in tissue building blocks. A new class of targets for therapy?

Garry P. Nolan, PhD, Rachford and Carlota A. Harris Professor, Department of Pathology, Stanford University School of Medicine, Center for Clinical Science Research

High parameter single cell analysis has driven deep understanding of immune processes. Using a next-generation single-cell “mass cytometry” platform we quantify surface and cytokine or drug responsive indices of kinase target with 45 or more parameter analyses (e.g., 45 antibodies, viability, nucleic acid content, and relative cell size). Similarly, we have developed two advanced technologies termed MIBI and CODEX that enable deep phenotyping of solid tissue in both fresh frozen and FFPE formats (50 – 100 markers). Collectively, the systems allow for subcellular analysis from the 70nm resolution scale to whole tissue in 3D.

I will present evidence of deep internal order in immune functionality demonstrating that differentiation and immune activities have evolved with a definable “shape”. Further, specific cellular neighborhoods of immune cells are now definable with unique abilities to affect cellular phenotypes—and these neighborhoods alter in various cancer disease states. In addition to cancer, these shapes and neighborhoods are altered during immune action and “imprinted” during, and after, pathogen attack, traumatic injury, or auto-immune disease. Hierarchies of functionally defined trans-cellular modules are observed that can be used for mechanistic and clinical insights in cancer and immune therapies.