Quantitative medicine for breast cancer patients

Charles M. Perou, Ph.D.
The May Goldman Shaw Distinguished Professor of Molecular Oncology
Co-Director of the UNC Computational Medicine Program
Professor in the Department of Genetics
Lineberger Comprehensive Cancer Center
University of North Carolina at Chapel Hill
North Carolina, U.S.A.

Gene-expression profiling has had a considerable impact on our understanding of breast cancer biology and clinical care. During the last 20 years, 5 intrinsic molecular subtypes of breast cancer (Luminal A, Luminal B, HER2-enriched, Basal-like and Normal-like), and a rare subtype with features of stem cells (Claudin-low), have been identified and intensively studied. The PAM50 subtyping assay provides important information within Hormone Receptor (HR)-positive breast cancer patients, where the Luminal A and B subtypes represent the majority of cases. Compared to Luminal A, Luminal B tumors are characterized by higher expression of proliferation/cell cycle-related genes and lower expression of several ER-regulated genes such as the progesterone receptor. The Luminal A vs B distinction, together with tumor size, is encompassed with the “PAM50 ROR Score”, which quantitatively predicts recurrence, and thus can inform decision making concerning the length of endocrine therapy treatments (i.e. 5 years vs 10 years).

In addition, genomic predictors of chemotherapy benefit for TNBC, and predictors of trastuzumab benefit for HER2+ patients, typically identify immune cell features as positive predictors of response, thus highlighting the importance of the microenvironment in response and survival. In particular, IgG/B-cell signatures were significantly associated with better metastasis-free survival. Overall, these data suggest that intrinsic molecular profiling, plus measures of the microenvironment focused on immune cells, can provide clinically relevant information beyond current pathology-based classifications.