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Analysis of Immune microenvironment in breast cancer by utilizing tissue microarray and computerized image analysis techniques.

Abstract

Breast cancers are considered to be less immunogenic as compared to some other cancers, but now the role of immunity has emerged during the last decade. Subtyping of tumour infiltrating lymphocytes (TILS) requires the use of several markers along with a routine breast panel of markers which includes estrogen receptor, progesterone receptor and her2 neu, thereby limiting the amount of tumour tissue.

Tissue microarray (TMA) is a recent innovation on field of pathology which allows the analysis of small representative tissue samples from hundreds of different cases assembled on a single histologic slide, allowing high throughput analysis of multiple specimens at the same time. It can permit simultaneous analysis of molecular targets at the DNA, mRNA, and protein levels under identical and standardized conditions. However, this technique is still not very commonly used in routine practice.

Estimation of TILS is crucial to understand different physiological and pathological conditions as well as effects of different immunotherapeutic interventions. Immunohistochemistry has been the standard method for evaluation of immune cell infiltration. Quantification of immunohistochemistry has traditionally been performed by manual counting or semiquantitative scoring which in time consuming, observer dependent and area cannot be estimated. The use of computerized digital image analysis (CIA) has made it possible to quantify larger samples of tissue in a more time-efficient and unbiased way.

However, this requires proper training on core concepts from image acquisition to image filtering, and segmentation is required to help tackle image analysis workflows. Emphasis on good practices and typical pitfalls in image analysis is equally essential. In recent years, digital pathology has received increasing attention. However, despite successful standardization efforts, visual assessment requires extensive training by pathologists. Automated image analysis methods can help improve quantification accuracy, save time and facilitate the analysis of more complex spatial patterns and provide standardized metrics for rigorous validation by expert pathologists and quality assurance through regulatory agencies.

Therefore, in addition to TIL detection through morphological (H&E) features, subtyping of TILs through immunohistochemistry or more advanced multiplex imaging approaches may become necessary and will also require adequate image analysis strategies.

Hence with the help of this fellowship my primary aim to study immune environment in breast cancer by using immunohistochemical markers on tissue microarrays along with the analysis of various sub-types of infiltrating immune cells using Computerized image analysis.