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ASO Author Reflections: "From Computer to Bedside" – A New Translational Approach to Immunogenomics

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Past:

There have long been intensive efforts to better understand how immune cells recognize and attack cancer cells in vivo. One of the early discoveries was made by William B. Coley, who reported the regression of certain sarcomas upon introduction of heat-killed streptococcal bacteria (Coley's toxin) [1]. This was the initial conceptualization of using the body's native inflammatory and immunologic responses as potential treatments for cancer. Burnet and Thomas subsequently proposed the cancer immunosurveillance theory that malignant cells frequently arise as the result of genetic abnormalities, but are typically recognized and eliminated by the immune system [2]. Advancement of the field of cancer immunology was put on hold for decades as a result of negative reports. However, during the 1990s, the cancer immunosurveillance theory was proven in animal models due to the advancement of molecular techniques. Further molecular mechanisms of cancer immunosurveillance have been gradually elucidated in humans with identification of human cancer antigens.

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Present:

Today, the molecular mechanisms of cancer immunosurveillance have been classified as cancer immunoediting. In solid tumors, the relationship between tumor infiltrating lymphocytes (TILs) and neoadjuvant chemotherapeutic response has been determined utilizing immunohistochemistry and flow cytometry techniques. Higher quantity of intra-tumoral TILs has also been reported to associate with improved patient outcomes. Improvements in genomic sequencing technologies and data analysis have led to the advancement of the field of immunogenomics. This approach clarifies the tumor immune microenvironment at the genomic level. Some techniques include: computational biological algorithms that estimate the quantity of tumor infiltrating immune cells from gene expression levels within a tumor sample as well as algorithms that estimate the T-cell receptor repertoire from RNAsequencing data.

Future:

Recently a scoring system (the immune Cytolytic Activity Score (CYT) was developed which reflects cancer immune responses at a molecular level via comprehensive analysis of gene expression data [3]. Our group aimed to utilize cutting-edge computational biological algorithms [4] to analyze immunogenomic data gleaned from the tumor immune microenvironment and correlate it with clinical outcomes. We found that CYT strongly associated with colorectal cancer immune responses as well as with survival [5]. One of the advantages of this bioinformatics approach compared with gold standard techniques such as flow cytometry, is its ability to use the same tumor sample to analyze gene expression as well as to generate an immune cell profile; thereby, avoiding the bias of tumor heterogeneity. We expect that molecular mechanisms of cancer immune responses may be further clarified by this bioinformatics immunogenomics approach, leading to the further discovery of therapeutic targets which may have a positive clinical impact on patient outcomes. Thus, in contrast to the “bench to bedside” methodologies which have been used up till the present, we propose that from “computer to bedside” will be the future of translational research.

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