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Novel approaches based on immune checkpoints for cancer immunotherapy

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Introduction: Cancer immunotherapy is one of the best therapies compared to traditional therapies that may cause potential toxicities such as chemotherapy and radiation. The potential use of immunotherapy is to restore the immune system of patients in attempt to stimulate it to reject and destroy cancer cells. With the recent approval of the monoclonal antibodies against CTLA-4 and PD-1 for the treatment of melanoma, renal carcinoma cancer and non-small cell lung have attracted wide interest for strategies that enhance T-cell-mediated response against cancer. A complex network of biological pathways governs interactions between the immune system and cancer cells. The balance of signaling via co-inhibitory or co-stimulatory molecules expressed on T cells has demonstrated to be a powerful approach to intensify antitumor immune responses. This approach has been used effectively for the generation of a new class of anticancer therapies called checkpoint-blocking antibodies. Exploiting on the success of CTLA-4 blockade, agents that target a second co-inhibitory receptor, PD-1 (Programmed cell death protein 1), or its ligand, PD-L1, are in clinical development.

Research: The presence of several inhibitory pathways that block T cell responses offers particular strategies for mobilizing the immune system to attack cancer cells.There are some strategies to modulate the microenvironment - targeting regulatory cells, blocking differentiation or recruitment, blocking immunosuppressive enzymes, regulatory cell depletion, re-programming immunosuppressive cells, modifying the chemokine and cytokine profile are some examples. The attractively of new strategies for immunotherapy is driven by immune response and microenvironment discovery.Usually, scientists have relied on conventional laboratory research tools to identify several biomarkers, for example, altered genes transcription factors changes in mRNA and protein expression. To put these cancer biomarkers in the context the researchers can use several strategies to find a good parameter to take care of patient and drug development.As more and more immunotherapies are made available, the overall goal will be to screen patients and determine which of the immunotherapies will be more effective for each cancer type and each patient, including the analysis of new immune cell population.

Results: Currently there are several Clinical Trials across more than 20 different cancers including, melanoma, ovarian, prostate, breast, lung, gastric, kidney, bladder, cervical, anal, colorectal and pancreatic cancers, as well as in leukemia, lymphoma, sarcoma and glioblastoma. Inhibitory molecules like CTLA-4, PD-1, LAG-3, TIM-3, VISTA and BTLA besides co-stimulatories molecules such as ICOS, OX40 and 4-1BB are potent agents for combination therapy in order to improve antitumor responses.The analysis of tissue and blood samples from cancer patients is being conducted with new technologies as Flow Cytometry (FACS) and mass cytometry (Cytof). Here, we will share some strategies in order to pursuit molecules that could help us to better understand cancer immunotherapy responses.

Conclusion: A harmonized struggle to assess the value biomarkers that address different aspects of the cancer-immunity cycle in T cell checkpoint blockade will allow us to integrate information on individual aspects of tumor-immune interaction.

Biography:

Dr. Jorge Augusto Borin Scutti is currently Research Scientist of Immunotherapy Platform (Immunology Department) at the MD Anderson Cancer Center (Houston-Texas). As Research Scientist hisworks focuses onanalyzing the activity of innate and adaptive cell populations like T cells, B cells, tumor cells, Myeloid Derived Suppressor Cells (MDSC) and Natural Killer (NK) cells that are critical on immune response against cancer and then might regulate positively or negatively T-cell responses.Dr. Scutti earned his Master and PhD in Microbiology and Immunology Department at Federal University of São Paulo (UNIFESP) working on cancer vaccines and peptides derived proteins to stimulate immune system against melanoma. Postdoctoral at MD Anderson Cancer Center (MDACC) - Pediatrics Department, where he began evaluating pediatrics cancer - DIPG (Diffuse Intrinsic Glioma Pontine) its microenvironment, Natural killer cells and histone deacetylase inhibitors (iHDAC) as cancer immunotherapy tool. Experience in cancer immunology and immunotherapy in experimental studies and clinical research.