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Session Topic : Gene Therapy / RNA Therapy

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Polysaccharide-Based Nano-PAMP Strategy for mRNA Cancer Vaccine Development

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Effective immunotherapy largely relies on the cytotoxic T lymphocytes (CTLs)-mediated elimination of cancer cells, for which the type, density, and location of CTLs in tumors determine clinical outcome. Tumors can be classified as "HOT" vs. "COLD" phenotype based on CTLs status; hot tumor is characterized by high number of CTLs in the proximity to cancer cells whereas cold tumors have few or no CTLs. Hot tumors with pre-existing CTLs are consequently more susceptible to immunotherapies, showing favorable clinical response in multiple cancers. Tumors develop physical and chemical barriers against antitumor functions of CTLs, by fostering immune-resistant tumor microenvironment (TME) that exhibit inter- and intra-tumor heterogeneity at multiple levels. Therefore, it is necessary to disrupt the immune-resistant TME to exploit the full therapeutic potential of CTLs against tumors, but such heterogeneity and complexity of TME poses numerous challenges for the field to overcome. In this talk, a new paradigm of cancer treatment with emphasis on a personalized cancer vaccine will be introduced and messenger RNA (mRNA) will be highlighted as a next generation therapeutics beyond vaccine platform. Then various immunoengineering strategies to manipulate antitumor T cells in TME will be introduced; 1) peptide-based neoantigen cancer vaccine development; 2) messenger RNA (mRNA)-based cancer vaccine development; 3) in situ vaccination strategies - photothermal therapy-induced immunogenic cell death, and mannan-based nano-PAMP to elicit anti-tumor T helper 17 (Th17) immune response in local tumors. The unique and highly multidisciplinary biomaterials-based tools and approach to precisely modulate immune responses are widely applicable to other diseases including autoimmunity, gut microbiome modulation, inflammation, and infectious diseases.

Keywords: Cancer vaccine, mRNA , Nanoparticle, Cancer immunotherapy, Polysaccharide Mannan