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The tumor immune microenvironment as a target for nano-therapies and patient-tailored treatments.

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Abstract

Cancer is a complex illness with local to systemic expression. Cancer cells in relation with the constitutive components of the tissue from which they develop and the immune system elements, that interact with them to ablate the cancer cells and promote tissue repair, form the tumor microenvironment. The interactions between all these elements decide the tumor evolution either toward its elimination (inflammation, immune recognition and direct cytotoxicity) or its establishment and progression (inversion of the immune response, chronic and smoldering inflammation, immune cell exhaustion and establishment of an immune suppressive and tissue remodeling environment). The alteration of the tissue collagen scaffold influenced by the immune environment continuous modifications collaborates to impede adequate access to immune cells and drugs and solicitate epithelial to mesenchymal transition allowing metastatic cell behavior. Under these conditions, the altered immune environment can bias the efficacy of the treatments and favor the tumor heterogeneity. Many therapeutic approaches were developed, from surgery to chemo- and radiotherapy until the recent advances in immunotherapy. However, if the therapeutic approach is systemic, sensible side effects can accompany the treatment because of the involvement also of non-tumoral tissues. Therefore, from the last years of the XX century, a progressive interest and improvement in technical possibilities started to focus on targeting therapies using monoclonal antibodies (e.g. against cellular pathways, growth-factors, immune check-point molecules) and/or organic/inorganic nano-constructs (e.g. ferritin-based, iron-based nanoparticles) studied for directly affect the cancer cells or other microenvironment components (immune cells). Focusing the intervention to the pathological component and selectively foster the anticancer response is the aim of modern oncology. In this presentation, we will highlight some of our observations done on components of the microenvironment favoring the tumor escape and our experience of tumor targeting by nanoparticles in experimental models looking to achieve more tumor and antigen specific treatments for enhancing the anti-cancer immune response, possibly with a patient-tailored approach.