Microbiota Modulation: A New Breakthrough in the Understanding of Tumor Progression in HGSOC.

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Ovarian cancer is the fifth cause of cancer deaths among women, and has the highest mortality rate among all gynecologic cancers. Most patients are diagnosed in late stages of disease, due to nonspecificity of initial symptoms and inefficiency of current screening biomarkers. The most frequent and aggressive types of ovarian cancer are usually associated with hypoxia and expression of chemotactic factors — as the CCL28 chemokine, leading to the recruitment of Treg cells, and impairment of the immune system. Therefore, the constitution of the immune cell infiltration into the tumor site correlates with clinical outcomes, but the mechanisms underlying these observations are unclear.

The immune system function is profoundly shaped by the gut microbiota. Microbial surface antigens and their metabolic products can trigger down-stream pathways resulting in the activation of immune cells and the production of cytokines, that can play both pro and anti-inflammatory roles. Here, we hypothesized that the gut microbiota can act as a modulator of anti-tumor immune response affecting tumor progression in ovarian cancer tumor models. C57/BL6 mice with the same genetic background but bred in different environments (Jackson and Harlan Laboratories) harbor distinct microbiota; previous results from our lab demonstrated that they also have singular baseline immune status that correlate with their microbiome.

There is evidence that the bacterial contents differentially affect tumor progression following inoculation with ID8CCL28 tumor cells in vivo. We determined that not only differences in baseline microbiome but also dysbiosis, induced by different antibiotics treatments, can be one of the mechanisms shaping the tumor inflammatory environment (ascites), and dictating the magnitude of tumor proliferation in vitro. This study introduces microbiome modulation as a new piece in the understanding of carcinogenesis, suggesting that, in the future, microbial signatures can possibly act as biomarkers with screening, therapeutic or prognostic values.

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