The role of microbiota in driving castration-resistant prostate cancer.

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Background: Prostate cancer cells depend on the tumor microenvironment, suggesting that tumor cell-extrinsic mechanisms might control prostate cancer progression and the emergence of therapy resistance. The microbiota is the ensemble of the microorganisms living in symbiosis with the host and is fundamental in shaping systemic immune responses. To date limited knowledge is available regarding intestinal microbiota alterations in prostate cancer and possible implications for the disease. Over the last years the microbiota has taken the stage and its role in the physiopathology of cancer as well as in the modulation of the effectiveness of anti-cancer treatments and infiltrating immune response are now established. Moreover, interventions aimed at manipulating the intestinal microbiota are being translated to the clinics with promising results. However, studies addressing the alterations of the intestinal microbiota in castration resistant prostate cancers (CRPC) as well as their functional implication in disease progression are still missing. Our aim is to fill this hole with the intent of finding therapeutic strategies based on the intestinal microbiota to be coupled with the standard of care therapies for CRPC.

Methods: To address this clinical need and its related biological questions we relied on several castration resistant prostate cancer mouse models and human specimens. We analyzed the gut microbiota by 16S ribosomal gene sequencing and characterized the immune response in the tumor, in secondary lymphoid organs and in the intestine by multiparametric flow cytometry.

Results: We identified the composition of the gut microbiota in animals and patients affected by CRPC compared with subjects affected by castration sensitive prostate cancer. In parallel, we provided a comprehensive characterization of the immune response in the tumor and in the intestine of mice harboring different microbiota composition.

Conclusions: Our study has the ambition to shed light on a novel and until now neglected component that plays a role in driving castration resistance, opening the way to novel therapeutic opportunities that could act as adjuvants of the current standard therapies. Moreover, we aim at identifying new prognostic markers that can predict the response to androgen deprivation therapy in patients. So far, we reported significant compositional differences in the gut microbiota in prostate cancer patients responding or not to androgen deprivation therapy and we have identified the microbial signature of CRPC patients.

Conflict of interest: None

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