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LOCOREGIONAL TREATMENT OF PERITONEAL METASTASIS; ABSTRACT

Peritoneal metastasis (PM) is an advanced stage of cancer disease arising from different gastrointestinal tumors such as colon cancer, rectal cancer, gastric cancer and also gynecological tumors such as ovarian cancer. The treatment options range from systemic chemotherapy to a locoregional treatment including the resection of the macroscopic tumor lesions on the peritoneum followed by the application of hyperthermic intraperitoneal chemotherapy (HIPEC). After recovery, these patients are also treated with systemic chemotherapy. Only few patient with limited peritoneal disease qualify for such an invasive and radical treatment. Interestingly, some patients treated with this radical procedure present with a unexpected long-term disease-free survival of several years, suggesting a certain immune control of the PM lesions. Furthermore, the role of CD 8+ T-cells in controlling primary colon cancer is already known and described, but how PM lesions from colon cancer are controlled by the immune system isn`t investigated in depth. The peritoneal cavity might have its own microenvironment and treatment related changes need to be further explored. We are therefore interested in understanding the locoregional treatment effect on PM lesions and the anticancer immune response. To investigate treatment related effects on the immunogenicity of cancer cells and the functional consequences on the specific immune system, we have established the locoregional treatment on 2D cancer-cell lines and patient-derived organoid (3D culture) and established the PM mouse model and its locoregional treatment. The locoregional treatment, applied in HIPEC condition, resulted in the upregulation of certain cancer -testis antigens (CTAs), which could be confirmed on patient-derived organoids from PM lesions. The CTA expression profile is individual and doesn`t seem to depend on the location of the metastasis. The application of a single dose chemotherapy intraperitoneal in the murine PM model already shows reduced tumor load and the infiltration of CD 8 + T-cells. The functional contribution of these CD 8 + T-cells to the tumor control and their antigen specificity need to be elaborated in further experiments. The results gained so far give evidence, that the locoregional treatment changes the immunogenicity of PM cancer cells and attracts CD 8+ T-cells into the PM lesions.

A further project also includes the determination of CD 8 + T-cells in PM lesions from human patients with a colorectal primary tumor. The frequency and distribution of the CD8+ T-cells within the peritoneal lesion will be compared with its primary tumor from the same patients. Further correlation to disease-free and overall-survival are possible extensions.

SPECIAL TECHNIQUES AND EQUIPMENT

Peritoneal metastasis mouse model, locoregional treatment in mice including HIPEC application, PM patient-derived organoid treatment, PM patient tumor and serum samples