GiC XXXIX WEB CONFERENCE 14 - 18 GIUGNO 2021
CONFERENZA NAZIONALE DI CITOMETRIA
AGGIORNAMENTI E INNOVAZIONI DELLA CITOMETRIA NELLE APPLICAZIONI CLINICHE E DI RICERCA

DEVELOPMENT OF EXHAUSTION AND ACQUISITION OF REGULATORY FUNCTION BY INFILTRATING CD8+CD28- T LYMPHOCYTES DICTATE CLINICAL OUTCOME IN HEAD AND NECK CANCER

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Introduction. CD8+ T lymphocytes are among the immune cells reputed to kill tumor cells. Head and neck squamous cell carcinoma (HNSCC) has a poor clinical outcome despite the presence of a rich CD8+ T cell tumor infiltrate. This may be due to alterations of tumor infiltrating CD8+ T cells. Here, we performed a characterization of infiltrating CD8+ T cells in a cohort of 30 HNSCC patients.

Methods. Blood and tumor biopsies from untreated HNSCC patients were evaluated by multicolor flow cytometry to delineate: CD4+ and CD8+ T cell maturation, frequency of CD4+ and CD8+ T regulatory cells (Treg), expression of immune checkpoints (CD39, PD-1, CTLA-4, TIM-3). Combination of traditional analysis and computational tools based on particular algorithms (i.e., t-SNE) have been used to dissect the complexity of the data.

Results. The results showed that differential intratumoral frequency of CD8+CD28+ T cells, CD8+CD28- T cells, and CD8+CD28-CD127-CD39+ Treg distinguished between HNSCC patients who did or did not respond to treatment. Moreover, we identified an intratumoral CD8+CD28- T cell subpopulation, which expressed markers of both exhausted (i.e., with impaired effector functions) and regulatory (i.e., exerting suppressive activities) cells. This suggests that in HNSCC effector T cells progressively undergo exhaustion and acquisition of regulatory properties, hampering their anti-tumor functions.