LECTURE SERIES & WORKSHOPS 2021

CANCER RESEARCH

LUXEMBOURG INSTITUTE OF HEALTH
RESEARCH DEDICATED TO LIFE

UNIVERSITÉ DU LUXEMBOURG

22

April 2021
Thursday

WEBINAR
via Webex*
45' *(talk)* + 30' *(discussion)*

11.00am - **12.15**pm

8 9 10 11 12 1 2 3

Role of stromal heterogeneity in metastatic spread and immunotherapy resistance in cancer

ABSTRACT

Cancer Associated Fibroblasts (CAF) constitute one of the most abundant stromal components in solid tumors. By combining various approaches and CAF markers, we identified 4 CAF subsets (CAF-S1 to CAF-S4) in breast and ovarian cancers (Costa, Cancer Cell, 2018; Givel, Nat. Commun, 2018). Two myofibroblastic CAF subsets CAF-S1 (FAP+ SMA+ MCAM-) and CAF-S4 (FAP- SMA+MCAM+) accumulate strictly in cancer, while the two others are also detected in normal healthy tissues. CAF-S1 and CAF-S4 display pro-metastatic functions through complementary mechanisms (Pelon, Nat. Commun, 2020; Bonneau, Breast Cancer Res., 2020). In addition, CAF-S1 promote immunosuppression through a multi-step mechanism. Indeed, CAF-S1 attract CD4+CD25+ T lymphocytes, enhance their survival and stimulate their differentiation into CD25HighFOXP3High regulatory T cell (Tregs) (Costa, Cancer Cell, 2018; Givel, Nat. Commun, 2018). By using single cell technology on more than 19,000 single CAF-S1 fibroblasts from breast cancer and demonstrated that the CAF-S1 subset is heterogenous and composed of 8 cellular clusters. We validated the five most abundant clusters by flow cytometry and in silico analyses in other cancer types, highlighting their relevance. Myofibroblasts from clusters 0 and 3, characterized by extracellular matrix proteins and TGFβ signaling, respectively, are indicative of primary resistance to immunotherapies. Cluster 0/ECM-myCAF upregulates PD-1 and CTLA-4 protein levels in Tregs, which, in turn, increases CAF-S1 cluster 3/TGFβ-myCAF cellular content. Thus, our study highlights a positive feedback loop between specific CAF-S1 clusters and Tregs and uncovers their role in immunotherapy resistance (Kieffer, Cancer Discovery, 2020).

SPEAKER

Dr Fatima MECHTA-GRIGORIOU

Research Director of Exceptional Class (DRE) – Inserm
Scientific Director of the Cancéropôle Ile de France
Deputy Director of the "Genetic and Biology of Cancer" Unit, U830 Inserm
Director of the "Stress and Cancer" laboratory - Institut Curie, Paris

HOST:
Department of Oncology (LIH)

RESPONSIBLE LIH SCIENTISTS:
Elisabeth Letellier / (elisabeth.letellier@uni.lu)
Bassam Janji / (bassam.janji@lih.lu)

www.lih.lu
www.uni.lu

Supported by:

Fonds National de la Recherche Luxembourg

***To join the Webinar:**

JOIN

Event number: 183 749 6048
Event password: zpBsVK37hU6