

Poster Abstract Submission

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| Name | Rania Faouzi Zaarour |
| Position | Assistant Professor and Researcher |
| Organization | Gulf Medical University, Thumbay Research Institute for Precision Medicine |
| Email | |
| Phone Number | |
| Research Title | Role of the hypoxic secretome in inducing stemness and cell survival in normoxic lung cancer cell lines |

Abstract:

Role of the hypoxic secretome in inducing stemness and cell survival in normoxic lung cancer cell lines
Authors: Rania Faouzi Zaarour¹, Maisa Ribeiro¹, Salem Chouaib ^{1,2} ¹ Thumbay Research Institute for Precision Medicine, Gulf Medical University, Ajman, United Arab Emirates. ² INSERM UMR 1186, Integrative Tumor Immunology and Immunotherapy, Gustave Roussy, Faculty of Medicine, University Paris-Saclay, Villejuif, France. Hypoxia one of the main features of solid tumors induces signaling that promotes tumor cell survival, invasion, and metastasis. The role of hypoxia inducible factor (HIF) signaling in inducing cancer stem cells (CSC) quiescence and reawakening and its effects on the secretome of cancer cells is not fully understood. Evidence suggests that one of the major barriers limiting the efficacy of immunotherapy seems to coalesce with the hypoxic tumor microenvironment (TME). Several secreted factors modulate the behavior of the tumor and neighboring cells within the TME, which then determine tumor progression, malignancy, immune and drug resistance. In addition, cancer stem cells could release cellular cargo in the form of extracellular vesicles that can influence neighboring cells, promote cancer survival, and impair natural killer cells mediated cytotoxicity. Finally, quiescence and immune escape are emerging features of at least some CSCs, indicating significant overlap between dormant cancer populations and CSCs. Here, we are investigating the effects of the hypoxic secretome on the promotion of epithelial-mesenchymal transition (EMT) and cancer stem cells in cells grown in normoxia. We first confirmed that gene expression of the secretory machinery and exosome markers are upregulated in hypoxia exposed lung cancer cell lines. Interestingly, hypoxia conditioned media resulted in an increase in these markers in cells grown under normal oxygen tension. Preliminary data further indicated an increase of cancer stemness, EMT and inflammatory markers in response to the hypoxia conditioned media. The putative association of the pathways required for these secreted factors including HIF-1 α and autophagy as well as the influence of hypoxic secretome on cell-mediated cytotoxicity will be discussed. Keys-words: cancer stem cells, tumor microenvironment, cancer cells quiescence, stemnes