ID: 03214

Topic: INNOVATIVE THERAPIES

MV130 as a new innate memory-based mucosae vaccine against cancer

Luna Minute[1] , Laura Bravo[1] , Pablo Mata[1] , Jaime Fernandez[1] , Francisco Javier Cueto[1] , Eduardo Lopez[1] , Carlos Del Fresno[1]

1) Hospital La Paz Institute for Health Research - IdiPAZ

Trained immunity (TI), known as innate immune memory, is described as the ability of innate immune cells of responding to a homologous or heterologous secondary challenge with enhanced proinflammatory response upon the exposure to certain TI-inducing stimuli. The most studied TI-inducers are the BCG vaccine and the fungal ?-Glucan. However, BCG and ?-Glucan have limitation for their clinical application. MV130 is a mucosal immunotherapy based on heat-inactivated bacteria indicated for recurrent respiratory infections. MV130 was demonstrated to induce TI in pre-clinical models against respiratory viruses included Sars-Cov2 or *C. albicans*. However, the role of MV130 in conferring cancer protection is unexplored. We observed that C57BL/6J mice subjected to the prophylactic regimen of six doses of intranasally administered MV130 exhibited delayed tumor development and improved tumor control against subcutaneously injected LLCs (Lewis Lung Carcinoma) cells, administered seven days after the last immunization. The protection is maintained when tumor cells are injected 60 days after the last MV130 administration, indicating that MV130 induces a long-lasting memory, which is a main feature of TI. Furthermore, MV130-treated mice, show protection against orthotopic lung tumors and melanoma spontaneous lung metastasis, as well as a pro-inflammatory lung microenvironment. Upon *ex vivo* heterologous restimulation of MV130-treated lung innate populations, alveolar macrophages, interstitial macrophages and NK cells presented enhanced TNF production, revealing a potentiated response due to TI. Moreover, chromatin remodelling by ATAC-seq confirmed the training on an epigenetic level. scRNAseq from CD45+ cells from tumor-bearing lungs revealed profound modulation of the resident myeloid compartment concomitant with a differential distribution of lymphoid populations in MV130-treated mice. In conclusion, our data indicate that MV130 induces TI in innate immune cells by potentiating a proinflammatory antitumor response, paving the way for the induction of innate memory through mucosae as a novel cancer immnunotherapy strategy.