Background cDC1 cells are a subset of antigen presenting cells highly specialized in cell-associated antigen crosspresentation. The presence of this DC population in human cancer correlates with good patient prognosis and response to immunotherapy. Mice that are ontogenically deficient in cDC1 or crosspresenting mechanisms fail to effectively prime antitumor immune responses and therefore show poor response to immunotherapy. The mechanisms by which cDC1 support immunity during immunotherapy mediated responses have not been well defined.

Methods Using XCR-1-DTR venus mice we were able to track and deplete at will cDC1 cells at different time points during immunotherapy. Tumor growth studies were performed with different types of immunotherapies (adoptive T cell transfer, anti-PD-1, anti-CD13 and anti-CTLA-4 mAbs). Flow cytometry and multiplex immunofluorescence were used to characterize CD8 T cell responses and intravital imaging was used to track the behavior of cDC1 and antitumor CD8 T cells.

Results The presence of cDC1 cells was an absolute requirement at the onset of immunotherapy for most of the therapies tested but once the first dose of immunotherapy their absence had lesser impact on the antitumor response. We observed that immunotherapy affected cDC1 migratory capacities and interaction with anti-tumor T cells and that cDC1 were important to maintain a pool of TCF7+ CD8 cells in the TDLN and to some extent in the tumor preventing T cell exhaustion during immunotherapy.

Conclusions cDC1 presence is important during the onset of various immunotherapies to maintain CD8 T cell stemness and as a consequence to allow tumor rejection. However once immunotherapy has already been established cDC1 requirement is less pronounced.

References


Ethics Approval All animal experimentation have been approved by the institutional animal research ethics committee and the regional government.