

Mouse and human cutaneous squamous cell carcinomas harbor distinct dendritic cell subsets that can be reprogrammed by a local immunomodulatory treatment.

Cutaneous squamous cell carcinomas (cSCC) are invasive epithelial tumors of bad prognosis, difficult to cure with current therapies. Local immunotherapies stimulating the adaptive immunity should improve long-term patient survival without recurrence. Dendritic cells (DC) are critical actors of antitumoral immunity in charge of educating CD4+ and CD8+ T lymphocytes. Mouse and human skins contain ontogenically and functionally distinct DC subsets, including conventional DC1, DC2 and Langerhans cells (LC) as well as monocyte-derived DC. In this report, we have delineated the phenotype and functions of tumor-associated DC subsets using a mouse model of chemical skin carcinogenesis and human cSCC biopsies. We have elucidated the impact of a local immunotherapy on DC functional maturation and antitumoral immunity. We found that mouse and human cSCC are infiltrated by the DC subsets described in the skin but in lower proportions for LC and DC1. In the tumor environment, conventional DC subsets displayed a regulatory phenotype. Surprisingly, tumor-derived migratory DC2 primed tumor antigen-specific CD8 T lymphocytes while tumor-derived migratory DC1 failed to do it contrary to their steady state counterpart. An immunostimulatory local immunotherapy was shown to induce the reprogramming of IL-12 producing tumor-associated DC and the regression of established skin tumors. This treatment discretely modulated the functions of migratory LC and DC1 and strongly increased the functional maturation of conventional DC2 leading to the massive priming of IFN γ -producing and IL17-producing CD8+ T cells. Consistent with these data, this local immunotherapy induced a CD8 memory response that delayed the progression of secondary tumors. These findings underscore the importance of environmental cues on DC functions that might be important for local immunotherapies targeting DC subsets.

Keywords : cutaneous squamous cell carcinoma, dysfunctional dendritic cells, local immunotherapy, DC reprogramming
Authors :
References : , , ,

Authors

Ophélie Vermeulen 1, Pierre Bourdely 1, Franck Bihl 1, Julie Cazareth 1, Belinda Desrues 2, Sokchea Khou 1, Carmelo Luci 1, Gilles Poissonnet 3, Anne Sudaka 2, Véronique Braud 1, Fabienne Anjuère 1,

1. IPMC, Valbonne, FRANCE
2. CAL, Nice, FRANCE
3. IUFC, Nice, FRANCE