Sensory neurons regulate dermal macrophage functions and tissue repair after skin exposure to UV radiation

---
Guillaume Hoeffel1, Guilhaume Debroas1, Rafaelle Rossignol1, Ana Reynders2, Aziz Moqrich2 & Sophie Ugolini1

1Aix Marseille Univ, CNRS, INSERM, CIML, Centre d'Immunologie de Marseille-Luminy, Marseille, France
2Aix-Marseille-Université, CNRS, Institut de Biologie du Développement de Marseille, UMR 7288, Case 907, 13288 Marseille, France

The existence of a bidirectional communication between the nervous and the immune system is now well accepted. Tissue-resident macrophages are key players in tissue homeostasis and highly rely on their niche microenvironment to acquire and sustain their functions throughout the lifespan. In tissue barriers such as the skin, the dense sensory neuron network could provide such signaling to dermal macrophages.

We identified here a particular subset of sensory neurons called low-threshold mechanoreceptor type C (C-LTMR) as crucial in tissue repair after sunburn-like lesion. Depletion of these neurons increased tissue-damage and residual dermal fibrotic scar upon UV irradiation. Exploring the ontogeny of dermal macrophages, we identified that embryonic-derived long-lived macrophages are rapidly outnumbered by monocytes-derived macrophages in UV-irradiated mice. Depletion of sensory neurons increased inflammatory monocyte infiltration concomitantly with a defect in specific anti-inflammatory dermal macrophage subsets. Finally, we identified a particular neuropeptide promoting the anti-inflammatory properties of dermal macrophages. Without this neuropeptide, UV-irradiated skin expresses more IL1β and TNFα during the inflammatory phase. On the other hand, dermal macrophages tend to overproduce TGFβ during the recovery phase leading to anarchical expansion of mesenchymal fibroblast and unresolved skin fibrosis.
Our results suggest that sensory neurons could provide signals allowing dermal-resident macrophages to optimize their pro-repair activities during inflammation and protect the skin from overwhelming fibrosis.

Keywords : Sensory neurons, dermal macrophages, tissue repair, skin fibrosis
Authors :
References : , , ,

Authors

Guillaume Hoeffel 1, Guilhaume Debroas 1, Rafaelle Rossignol 1, Ana Reynders 2, Aziz Moqrich 2, Sophie Ugolini 1,

1. CIML, Marseille, FRANCE
2. IBDM, Marseille, FRANCE