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INTRODUCTION

Acute postoperative pain results from a dynamic cross talk between the immune and the nervous system. In particular, previous research in our laboratory revealed that skin-resident dendritic cells mediate mechanical inflammatory pain hypersensitivity by releasing chemokines that induced sensory neurons hyperexcitability (Silva et al., 2022).



• While communication from skin resident cells to sensory neurons has been well described, it is still unknown whether sensory neurons can alter dendritic cell activation in models of inflammatory pain.

Here, we hypothesized that mediators released by sensitized sensory neurons in the periphery are sufficient to alter the activation profile of these tissue-resident myeloid cells.



METHODS

We performed in vitro experiments where DC2.4 dendritic cell line was incubated with either supernatant from sensory neurons collected in non-injured mice or in mice 24h after plantar incisional wound. Potential anti-inflammatory effect of neuronal mediators were assessed by prestimulating dendritic cells with LPS (1000ng/ml). Dendritic cells activation were assessed by flow cytometry and ELISA.



Sensory Neurons Mediate Activation of Skin-Resident Dendritic Cells in a Model of Postoperative Pain Brécier, A. ^{1,2}, <u>Silva, J. R.</u> ^{1,2} & <u>Ghasemlou, N.</u> ^{1,2,3,4}

IL-23 concentration increases when DCs are incubated with neuronal supernatant of injured mice



ELISA analysis revealed that supernatant from injured sensory neurons significantly increase the concentration of the inflan cytokine IL-23, likely secreted by dendritic cells., but not the concentration of the chemokine CCL22.

Markers of immune activation are overexpressed in DCs after an incubation with neuronal supernatant of injured



A larger proportion of dendritic cells expressing markers of immune activation such as CD80, CD86, CD40 and MCH II were for cultures incubated with the supernatant from injured sensory neurons. This suggests a direct pro-inflammatory effect of sensory n on dendritic cells.

Our findings revealed that sensory neurons challenged by incisional wound might maintain and promote the activation of dendrit Targeting signalling from sensory neurons to skin-resident dendritic cells could represent a new strategy to mediate mechanical hypersensitivity following a surgical procedure.



Silva, J. R., Iftinca, M., Gomes, F. I. F., Segal, J. P., Smith, O. M. A., Bannerman, C. A., Mendes, A. S., Defaye, M., Robinson, M. E. C., Gilron, I., Cunha, T. M., Altier, C., & Ghasemlou, N. (2022). Skin-resident dendritic cells mediate postoperative pain via CCR4 on sensory neurons. Proceedings of the National Academy of Sciences of the United States of America, 119(4), 1–10. https://doi.org/10.1073/pnas.2118238119



RESULTS Neuronal supernatant of injured and non-injured mice do not change CCL22 concentration

DISCUSSION

CD80, CD86, CD40 & MCH I

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