Histone demethylase LSD1 is required for LC embryonic development but dispensable for LC maintenance and repopulation

X Wang, B Keuning and J M Quinn

Langerhans cells (LCs), the sole dendritic cell subpopulation in the epidermis, are potent regulators of immune surveillance and tolerance. Unlike conventional DCs, LCs follow a heterogeneous pathway with unique differentiation, migration and function in skin. Several studies have shown that demethylase LSD1, known to mediate the demethylation of lysine amino acids on histone proteins, plays a key role in the maintenance and differentiation of hematopoietic stem cells. However, the role of LSD1 in LC ontogeny and homeostasis remains unknown. To address this, we generated Csf1rCreLSD1fl/fl conditional knockout (Csf1rLsd1 KO) mice in which the Csf1r promoter was inactivated in macrophage/microglia and LC precursors from embryonic stage. We found a robust reduction of LC precursors in Csf1rLsd1 KO mice at embryonic day 18.5 and postnatal day 0, suggesting that LSD1 is required for LC ontogeny at late embryonic stage. To investigate whether LSD1 is involved in LC maintenance and repopulation, we created Csf1rCreLsd1LysmCreLsd1fl/fl double knockouts. Loss of LSD1 in LCs was sufficient to decrease the number of LCs in all DC populations including epidermal LCs after birth. Flow cytometry and immunofluorescent staining of skin showed that the frequency and number of LCs were unaltered in 2-week-old and adult Csf1rLsd1 KO mice compared to wild-type mice. Using an ultraviolet C (UVC)-induced skin damage model, we found that long-term LCs were able to repopulate to the epidermal epidermis of Csf1rLsd1 KO mice 2 weeks after UVC treatment. Overall, these findings strongly argue against the hypothesis that LSD1 is critical, but not required for the LC maintenance at steady state and repopulation under inflammatory conditions.

IL-34 differentiation of immunosuppressive macrophage

K Kelly-Scumpia, R Shrair and RL Modlin

Innate lymphoid cells in healthy and atopic skin

N Allison, W Baer, C Bangert, C Staaf, T Krausgruber, C Bock, PM Brunner and G Stingl

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