E-cadherin is dispensable for epidermal localization of Langerhans cells

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Background

- Epidermal Langerhans cells (LC) express high levels of E-cadherin (E-cad)
- E-cad has been suggested to be responsible for LC adhesion to keratinocytes and therefore LC localization to the epidermis
- This hypothesis is supported by:
  - Formation of adherens junctions between E-cad expressing LC like DC and keratinocytes
  - Down regulation of E-cad during activation, maturation and emigration of LC
  - Requirement of TGF-ß for E-cad expression in DC and lack of epidermal LC in TGF-ß null mutants

Question addressed

Here we address the question wether E-cad is responsible for epidermal localization of LC by using a Cre/loxP mouse in which all CD11c$^+$ cells are devoid of E-cad (E-cad$^{fl/fl}$CD11c$^+$ Cre mice)

Epidermal localization of LC

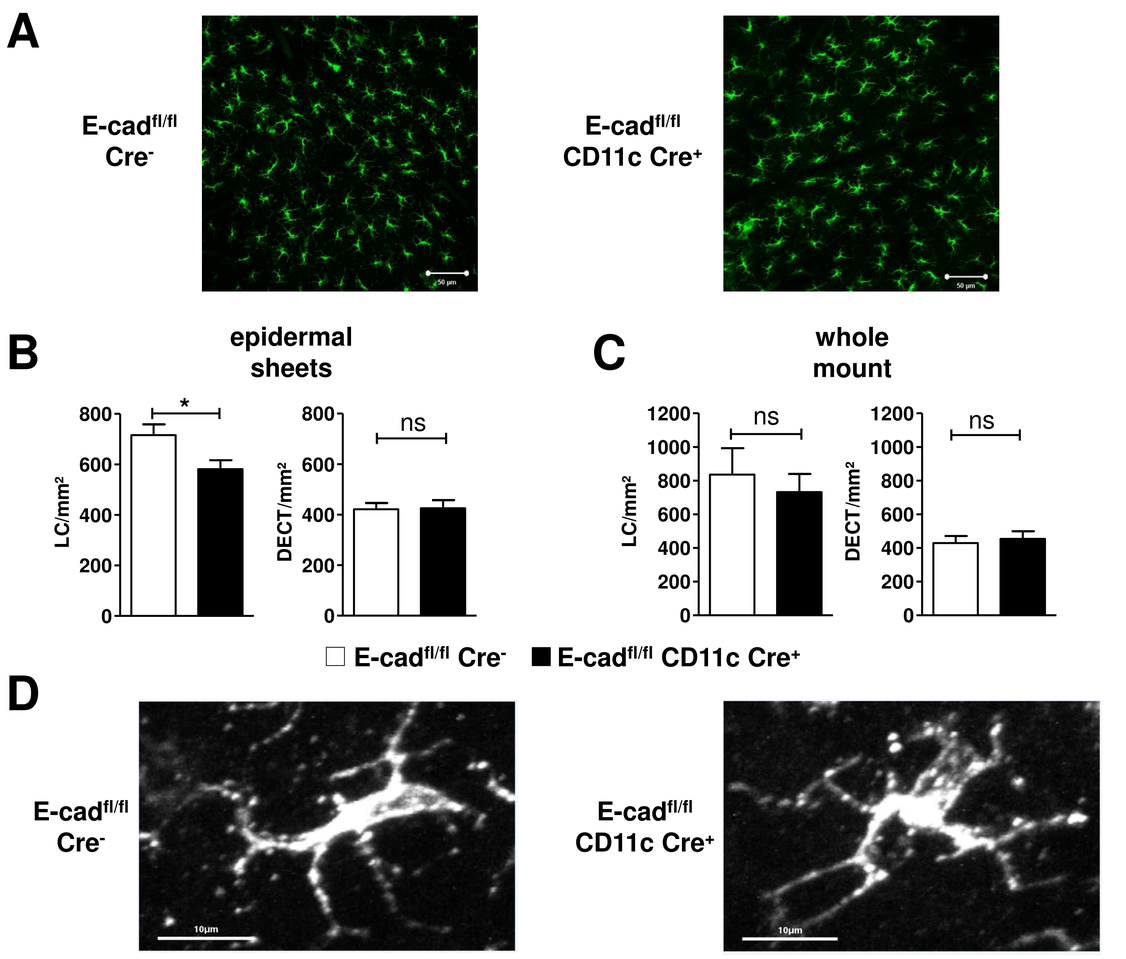

Figure 1: (A) Examplary pictures of whole mount IF stained ear sheets. Pictures show MHCII staining in green, scale bar = 50 µm **(B)** LC and DETC count in epidermal sheets, evaluated from IF staining, pooled data of 3 independent experiments shown as mean + SEM; n=11-12 mice per group **(C)** LC and DETC count in epidermis analyzed by whole mount IF staining and confocal microscopy, n = 4 mice per group **(D)** Morphology of LC in epidermis analyzed from whole mount stained ear with confocal imaging, scale bar = 10 µm

LC percentages in different cell suspensions

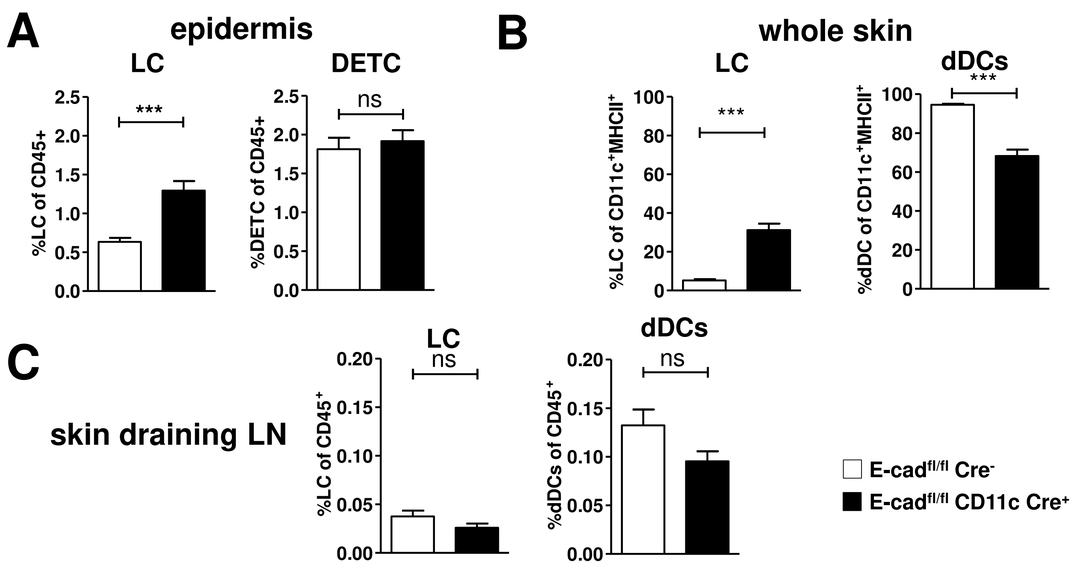

Figure 2: (A) Percentage of LC and DETC of all living cells in epidermal cell suspension **(B)** Percentage of LC and dermal DC (dDC) of all DC in single cell suspension of digested ear skin **(C)** Percentage of LC and dDC in skin draining LN single cell suspension. Pooled data of 3 independent experiments are shown as mean + SEM, n = 11-12 per group

Activation status of LC

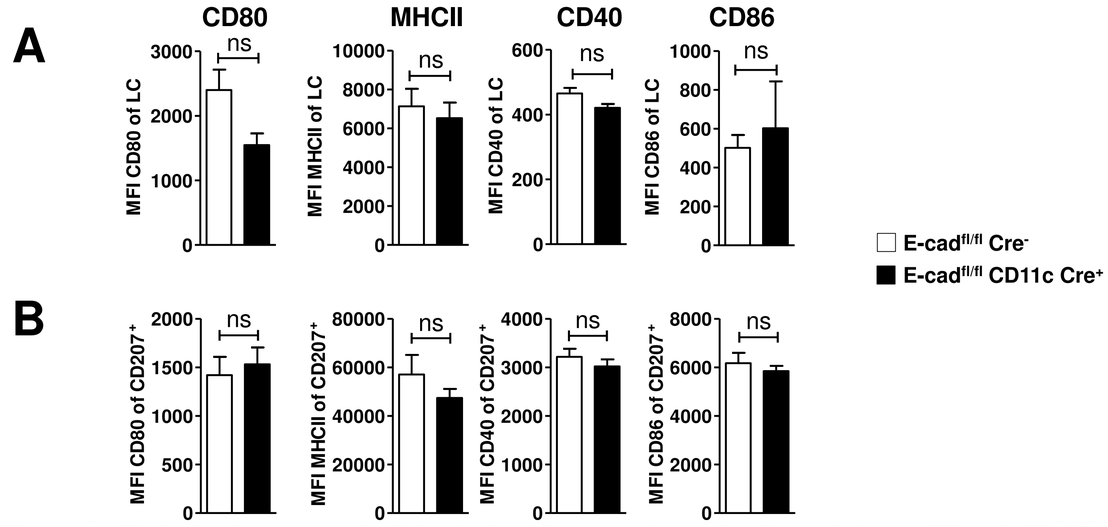

Figure 3: (A) Activation status of LC in single cell suspensions of epidermal sheets **(B)** and CD207$^+$ skin derived DC in skin draining LN. Pooled data of two independent experiments are shown as mean + SEM, n = 7 per group

Migratory properties of LC

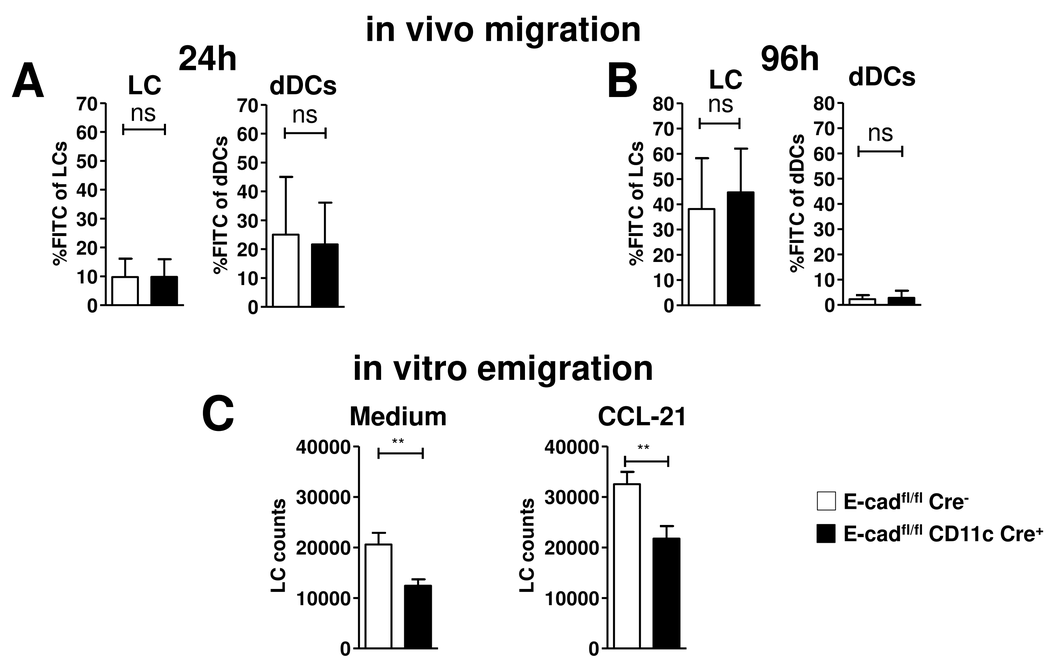

Figure 4: (A and B) Analysis of skin draining lymph node cells 24h **(A)** and 96h **(B)** after FITC painting on the ear, pooled data of three independent experiments are shown as mean + SEM, n = 10-15 per group
(C) Emigration of LC from skin explants in vitro without or with the chemokine CCL-21, pooled data of four independent experiments are shown with mean + SEM, n = 18-19 mice per group.

Contact hypersensitivity

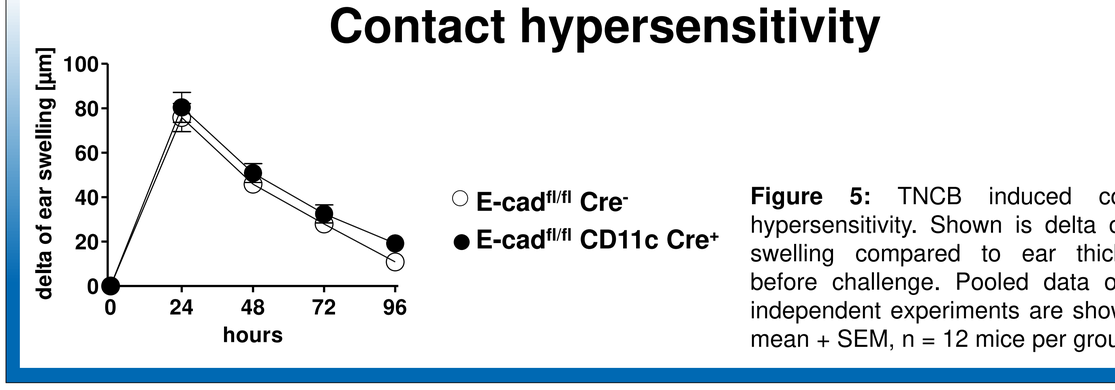

Figure 5: TNCB induced contact hypersensitivity. Shown is delta of ear swelling compared to ear thickness before challenge. Pooled data of two independent experiments are shown as mean + SEM, n = 12 mice per group

Summary

E-cadherin$^{fl/fl}$ CD11c$^+$ Cre mice display:

- Marginally reduced LC numbers in the epidermis
- Elevated LC numbers in epidermal and whole skin cell suspensions
- No difference in activation status of steady state LC
- No difference in migration in vivo
- Reduced emmigration of LC from skin explants in vitro
- No difference in ear swelling response during contact hypersensitivity

Conclusion

- E-cad seems to be dispensable for epidermal localization of LC