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PD-L1 on radio-resistant cells regulates effector CD8⁺ T-cell activation during the elicitation phase of contact hypersensitivity

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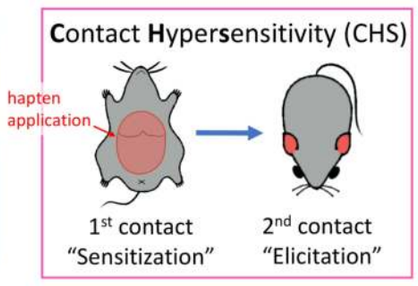
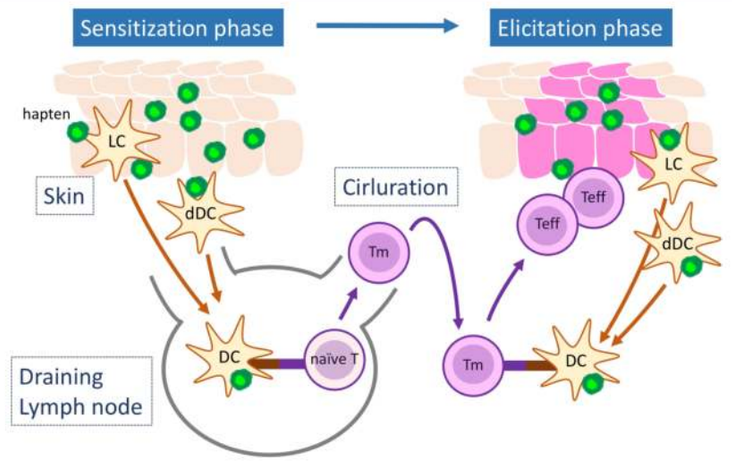
Contact hypersensitivity is a murine model for allergic contact dermatitis

Allergic Contact Dermatitis
- Common skin disease
- Type IV hypersensitivity

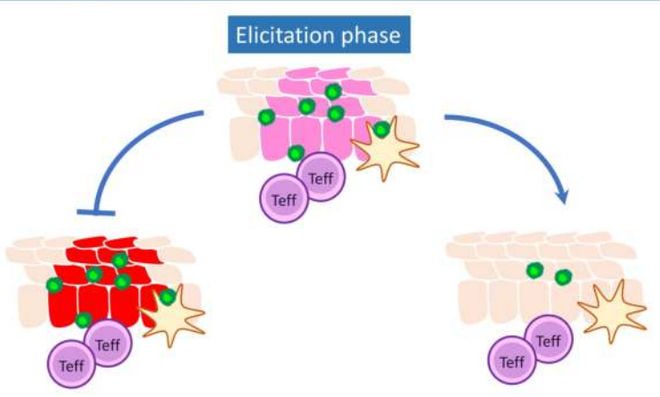
Contact Dermatitis (2016)



CHS consists of two phases; sensitization and elicitation



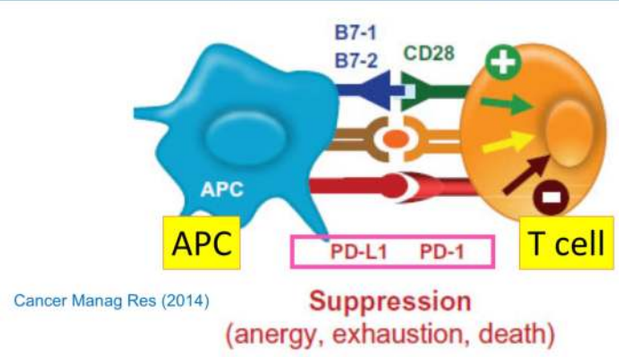
During the elicitation phase, negative regulation should be introduced



To avoid excessive inflammation.

To terminate inflammation.

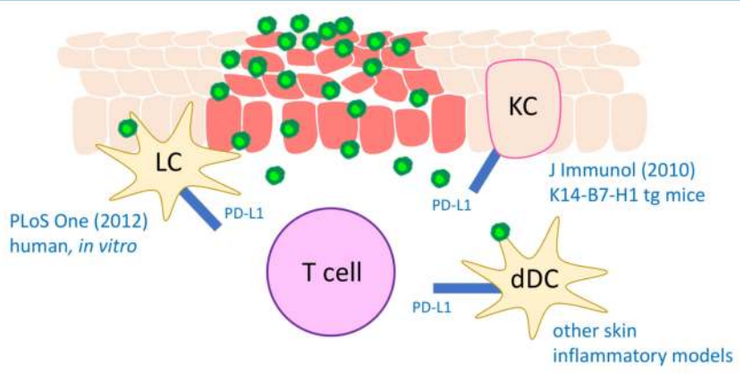
The programmed cell death protein-1/ -ligand 1 pathway; an important negative regulator



Cancer Manag Res (2014)

The PD-1/L1 pathway is physiologically important in immune tolerance and homeostasis.

The role of PD-1/L1 interaction in the elicitation phase of CHS is not fully understood



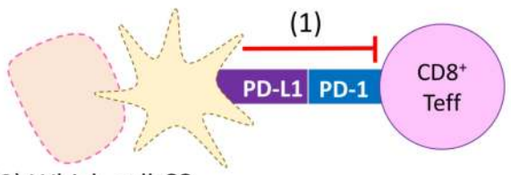
Many possibilities should be considered even today.
Further studies in more physiological conditions are necessary.

Purpose of this study

To investigate

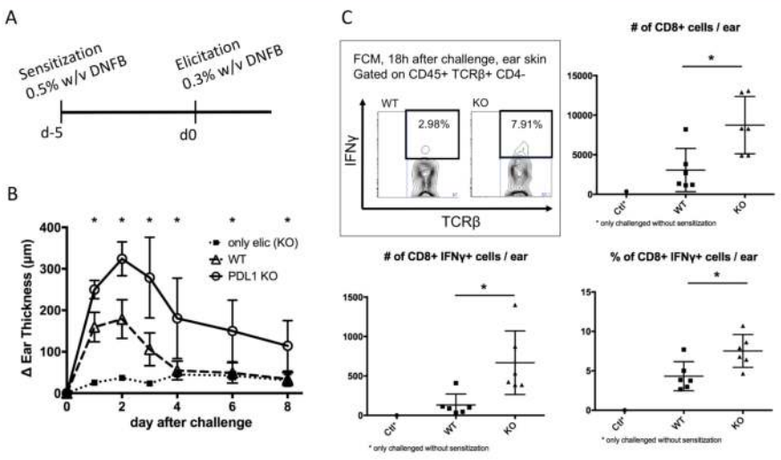
(1) the involvement of the PD-1/PD-L1 pathway in CHS responses during the elicitation phase.

(2) if so, on which cells PD-L1 is the most important for this regulation.

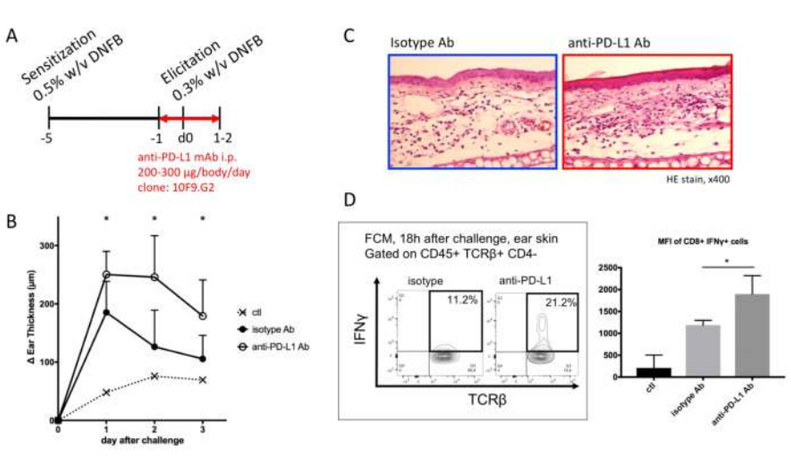


(2) Which cells??

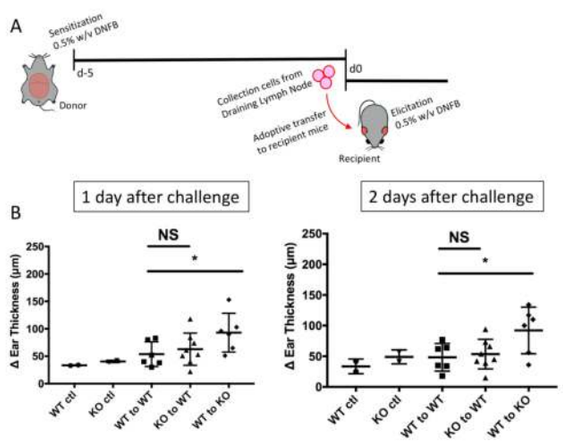
Result 1 : PD-L1 deficient mice exhibited exacerbated and prolonged CHS responses



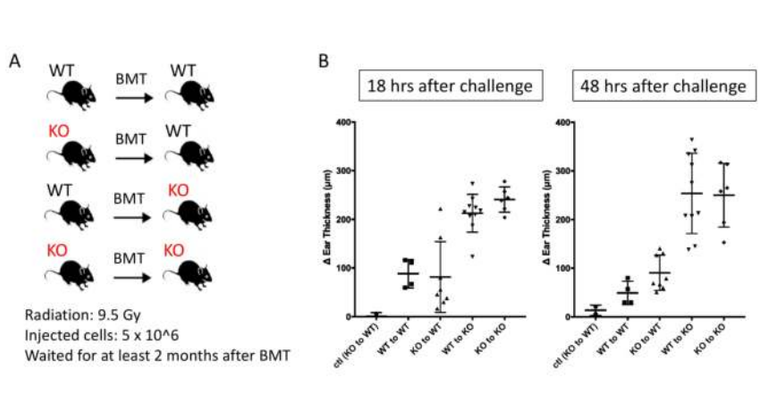
Result 2 : Blockade of the PD-1/PD-L1 pathway during the elicitation phase exacerbated CHS responses



Result 3 : PD-L1 KO mice transferred with sensitized LN cells from WT mice exhibited increased CHS responses

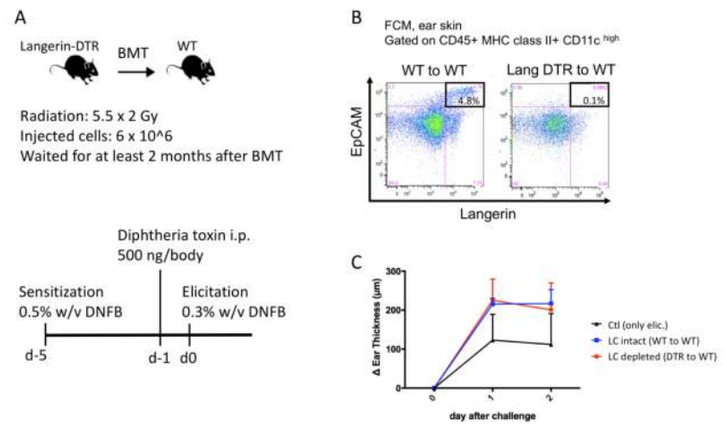


Result 4 : Bone marrow chimeric mice (WT to KO) exhibited increased CHS responses



Radiation: 9.5 Gy
Injected cells: 5 x 10^6
Waited for at least 2 months after BMT

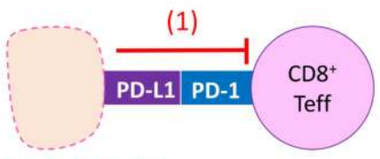
Result 5 : Depletion of Langerhans cells did not affect CHS responses



Summary

(1) PD-1/PD-L1 pathway negatively regulates CHS responses during the elicitation phase.

(2) PD-L1 on radio-resistant cells is the most important for this regulation.



(2) Radio-resistant cells

Acknowledgements