SELECTED OPPORTUNITIES IN ALLERGY & ASTHMA

METHODS AND COMPOSITIONS FOR TREATING ASTHMA AND ALLERGIC DISEASES (BIO 18315)

METHODS AND COMPOSITIONS FOR TREATING ASTHMA AND ALLERGIC DISEASES (BIO 18315)

Product factsheet

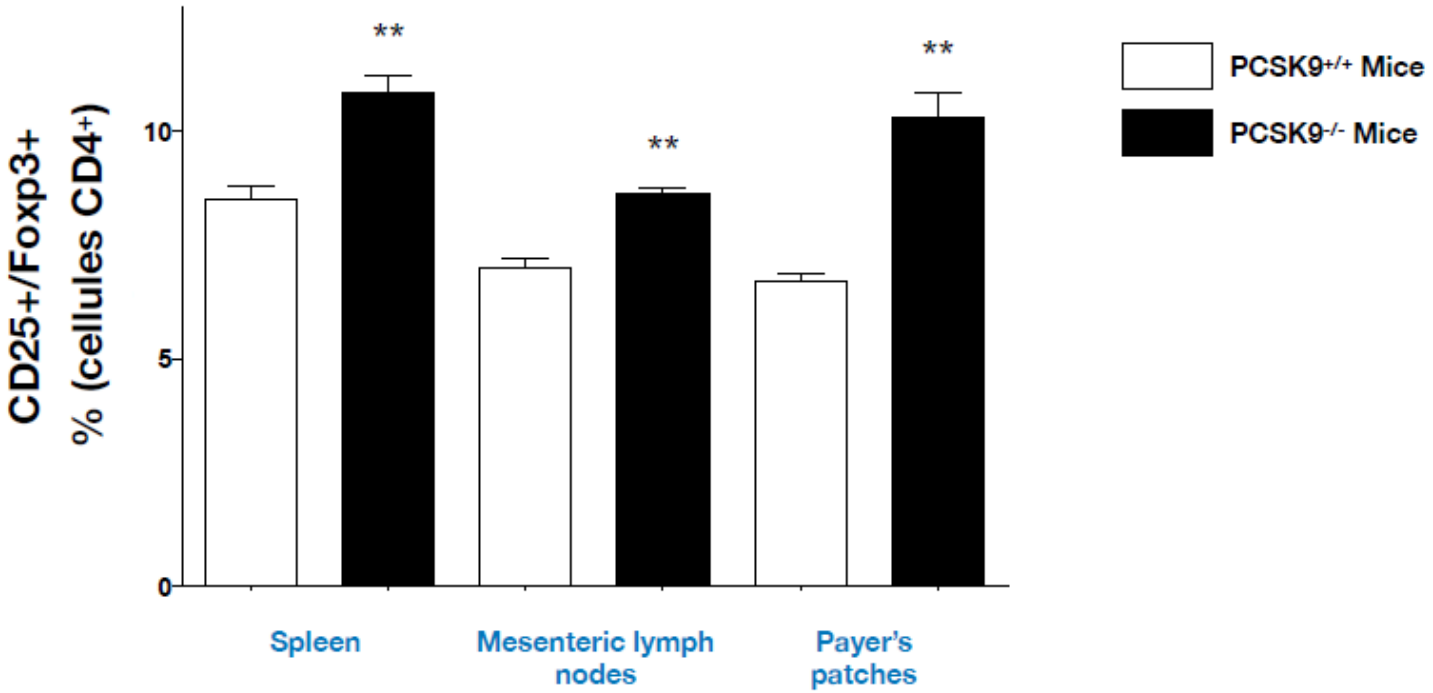
PoC in vivo

- **Target:**
  - PCSK9
- **Product:**
  - Could be tested: PCSK9 inhibitors (antibodies, small molecules, oligonucleotides…)
- **Application:**
  - Allergic diseases and asthma
- **Rational:**
  - PCSK9 (proprotein convertase subtilisin kexin type 9) is a critical regulator of cholesterol metabolism
  - Beyond its role in lipid metabolism, some studies suggest that PCSK9 may also be involved in inflammatory response
  - Several independent groups have recently investigated the implication of PCSK9 on sepsis but none of them have determined its impact on allergies and/or asthma which is a global health burden
- **POC:**
  - Regulatory T cells are significantly more abundant in the spleen, mesenteric lymph nodes and Peyer's patches of $PCSK9^{-/-}$ mice
  - HDM allergens increase the intracellular PCSK9 expression and possibly its secretion in human cells
  - PCSK9 deficiency attenuates the allergic responses
- **Patent and publication:**
  - PCT/EP2019/073546: METHODS AND COMPOSITIONS FOR TREATING ASTHMA AND ALLERGIC DISEASES
  - Publication in progress

METHODS AND COMPOSITIONS FOR TREATING ASTHMA AND ALLERGIC DISEASES (BIO 18315)

Proof of concept

PSCK9 deficiency increases regulatory T cells population



Regulatory T cells are significantly more abundant in the spleen, mesenteric lymph nodes and Peyer's patches of PCSK9-/- mice.

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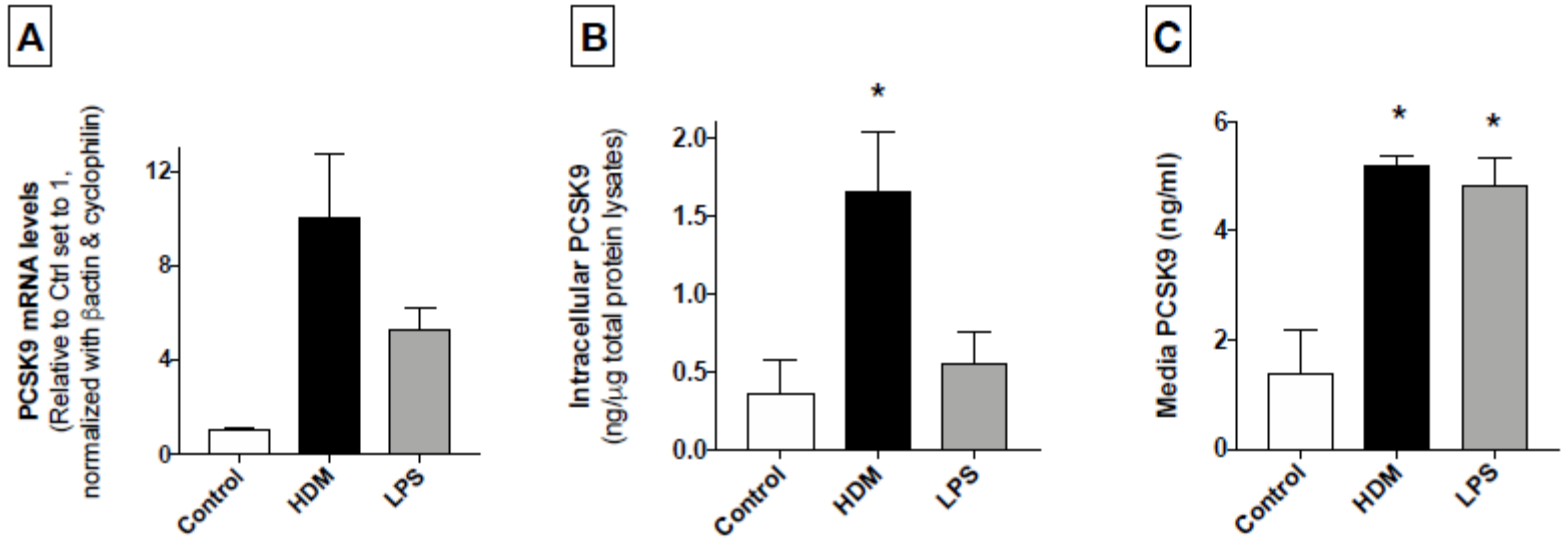
Proof of concept

HDM allergens increase the intracellular PCSK9 expression and possibly its secretion



*Human primary BECs were cultured for 48 hours with HDM allergens or LPS (10µg/ml). (A) PCSK9 mRNA levels (B) Intracellular PCSK9 protein and (C) "secreted" PCSK9 protein levels. Protein levels were assayed by ELISA. * P<0,05.*

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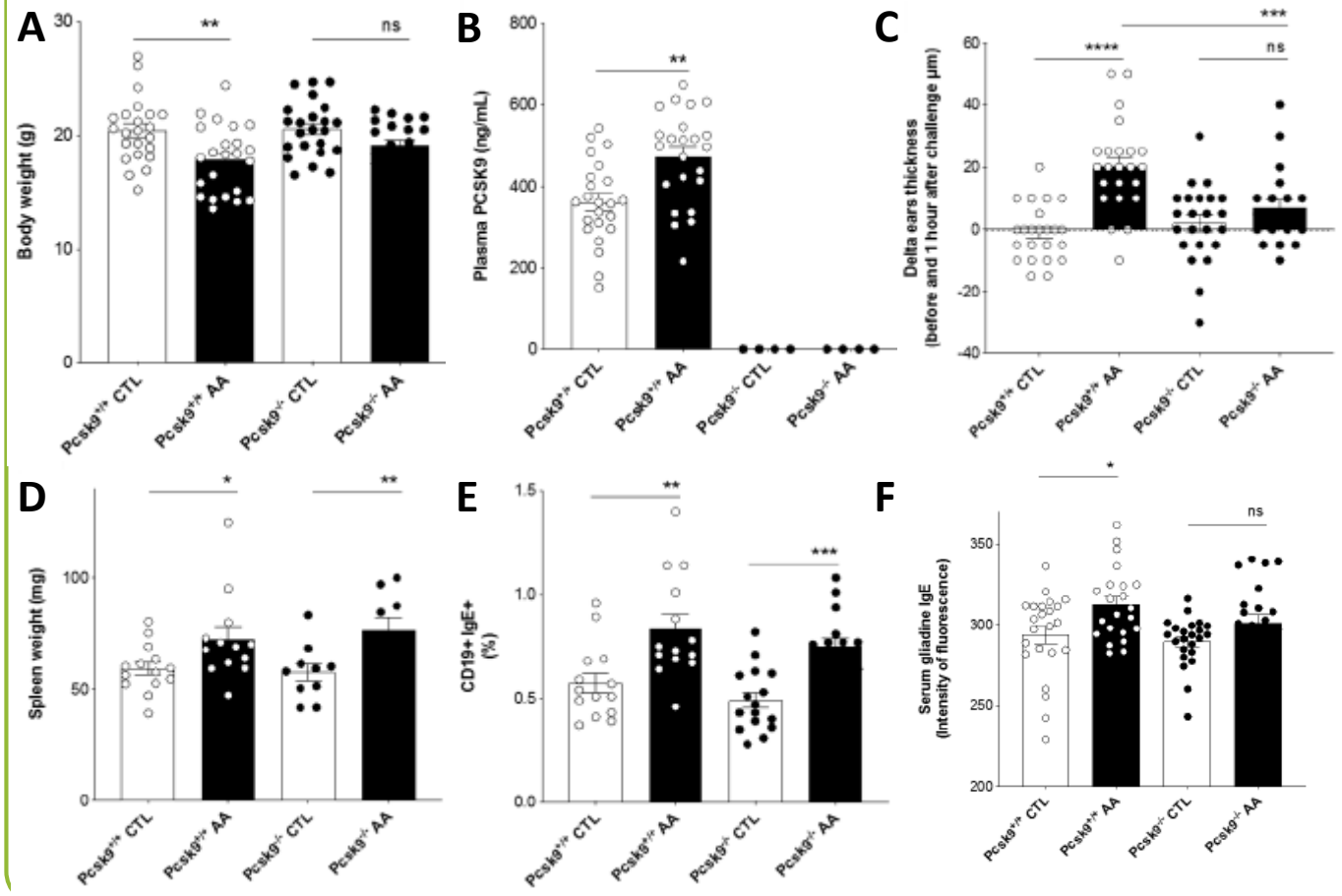
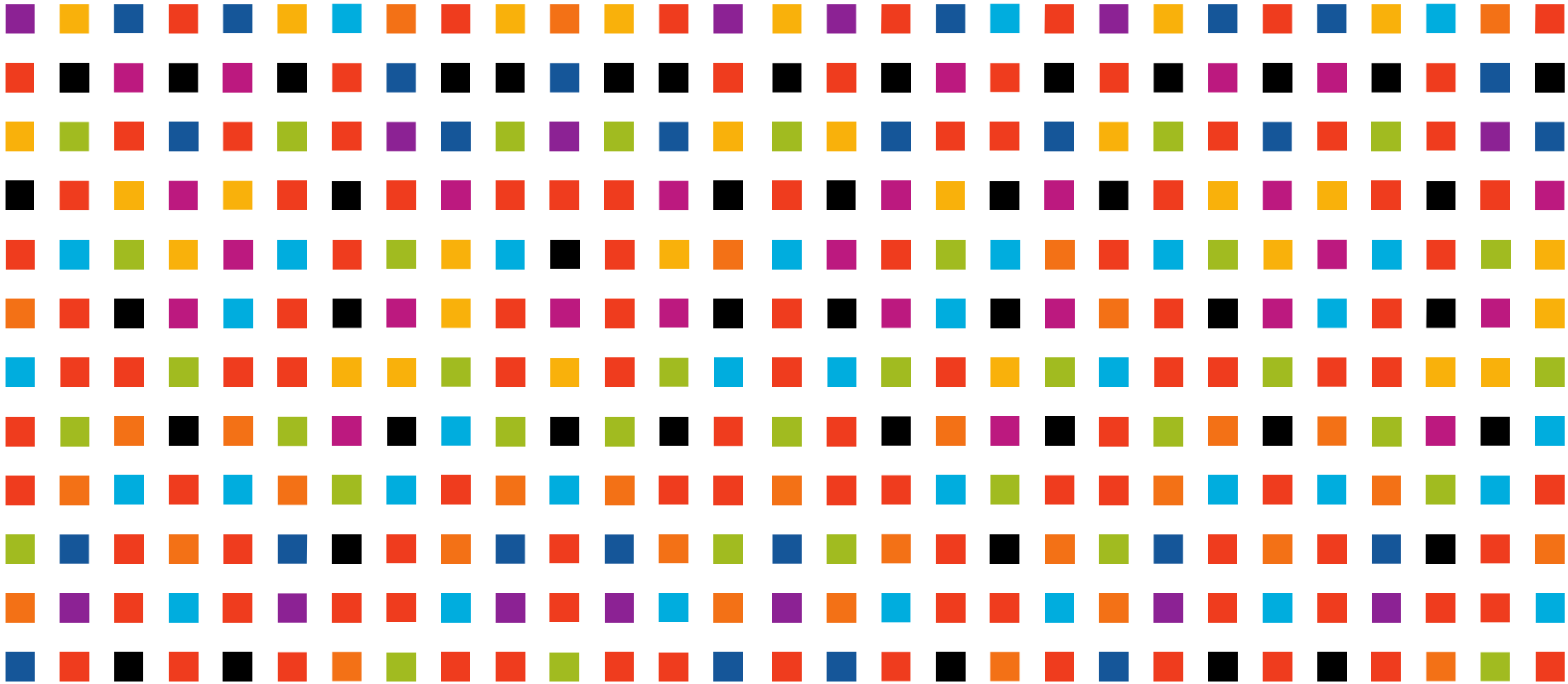
PCSK9 deficiency attenuates the allergic responses



PCSK9$^{+/+}$ (white circle) and PCSK9$^{-/-}$ mice (black circle) were sensitized by intra-peritoneal injection of vehicle (white bars) or gliadins (black bars) and then challenged twice with water or gliadins by gavage. One hour after the second oral allergic challenge body weight (**A**), plasma PCSK9 concentrations (**B**) ear thickness (**C**) were measured and represented as dot plots and histograms representing mean ± SEM. One hour after the second oral allergic challenge spleen weight (**D**), splenic CD19+ IgE+ cells percentage (**E**) and plasma gliadin specific IgE concentrations (**F**)



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