Allergy development – intrauterine and onwards

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IgE 50 years, 6th October 2017
IgE in the intrauterine environment

Intrauterine/neonatal microbial environment – Immune profile in the offspring? Relevance to allergy?
IgE in the intrauterine environment
IgE in the intrauterine environment – what was known?

- Allergic diseases often present in early years
- Maternal allergy is considered to be a stronger risk factor than paternal allergy
- IgE present in cord blood
  - Origin?
  - Predictor for allergy?

-> Suggested a role of the intrauterine environment
IgE in the intrauterine environment – what was known?

  - IgE in the amniotic fluid

- *Jones et al Lancet 1998:*
  - Exposure to IgE in the intrauterine environment
  - Correlation between maternal plasma- and amniotic fluid levels of total IgE
  - -> Postulated fetal swallowing of IgE
When life was easy: Th1 vs Th2

“A Th2 environment promotes allergy”

IgE in the intrauterine environment

- Does the local environment in the placenta contain IgE? On which cells? Does this differ between allergic and non-allergic mothers?
IgE in the human placenta

Term placentas (n=86) from a prospective allergy cohort
Immunohistochemical stainings for IgE & receptors

No evidence of local placental IgE production

Will allergy or infection influence placental IgE?

- Placental IgE is independent of:
  - Maternal allergy
  - Malaria infection
  - Chorioamnionitis
IgE in the human placenta: maternal or fetal?

Joerink et al Allergy 2009
Transplacental passage of maternal IgE via FcRn in the form of IgG-IgE immune complexes

Bundhoo et al Clin Exp Allergy 2015
IgE in utero—beneficial, harmful, or?

- “Mucosal antibody”? 
- Protecting the fetus against harmful substances?
- “In symbiosis” with the Hofbauer cells, promoting their survival?
- Maternal origin (?), Promoting allergy?
Intrauterine/neonatal microbial environment – Immune profile in the offspring? Relevance to allergy?
T cell subsets today – from Th1/Th2 to Th”X” and a great plasticity
Microbiota & immune balance – the intestine in focus

Lasken & McLean Nat Rev Genetics 2014
Mowat & Agace, Nat Rev Immunol 2014
Walker Pediatr Res 2017
Bacterial metabolites influence the epigenome of T-cells

Luo et al Front Immunol 2017
Microbiota, intrauterine environment and immune development

Gomez de Agüero et al Science 2016
Macpherson et al Nature Rev Immunol 2017

Geuking et al Immunity 2011
Walker Pediatr Res 2017
Microbiota-mediated immune regulation in vivo

Sjögren et al Clin Exp Allergy 2009
Johansson et al PLoS one 2011
Björkander et al JACI 2016
Björkander et al manuscript 2017

Petursdottir, Nordlander et al submitted 2017
A gut microbiota connected to a high allergy risk in children, promotes a strong Th17 immunity

Petursdottir, Nordlander et al 2017
The mice “tolerate” the human microbiota well – no signs of intestinal inflammation

Petursdottir, Nordlander et al 2017
Significant differences in “allergy-protective” and “allergy-risk/Th17-promoting” floras but it is not a matter of diversity.....

Petursdottir, Nordlander et al 2017
Th17/2 cells contribute to allergic responses
Suppress by targeting RORγt

Cosmi et al JACI 2010
Na et al JACI 2017
Microbiota and the immune system

Belkaid & Harrison Immunity 2017
Acknowledgements

Gut microbiota & immune maturation:
Sophia Björkander
Sofia Nordlander
Dagbjört Petursdottir
Khaleda Rahman Qazi
Yeneneh Haileselassie
Claudia Carvalho-Queiroz

Velmurugesan Arulampalam – Karolinska Institutet
Stefan Roos - Biogaia
Caroline Nilsson – Sachs Children’s Hospital
Jan-Olof Persson & Klas Udekwu– Stockholm University
Diarmaid Hughes– Uppsala University

IgE in placenta:
Ulrika Holmlund
Ingeborg van der Ploeg
Bengt Sandstedt
Caroline Nilsson
Gunnar Lilja
Annika Scheynius

Vetenskapsrådet
Ragnar & Torsten Söderbergs Stiftelser
Engkviststiftelsen
Hjärt-Lungfonden
Cancer och allergifonden
Stockholms Universitet