

The Science of Food Allergy

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Food Allergy -definition

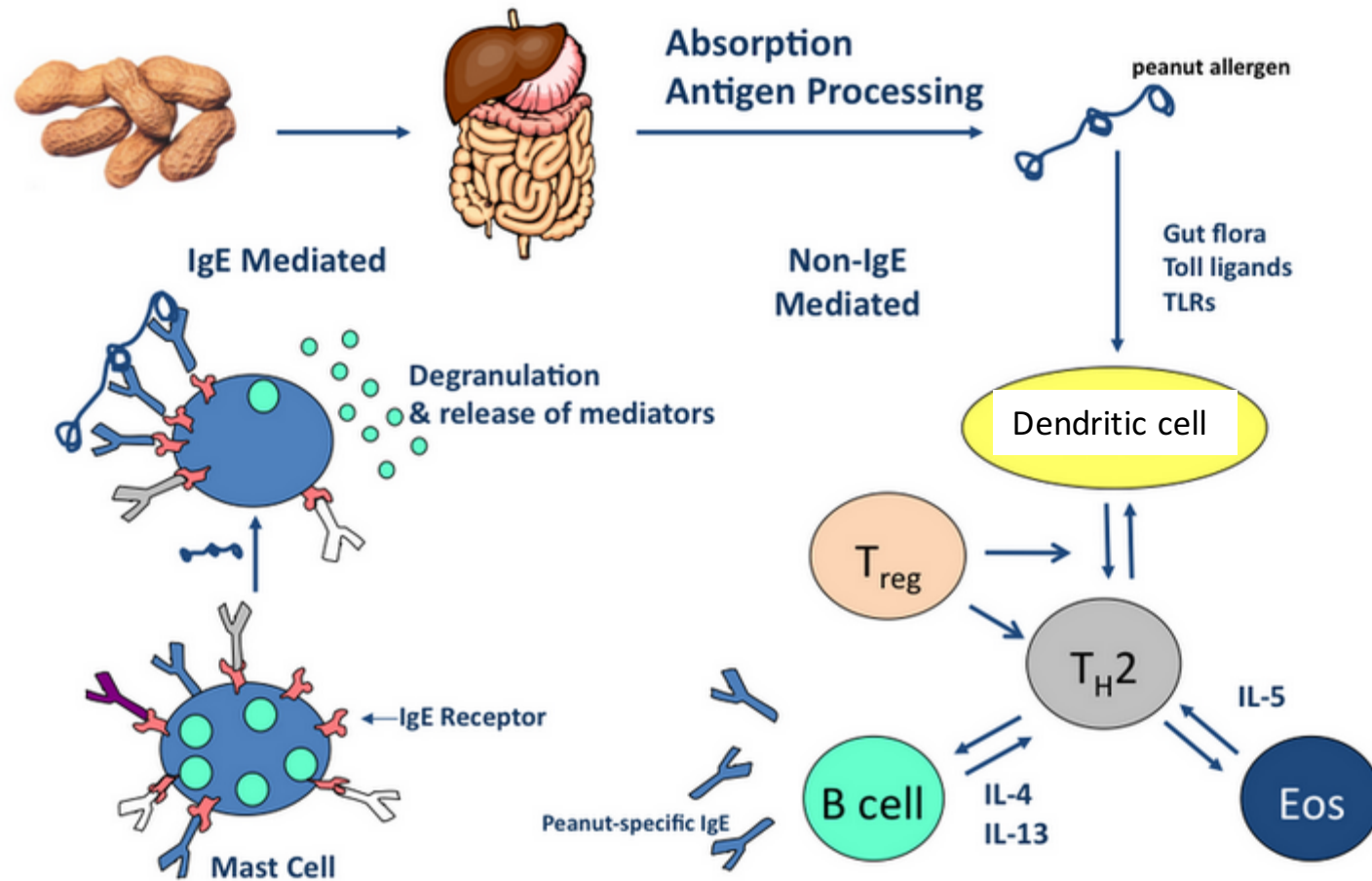
“People with food allergies have an allergic reaction when they come in contact with certain foods. This happens because their immune system overreacts to the proteins in that food”.

Eight kinds of food cause most food allergies:

- Cow's milk
- Eggs
- Peanuts
- Wheat
- Soy
- Fish
- Shellfish
- Tree nuts

AAAAI website, 2015

What happens in food allergy?



Where does food allergy begin – Lack of oral tolerance?

Oral tolerance is the acquired immunological unresponsiveness to food antigens.



Translation: When you eat food your immune system learns not to respond to it.

If you don't develop tolerance to a food there is a risk of developing food allergy

The process of tolerance development

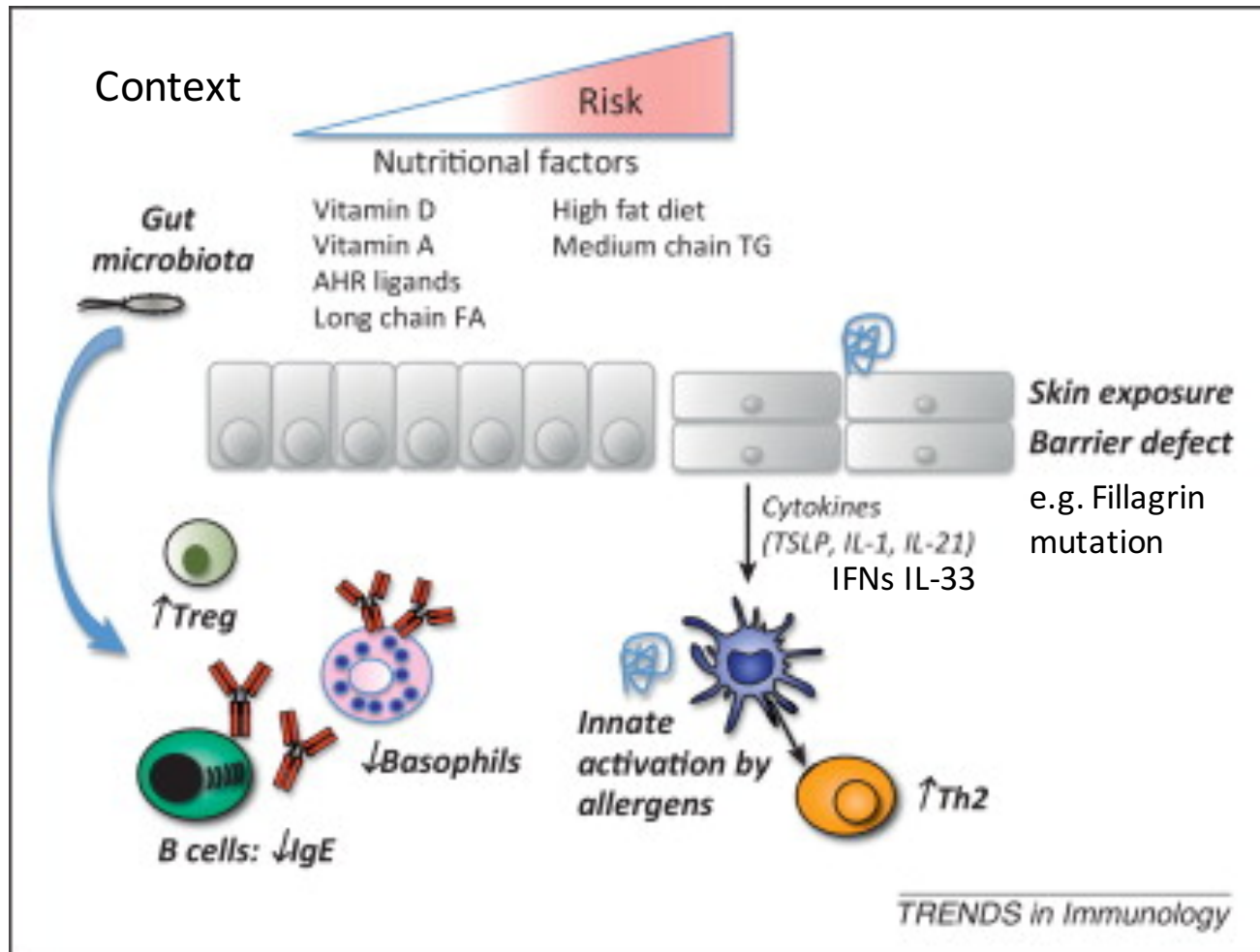
Tolerance

- Food proteins taken up into gut lymphoid follicles
- Special “tolerizing” dendritic cells, guided by local signals educate regulatory T cells and limit TH2 cells
- T cells inhibit immune response or only allow limited IgA response to antigen

Sensitization

- Food contacts immune system in another tissue or during infection
- Non- tolerogenic dendritic cells educate T cells that mobilize immune response
- T cells promote the development of an active immune response including IgE antibodies

Tolerance vs sensitization



Berin and Sampson, 2013

Whose at risk- Genetics

- No simple genetic pattern – gene environment interaction and multiple factors
- Associations found with....
 - CD14
 - NLRP3 – bacterial sensing

 - Stat 6
 - IL-10 (cytokine) – immune regulation

 - SPINK
 - Fillagrin – epithelial barrier

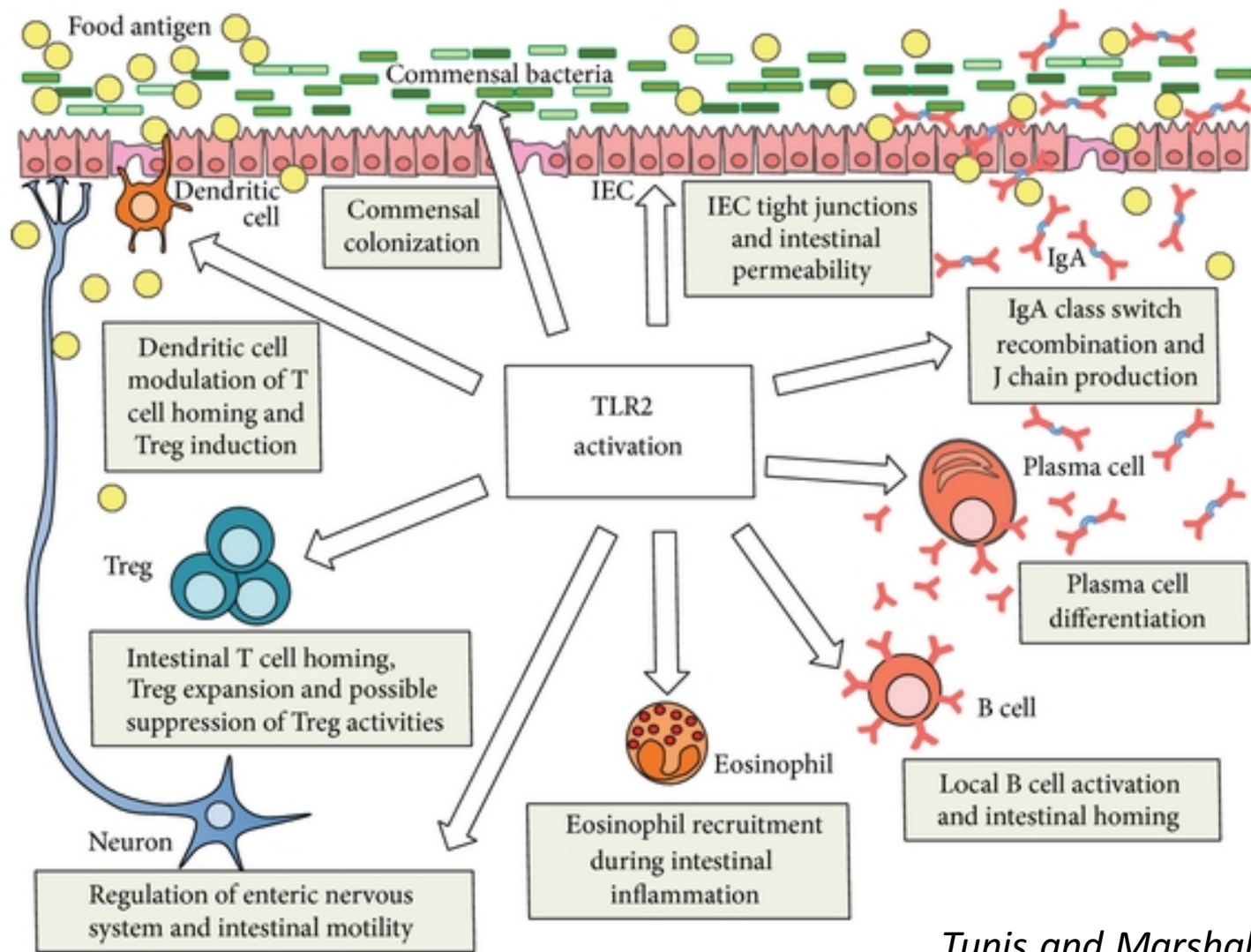
Can FAST and GETFACTS genetics studies

- Identify the genetic basis of peanut allergy, ensuring rare variants are not overlooked
- Examining epigenetics (functional genetic changes related to environment) in collaborative studies
- Using a second group of subjects to confirm findings and examine functional correlates
- Explore preventive strategies in those at highest risk, based on genetic markers

Bacteria and their products

- Intestinal flora altered in food allergy?
- Certain flora associated with development of allergy?
- Role for probiotics or early exposure to particular organisms?
- Tolerance to resident intestinal bacteria is an important factor in their survival, so altered tolerance regulation changes bacterial balance
- Some bacterial products are important in regulating tolerance (eg. Toll Like Receptor 2 ligands)
- Most work done on large intestinal bacteria, but small intestine might be more important site

TLR2 – just one receptor for bacterial products



Cows Milk – what's special?

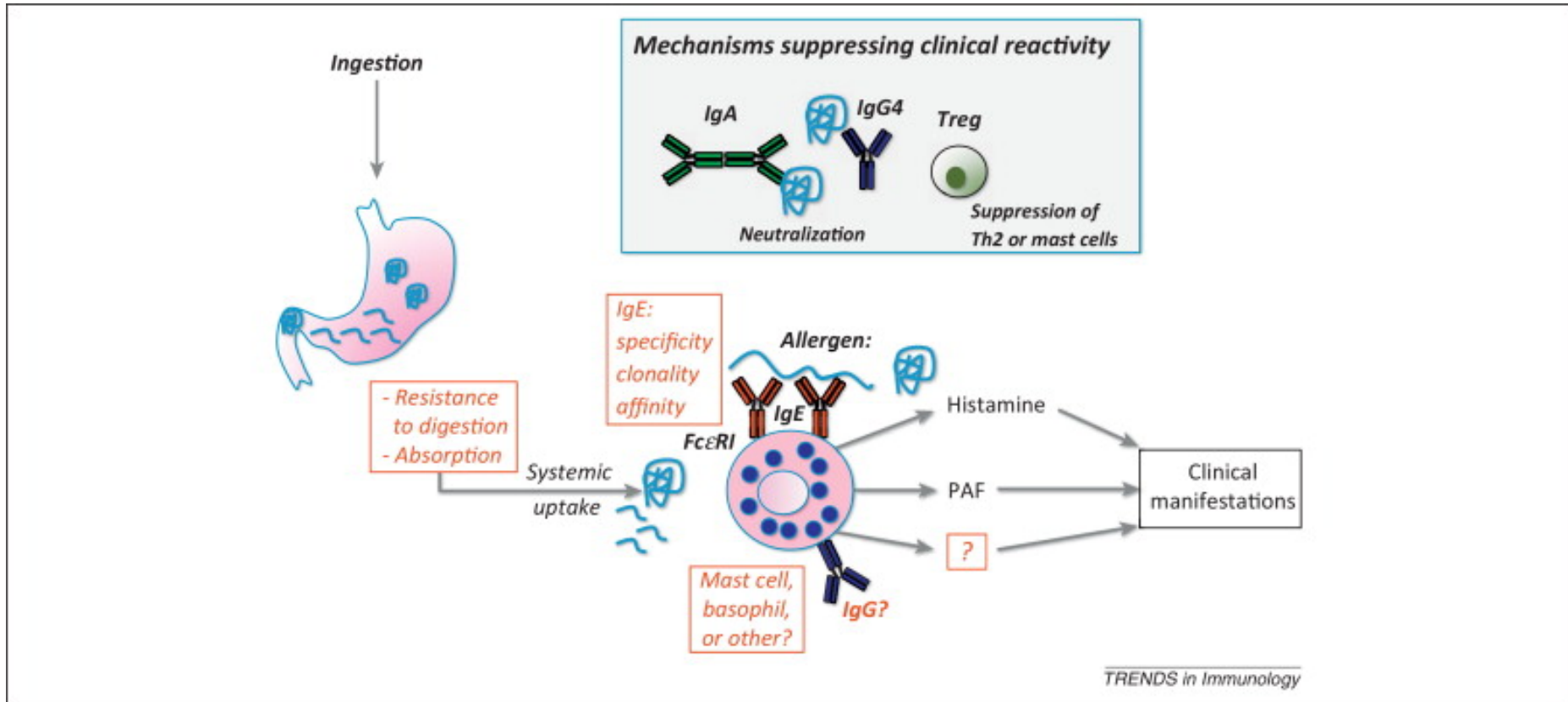
- Often the first food allergy to develop
- Common in young children – often resolves
- Human breast milk (and some cows milk products) contain multiple immune modulators
 - TGF-beta
 - Vitamin A
 - IgA to multiple pathogens and foods
 - Soluble TLR2 (inhibits TLR2 function)

To prevent disease we need more information...

Fundamental studies:

- Cohort studies of disease development (CHILD)
- Fundamental studies on the impact of dietary and microbial exposures on sensitization/tolerance, including the assessment of potential organisms which could reduce sensitisation – implication for prevention of disease
- Improved understanding of the role of TLR2, interferons and IgA in oral tolerance/sensitization with a view to developing improved food allergy prevention strategies in early life
- Information on novel approaches to preventing severe reactions – eg by developing by “tolerizing” dendritic cells or blocking key substances released during anaphylaxis

IgE to food does not always mean there will be an allergic response- opportunities?



Management and therapy – ongoing studies

- Thresholds: Produce Canadian data on peanut antigen thresholds that will inform public health regulations, industry etc.
- Anaphylaxis – identify management gaps, temporal trends, emerging allergens, and new diagnostic markers
- Identify strategies to reduce severe reactions, risk, mediator blockade etc.
- Oral tolerance induction – establish safe and efficient clinical desensitization protocols across multiple centres and evaluate biological correlates of success
- Dependent upon registries and clinical trial capacity

Summary

- Susceptibility – genetics/environment
- Tolerance vs sensitization - prevention
- Allergic response/anaphylaxis – blockade
- Management – thresholds, exposure
- Immune based treatment – Oral Immunotherapy, mediator blockade

Thank you
Questions?