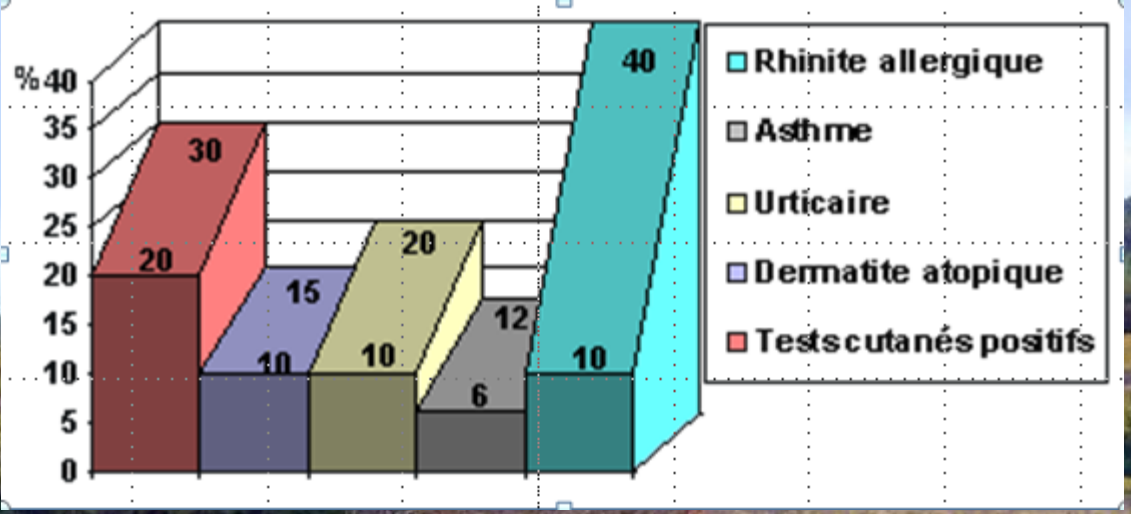
IgG alimentaires … POUR ou CONTRE ???

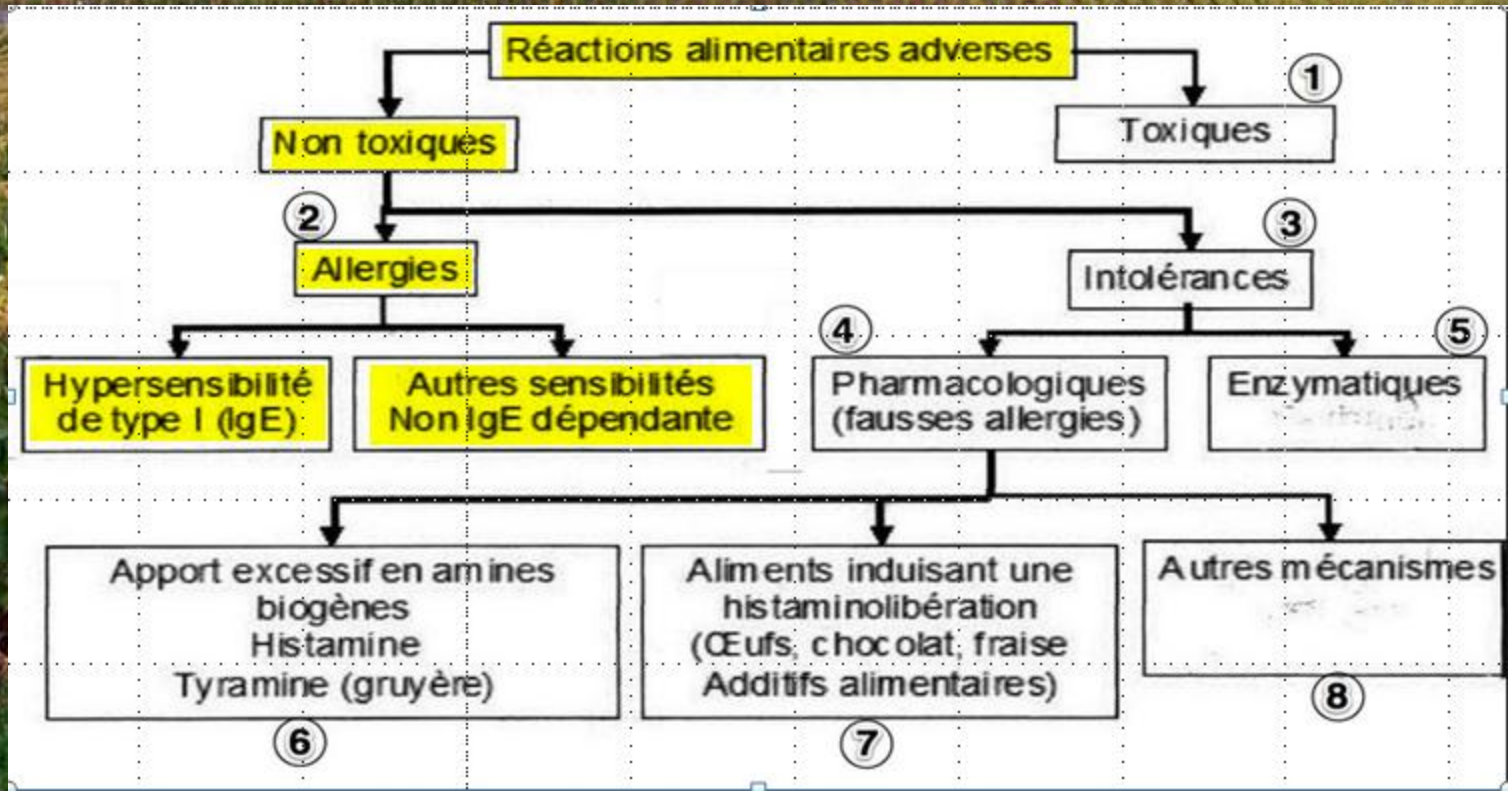
Je suis POUR, mais POUR QUOI …
ET POURQUOI …

- Dans une pratique médicale rigoureuse
- Dans une pratique biologique réfléchie
- Et avec modération … surtout à Beaune

P. Sottiaux



Evolution des allergies en 20 ans

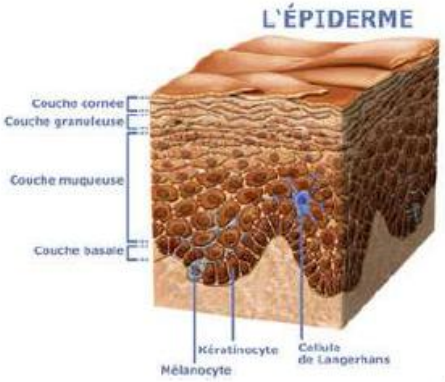


Mécanismes de défense non-spécifiques		Mécanismes de défense spécifiques
Barrières anatomiques et physiologiques	**Immunité innée (naturelle)**	**Immunité acquise**
• Peau • Muqueuses / sécrétions • Température corporelle	• Phagocytes • Médiateurs chimiques • Réaction inflammatoire	• Lymphocytes • Anticorps

BARRIERE INTESTINALE

1000 m²
5µm

PEAU

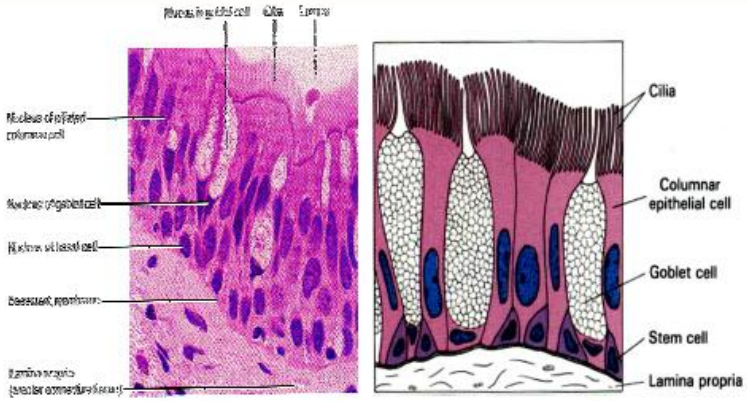


+/- 2 m²

Alvéoles Pulmonaires

130 m²

Epithelium Respiratoire



2 m²

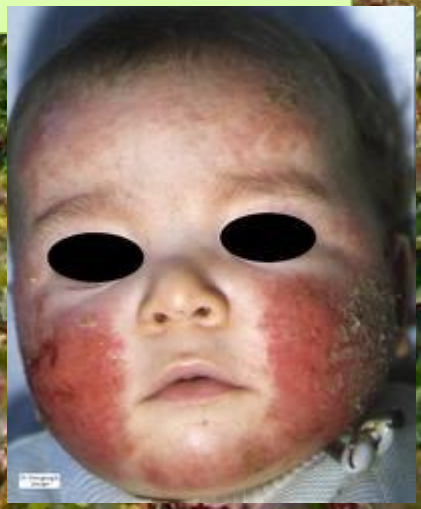
POUR SE COMPRENDRE …..

ALLERGIE: Ne concerne pas que des réactions d'hypersensibilité immédiate. Souvent confondue avec réactions de type 1 (IgE – Histamine).

L'ALLERGIE est un ensemble de pathologies caractérisées par une réponse du système immunitaire contre des molécules du non soi qui ne sont pas associées à un agent pathogène mais sont considérées comme telles par les cellules du système de défense de l'organisme.

ATOPIE: Expression clinique des réactions de type 1 (IgE).
Les antigènes non parasitaires de l'environnement sont appelés allergènes.
Les manifestations sont variées: rhinite, asthme, dermatite atopique, eczéma, urticaire, allergie alimentaire …..

Fig. 1.4 Arthur Fernandez Coca (1875–1959). Coca introduced the term "atopy" (now recognized as IgE-mediated hypersensitivity). (From Cohen & Samter 1992, with permission.)



POUR SE COMPRENDRE

HISTAMINE

- Constituant majeur des granules (10%)
- Formé par la décarboxylation de la L-histidine
- Effet immédiat (minutes qui suivent la dégranulation)
- Trois types de récepteurs
  - **H1**: contraction musculaire lisse (intestin, bronches), sécrétion de mucus, perméabilité vasculaire accrue
  - H2 : stimulation sécrétion acide par l'estomac
  - H3 : modulent la transmission de neurotransmetteurs au extrémités présynaptiques

ATOPIE

Certains individus produisent des IgE contre des antigènes non parasitaires de l'environnement

Ces individus sont dits *atopiques*, les antigènes (non parasitaires) en question sont dits *allergènes*

L'Histamine n'est pas seule …

Leukotriènes et prostaglandines

Mêmes types d'effets que histamine (notamment PGD_2)

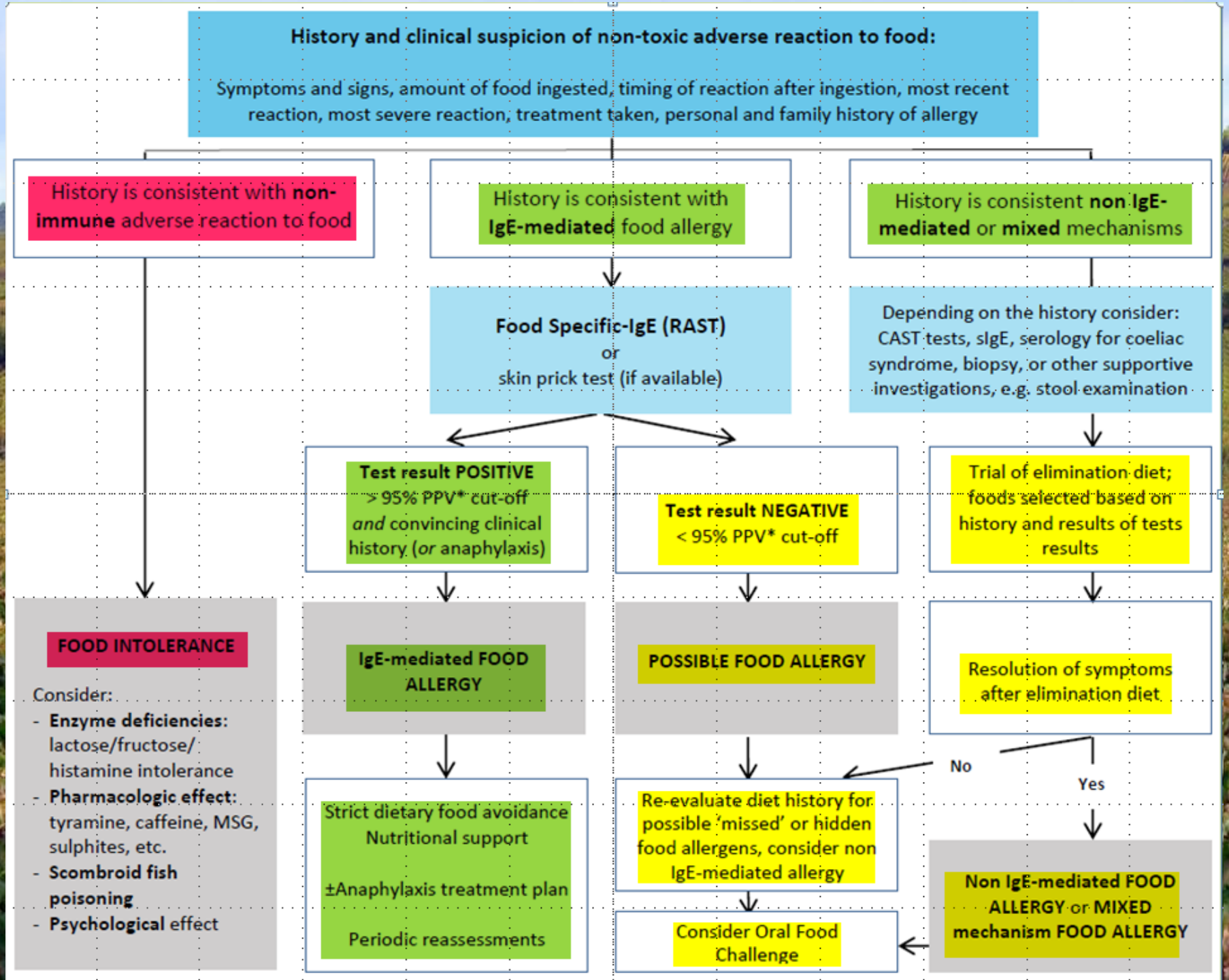
- plus tardifs
- plus prolongés
- beaucoup plus puissants que ceux de l'histamine

Qu'est-ce qui rend un individu atopique?

Facteurs génétique: Histoire familiale fréquente

- loci sur 5q lié à une région qui code pour plusieurs cytokines dont IL-3, IL-4, IL-5, IL-9, IL-13 et GM-CSF
- loci sur 11q lié à une région qui code pour la chaîne β du récepteur de haute affinité pour les IgE

Facteurs de l'environnement : Importants (concordance <50% chez jumeaux homozygotes)


History and clinical suspicion of non-toxic adverse reaction to food:
Symptoms and signs, amount of food ingested, timing of reaction after ingestion, most recent reaction, most severe reaction, treatment taken, personal and family history of allergy
History is consistent with non-immune adverse reaction to food
History is consistent with IgE-mediated food allergy
History is consistent non IgE-mediated or mixed mechanisms
Food Specific-IgE (RAST)
or
skin prick test (if available)
Depending on the history consider: CAST tests, sIgE, serology for coeliac syndrome, biopsy, or other supportive investigations, e.g. stool examination
Test result POSITIVE
> 95% PPV* cut-off
and convincing clinical history (or anaphylaxis)
Test result NEGATIVE
< 95% PPV* cut-off
Trial of elimination diet; foods selected based on history and results of tests results
FOOD INTOLERANCE
Consider:
- Enzyme deficiencies: lactose/fructose/ histamine intolerance
- Pharmacologic effect: tyramine, caffeine, MSG, sulphites, etc.
- Scombroid fish poisoning
- Psychological effect
IgE-mediated FOOD ALLERGY
POSSIBLE FOOD ALLERGY
Resolution of symptoms after elimination diet
No
Yes
Strict dietary food avoidance
Nutritional support
±Anaphylaxis treatment plan
Periodic reassessments
Re-evaluate diet history for possible 'missed' or hidden food allergens, consider non IgE-mediated allergy
Consider Oral Food Challenge
Non IgE-mediated FOOD ALLERGY or MIXED mechanism FOOD ALLERGY

DERMATITE ATOPIQUE
Mise au point au laboratoire d'immunologie et par un dispositif d'imagerie par lampes LED

Merci aux Drs JM Philippart de Foy et Isabelle Dequenne

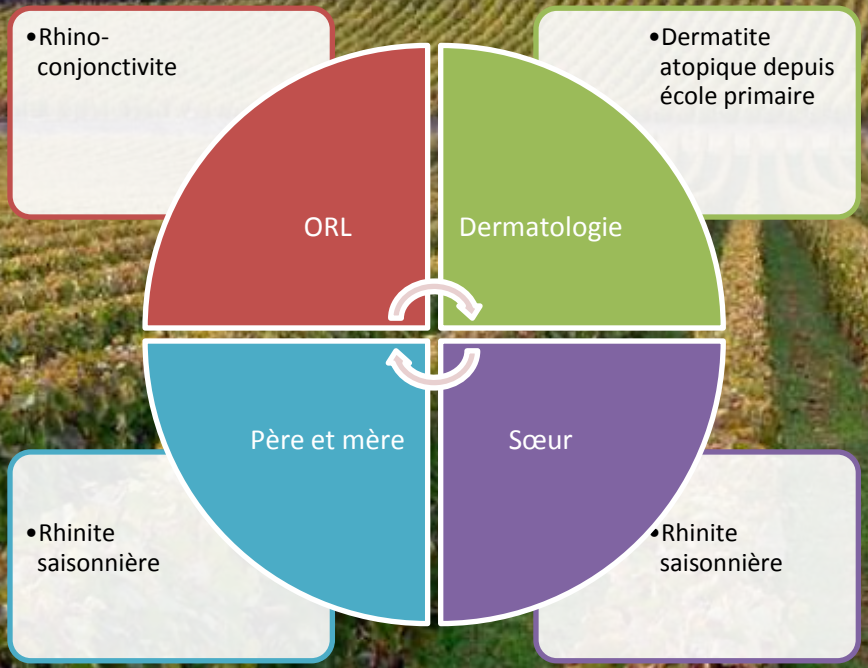
Candidat: Dr JM Philippart de Foy et Dr Isabelle Dequenne
Promoteur du mémoire : Docteur Chantal Dangoisse
Année académique 2012-2013
Certificat d'Université en immunoallergologie de l'ULB

Histoire clinique : JF, 26 ans, origine vietnamienne

- **Depuis l'enfance**
  - Dermatite atopique
  - Récidivant à l'arrêt des R
- **Depuis 2010**
  - Poussées plus fréquentes
  - Poussées plus marquées
- **Février 2013**
  - Retour sports d'hiver
  - SCORAD 38,2

ANAMNESE

ATCD personnels et familiaux



Environnement

Mise au point Diagnostic (1)

Examen clinique février 2013

Dermatologie

- Pas de xérose cutanée franche (en dehors des zones eczématisées)
- Dermographisme
- Quelques stries de grattage
- Eczéma : paupières, joues (dépigmentation inflammatoire), cou (lichénification), épaules, dos, plis des coudes (lichénification), creux poplités.

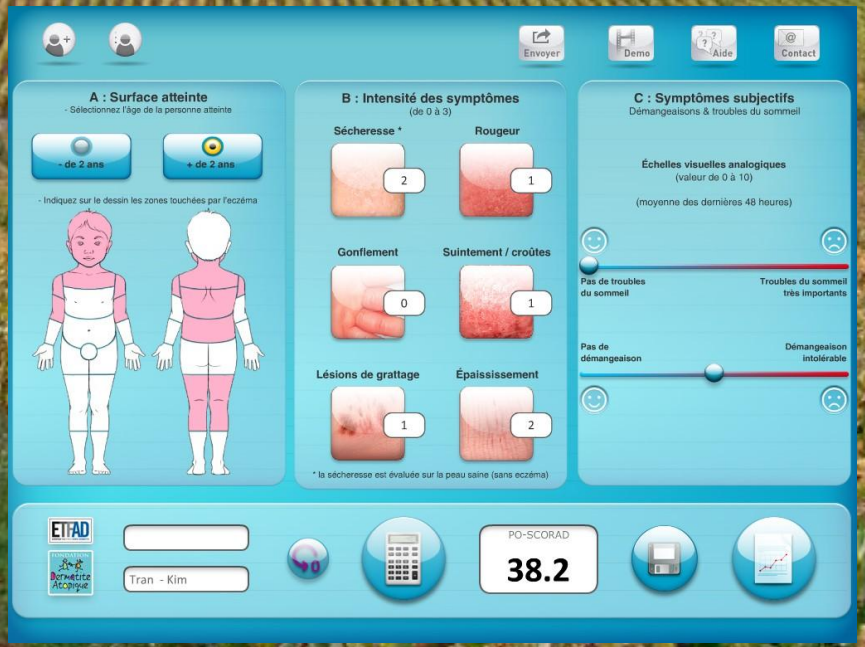
BMI

- 19,8
- Tour de taille 59 cm

Cardio-pulmonaire

- TA : 110/60 mm Hg
- Bruit respiratoire normal
- Pouls périphériques palpés

SCORAD



Mise au point diagnostic (2)

Examens antérieurs

2005 PT	2005 Rast IgE	2011 Patch Test Tous Négatifs	2011 IgE	2011 Nutrition
• Chien + • Chat + • Cheval +	• Chien + • Chat + • Cheval +	• Série standard • Allergènes médicamenteux + stéroïdes • Cosmétiques + parfums • 8 produits personnels	• 107 kU/l • RAST : **Ex1 Mixture d'animaux ➔ 20,3U/ml**	• ↓vitamine E • ↓ zinc

Mise au point diagnostic (3)

2013

Mg	IgE	Rast IgE	IgG spécifiques*
• 4,38 mg/dl • Norme : 4,4-6,79	• 116 kU/L	• Ex1 **Mixture d'animaux ➔ 16,7 U/ml**	• Œuf : < 2 mg/dl • **Caséine : 84,9 mg/L** • Gluten : < 2 mg/dl

***UniCAP (Phadia, Uppsala, Sweden)**

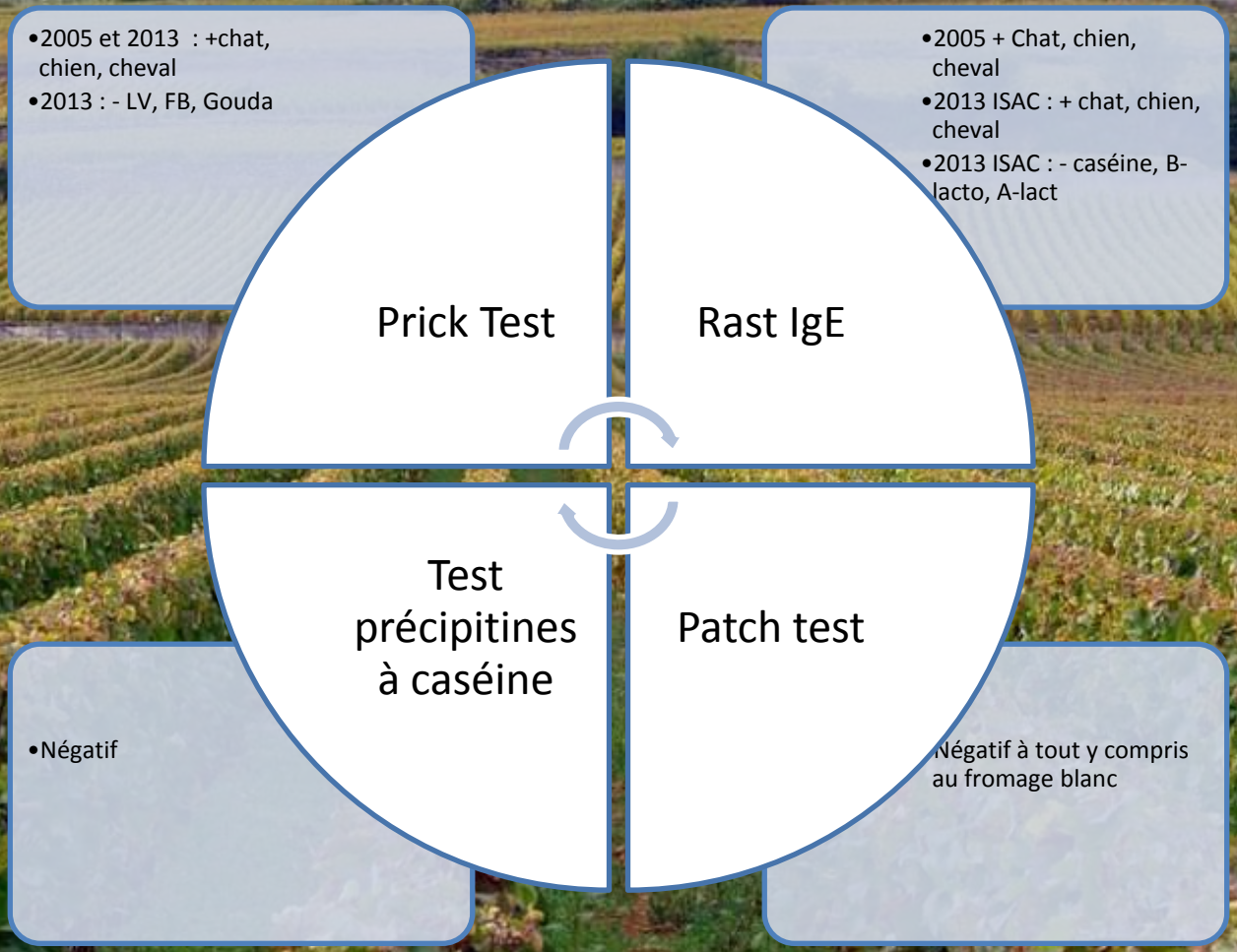
Mise au point diagnostic 2013 (4)

Test	Lieu	
Test de précipitines à la caséine	CHU Brugmann	négatif
Test ISAC *	CHU Brugmann	**Ci contre**
Prick test	Cabinet	**Ci contre**
Patch fromage blanc	Cabinet	Négatif à 48h Négatif à 72 h
Test de PO aux PLV**	Cabinet	Voir ci après

ISAC (Immuno Solid phase Allergen Chip)			
Chien	rCan f 5	Arginine estérase	**66 ISU-E**
Cheval	rEqu c 1	lipocalin	**15 ISU-E**
Chat	rFeld d 4	Lipocalin	**4.2 ISU-E**
Souris	nMus m 1	Lipocalin	**1.7 ISU-E**

Prick Test	
Chien stallergènes	Papule **5 mm**
Cheval stallergènes	Papule **5 mm**
Lait de vache stallergènes	Négatif
Lait de vache natif	Négatif
Fromage blanc natif	Négatif
Gouda natif	Négatif

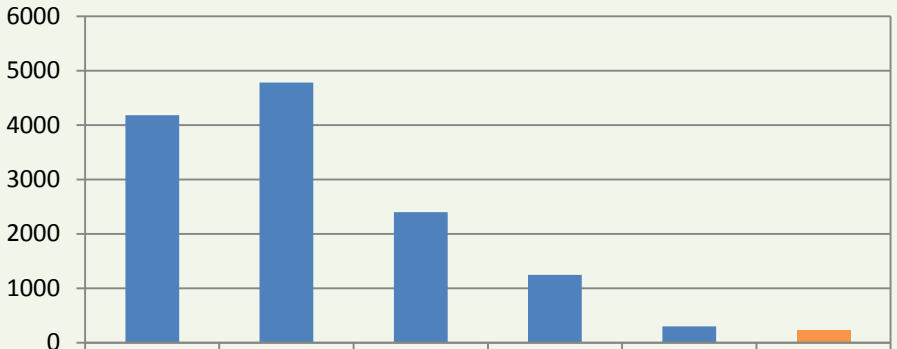
Résumé


•2005 et 2013 : +chat, chien, cheval
•2013 : - LV, FB, Gouda
•2005 + Chat, chien, cheval
•2013 ISAC : + chat, chien, cheval
•2013 ISAC : - caséine, B-lacto, A-lact
Prick Test
Rast IgE
Test précipitines à caséine
Patch test
•Négatif
Négatif à tout y compris au fromage blanc

Test éviction des produits laitiers : 4 arguments

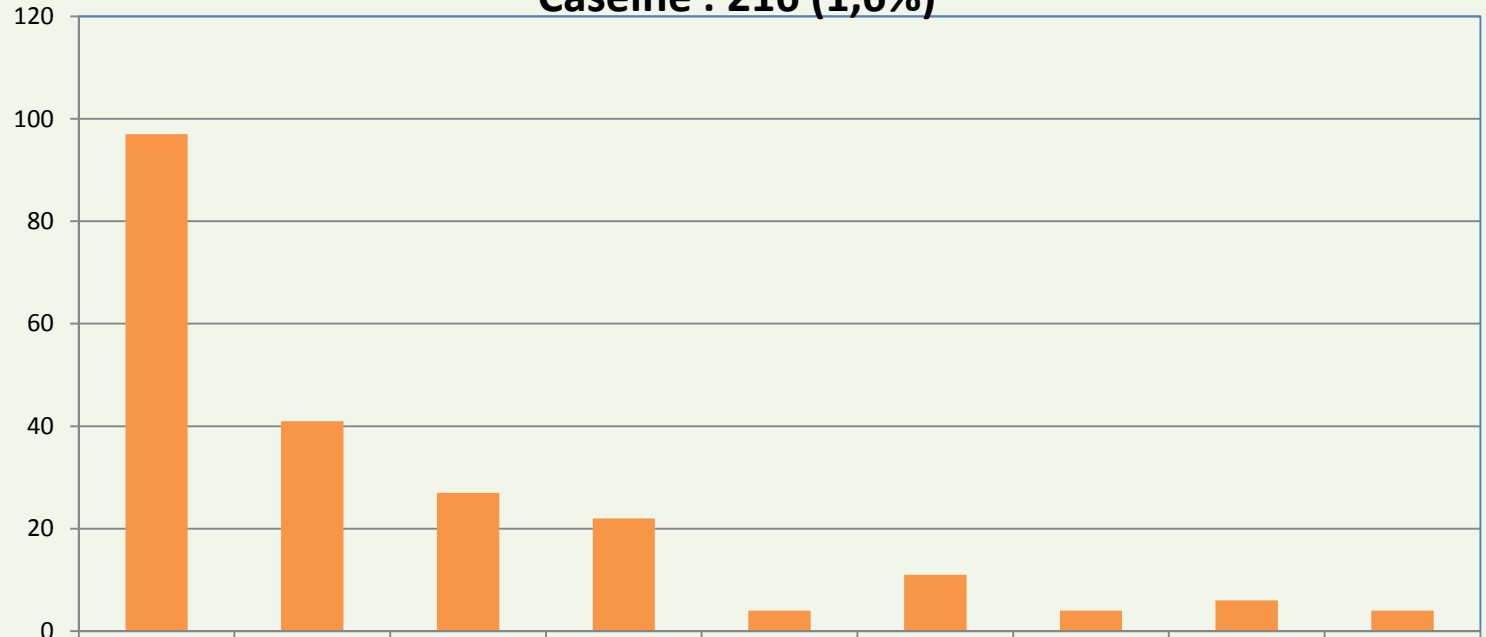
Biologique	• Réponse IgG ➔ caséine
Anamnestique	• Aggravation DA depuis mise en couple avec jeune caucasien gros consommateur de produits laitiers • Nette aggravation après une semaine en Savoie : tartiflette, raclette, fromage de montagne
Habitudes familiales vietnamiennes	• Peu de produits laitiers
Bilan allergologique	• Aucun résultat pertinent pour expliquer DA

Caséine : 13.115



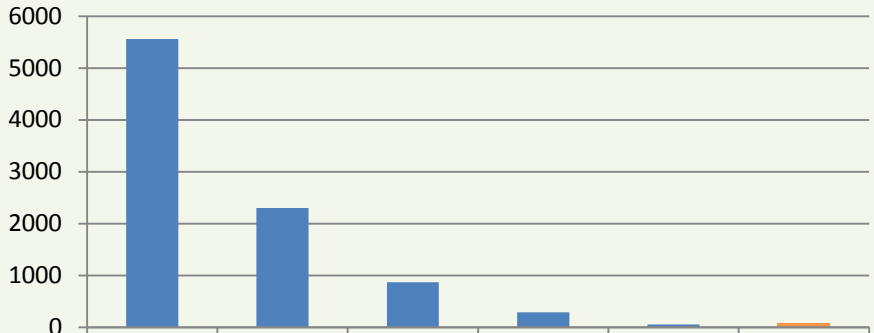
	0-2 mg/l	2-5 mg/l	5-10 mg/l	10-20 mg/l	20-30 mg/l	> 30 mg/l
Série1	4180	4780	2399	1243	297	216
Série2	31,9%	36,4%	18,3%	9,5%	2,3%	1,6%

Caséine : 216 (1,6%)



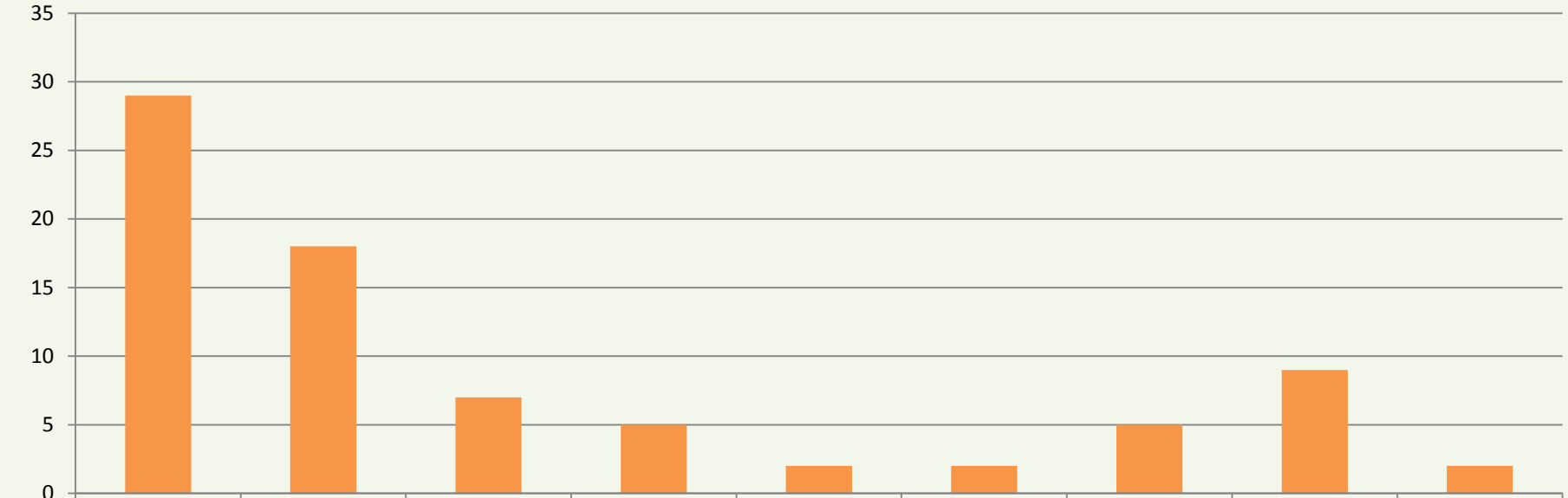
	30-40 mg/l	40-50 mg/l	50-60 mg/l	60-70 mg/l	70-80 mg /l	80-90 mg/l	90-100 mg/l	100-200 mg/l	>200 mg/l
Série1	97	41	27	22	4	11	4	6	4
Série2	0,74%	0,31%	0,21%	0,17%	0,03%	0,08%	0,03%	0,05%	0,03%

A-lactalbumine : 9.151



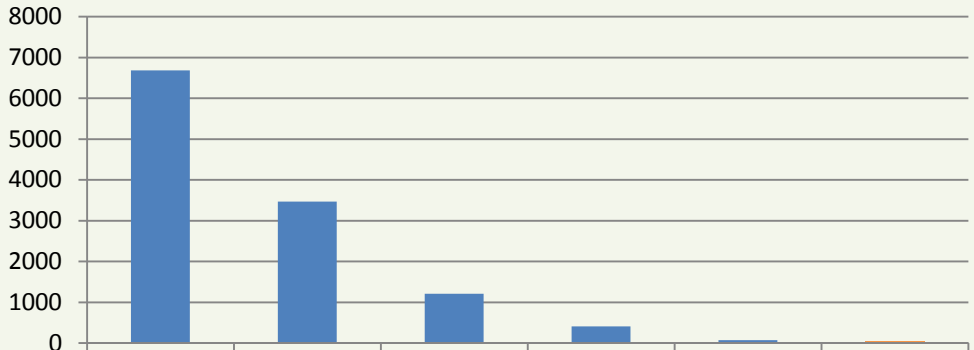
	0-2 mg/l	2-5 mg/l	5-10 mg/l	10-20 mg/l	20-30 mg/l	> 30 mg/l
Série1	5558	2302	867	288	57	79
Série2	60,7%	25,2%	9,5%	3,1%	0,6%	0,9%

A-lactalbumine : 79 (0,9%)



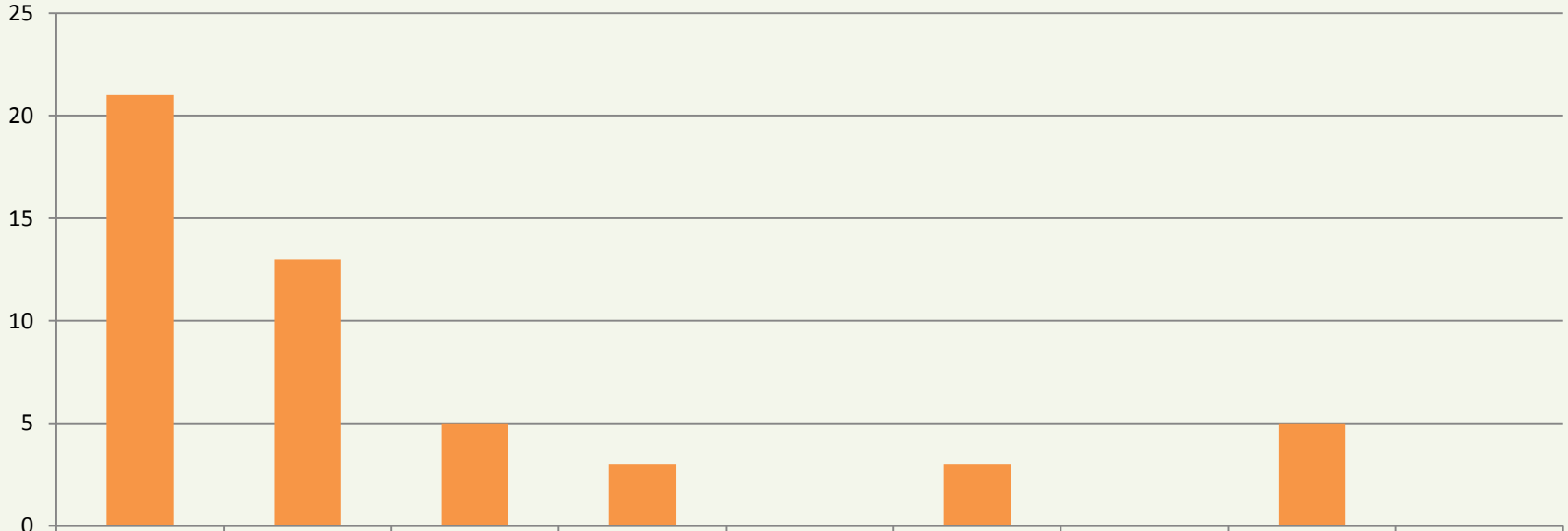
	30-40 mg/l	40-50 mg/l	50-60 mg/l	60-70 mg/l	70-80 mg /l	80-90 mg/l	90-100 mg/l	100-200 mg/l	>200 mg/l
Série1	29	18	7	5	2	2	5	9	2
Série2	0,32%	0,20%	0,08%	0,05%	0,02%	0,02%	0,05%	0,10%	0,02%

B-lactoglobuline : 11.892



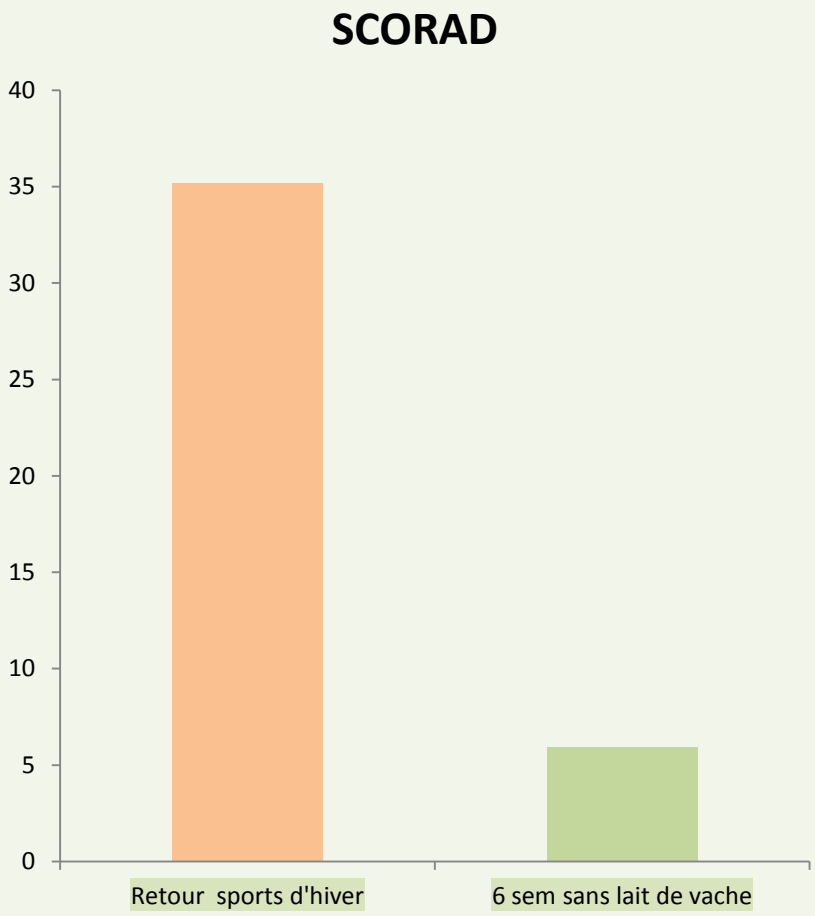
	0-2 mg/l	2-5 mg/l	5-10 mg/l	10-20 mg/l	20-30 mg/l	> 30 mg/l
Série1	6684	3470	1212	406	70	50
Série2	56,2%	29,2%	10,2%	3,4%	0,6%	0,4%

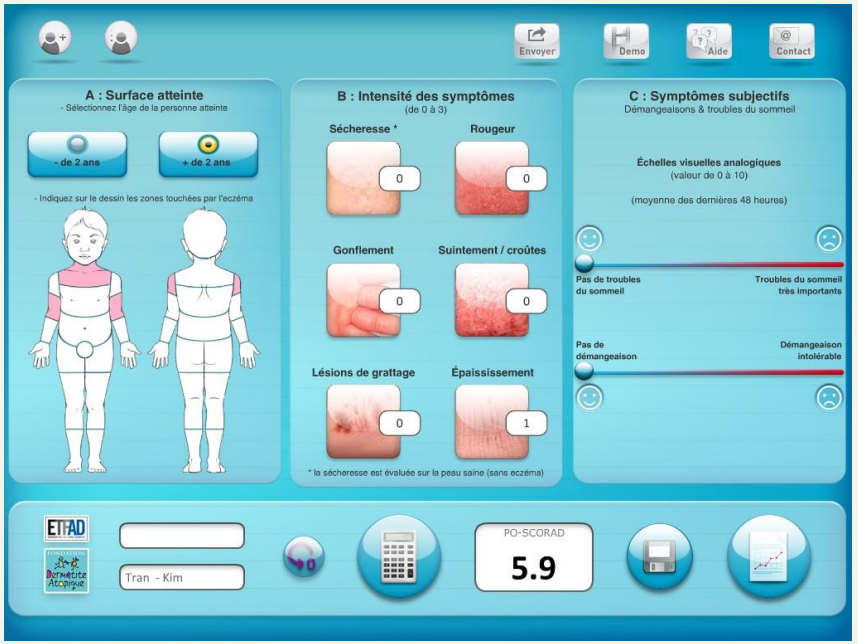
B-lactoglobuline : 50 (0,4%)



	30-40 mg/l	40-50 mg/l	50-60 mg/l	60-70 mg/l	70-80 mg /l	80-90 mg/l	90-100 mg/l	100-200 mg/l	>200 mg/l
Série1	21	13	5	3	0	3	0	5	0
Série2	0,18%	0,11%	0,04%	0,03%	0,00%	0,03%	0,00%	0,04%	0,00%

Evolution du SCORAD après éviction du LV



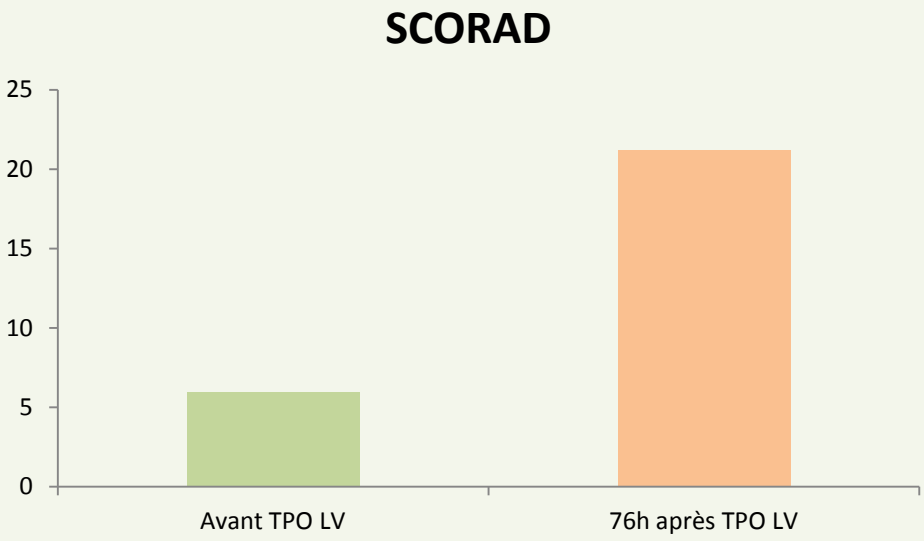


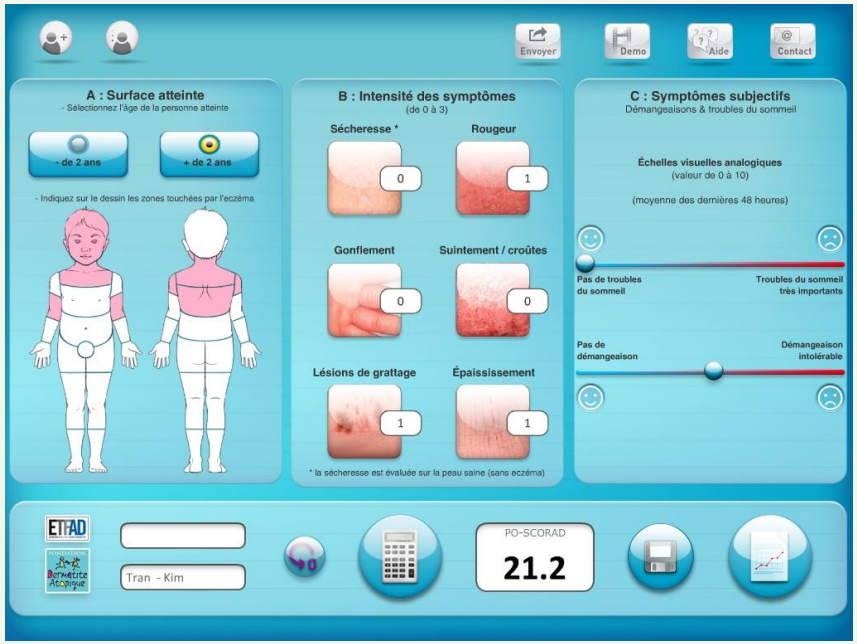
Test de provocation aux PLV

Qu'est ce que ça va donner???

« Beurk, c'est bien parce que c'est le futur grand père de mes enfants »

Evolution du SCORAD après 76h TPO aux PLV





Réflexions IgG caséine

Un point de vue

- Uniquement reflet de la consommation de l'aliment
- Monte le lendemain de la consommation de l'aliment
- Paradigme ↑ IgG_4 Bloquant au cours IT ➔ pas possible
- Elle n'a pas pris de la caséine en double aveugle

Un autre point de vue

- Que dire des 86,61% de échantillon < 10 mg/litre?
- Que dire des 1,6% de échantillon > 30 mg/litre?
- Que dire des 0,19% de échantillon > 80 mg/litre?
- Que dire du cas clinique présenté?
- Que dire des autres situations similaires?
- Autres épithélia : alvéolite extrinsèque allergique et préciptines?

Cas clinique

- Mécanisme ?
  - IgG
  - IC?
    - Complément?
    - GR CR1?
    - Neutrophiles ?
  - Mastocytes récepteur FCγ…?
  - LT?
- Refaire test de provocation : cinétique IgG, IC sur 72 heures?
- Elle ne consomme plus de PLV sinon eczéma / de manière itérative

De manière plus large

- Contact des médecins des patients aux valeurs les plus hautes?
  - Plaintes ?
  - ATCD médicaux / chirurgicaux?
  - Mises au point
  - Habitudes alimentaires?
- ….

Interaction de l'Ag avec l'épithélium

- Caséine

Antigène

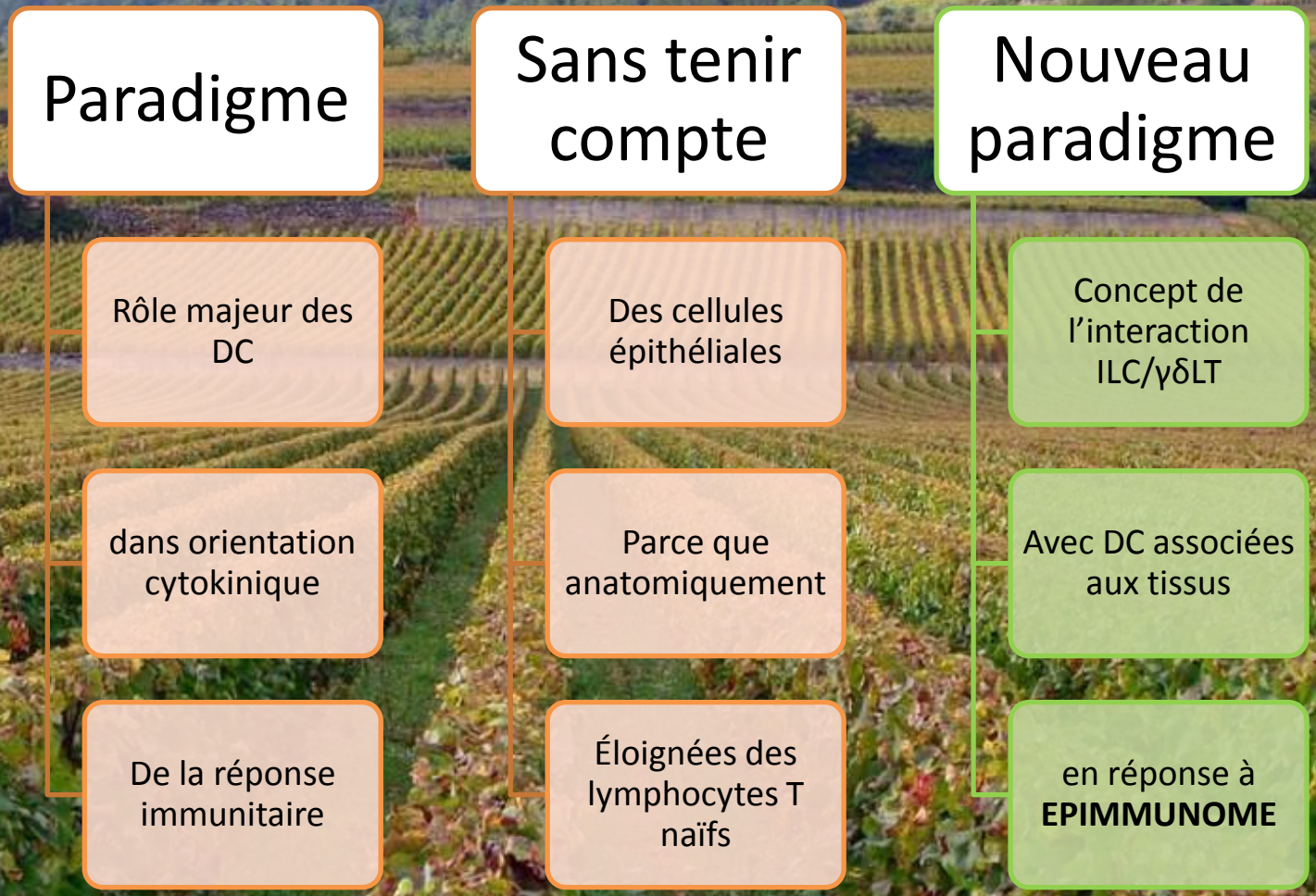
Épimmunome /ILC/DC

- Dans un statut particulier de l'épithélium

- switch isotypique IgG

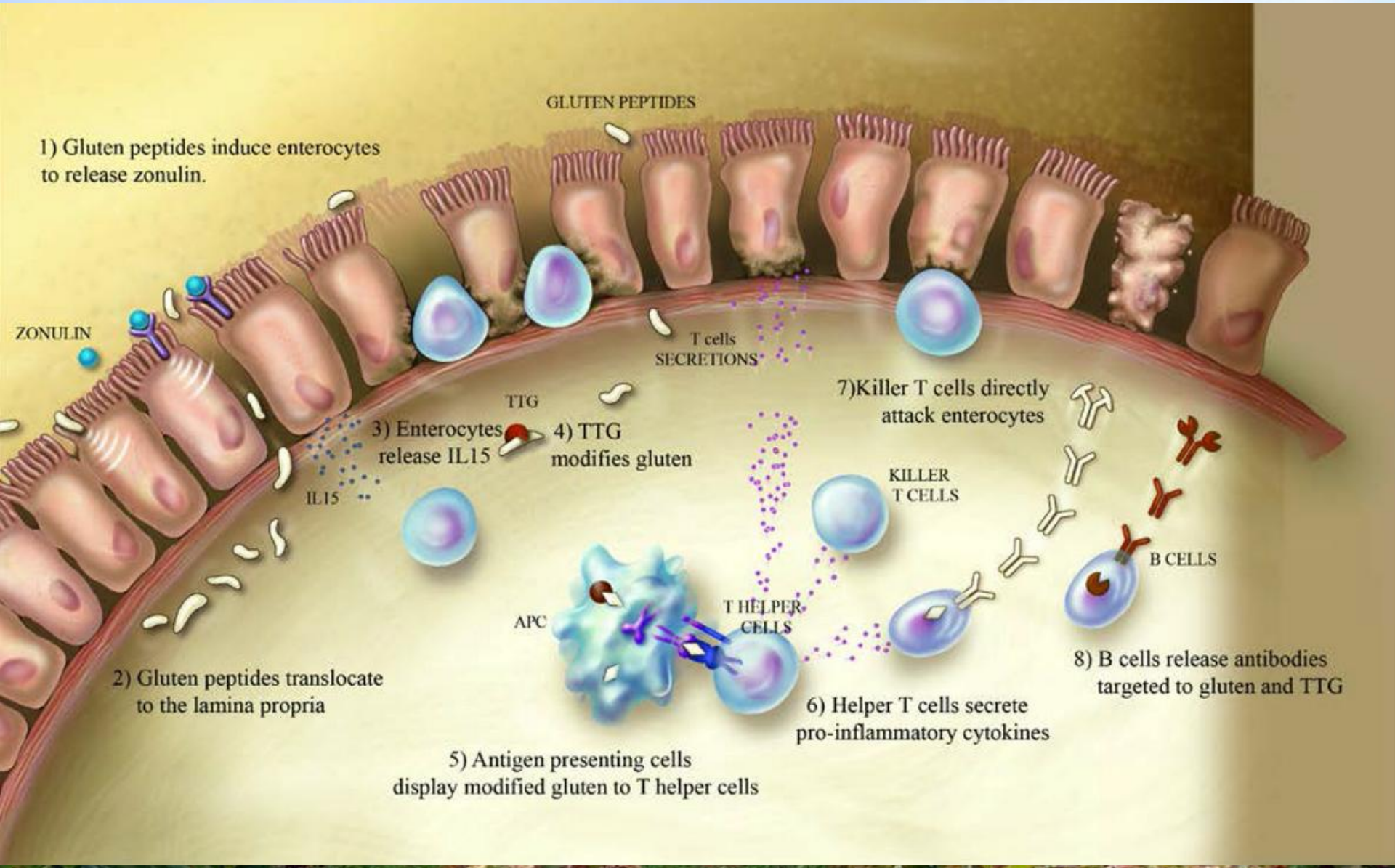
Réponse immune particulière

Interaction épithélium / DC / cellules lymphocytaires



Nature Rev Immunol feb 2013; vol 13: 88-99

Nature Rev Immunol 2010; vol 11: 656-665



Gloria Serena, Nutrients **2015**, *7*(9), 7143-7162

Conclusions et hypothèses

Rôle de IgG isolée ?

Rôle CIC?

Rôle des PMN?

IgG Caséine ?

Révélateur d'une réponse immunitaire en lien avec épimmunome digestif particulier à un moment donné?

Mécanismes LT cellulaires associés à eczéma?

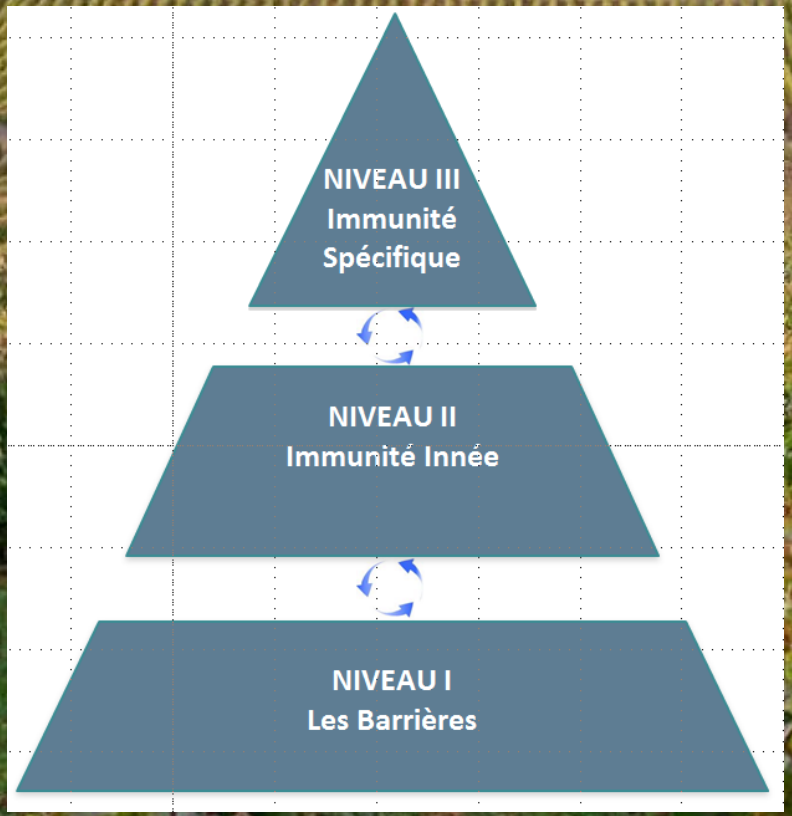
LA PAROLE DU SAGE

« Je boirai du lait le jour où les vaches mangeront du raisin. »

Vu à L'Essentiel, à Beaune

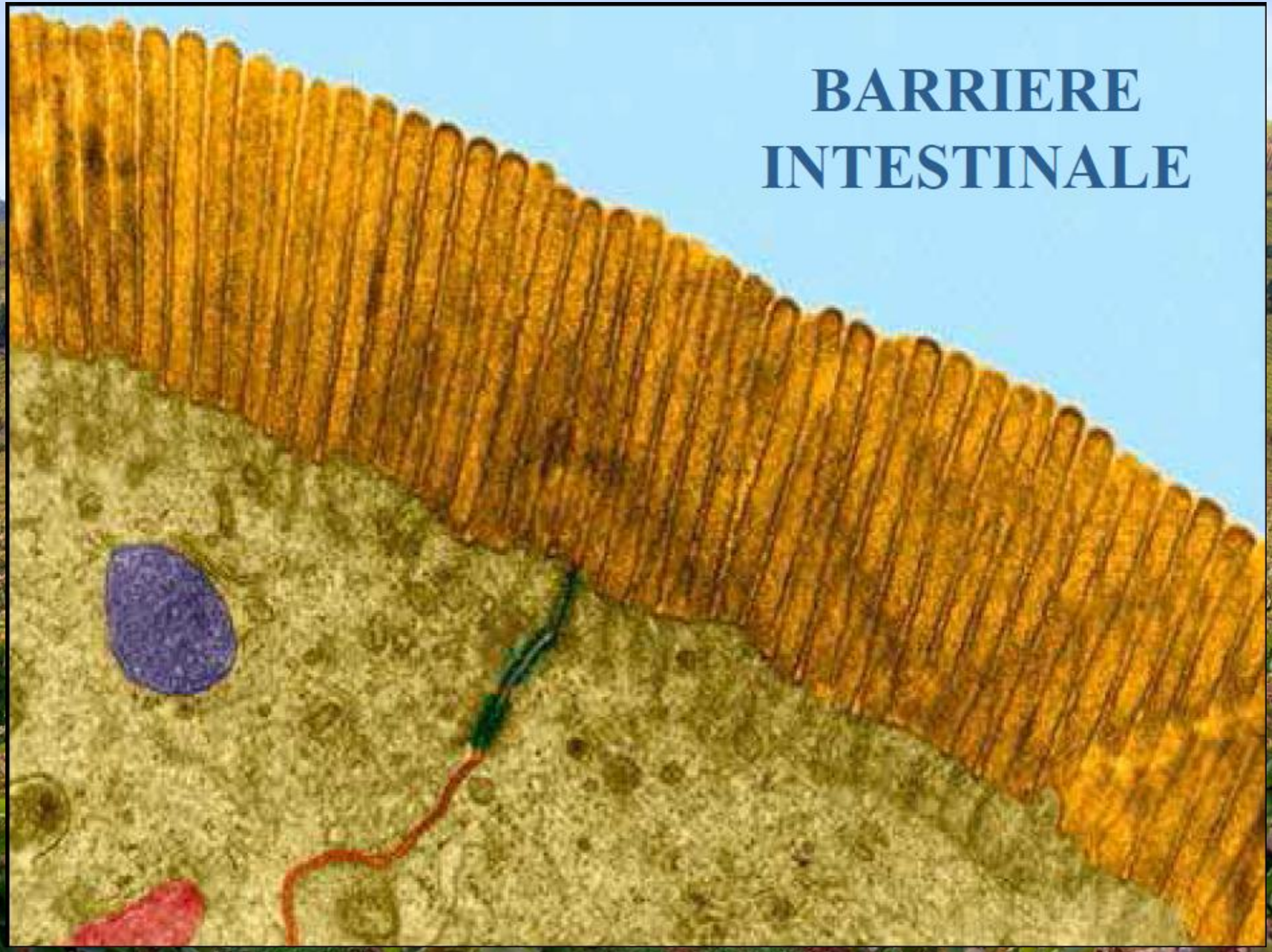
DEFENSES

BARRIERES

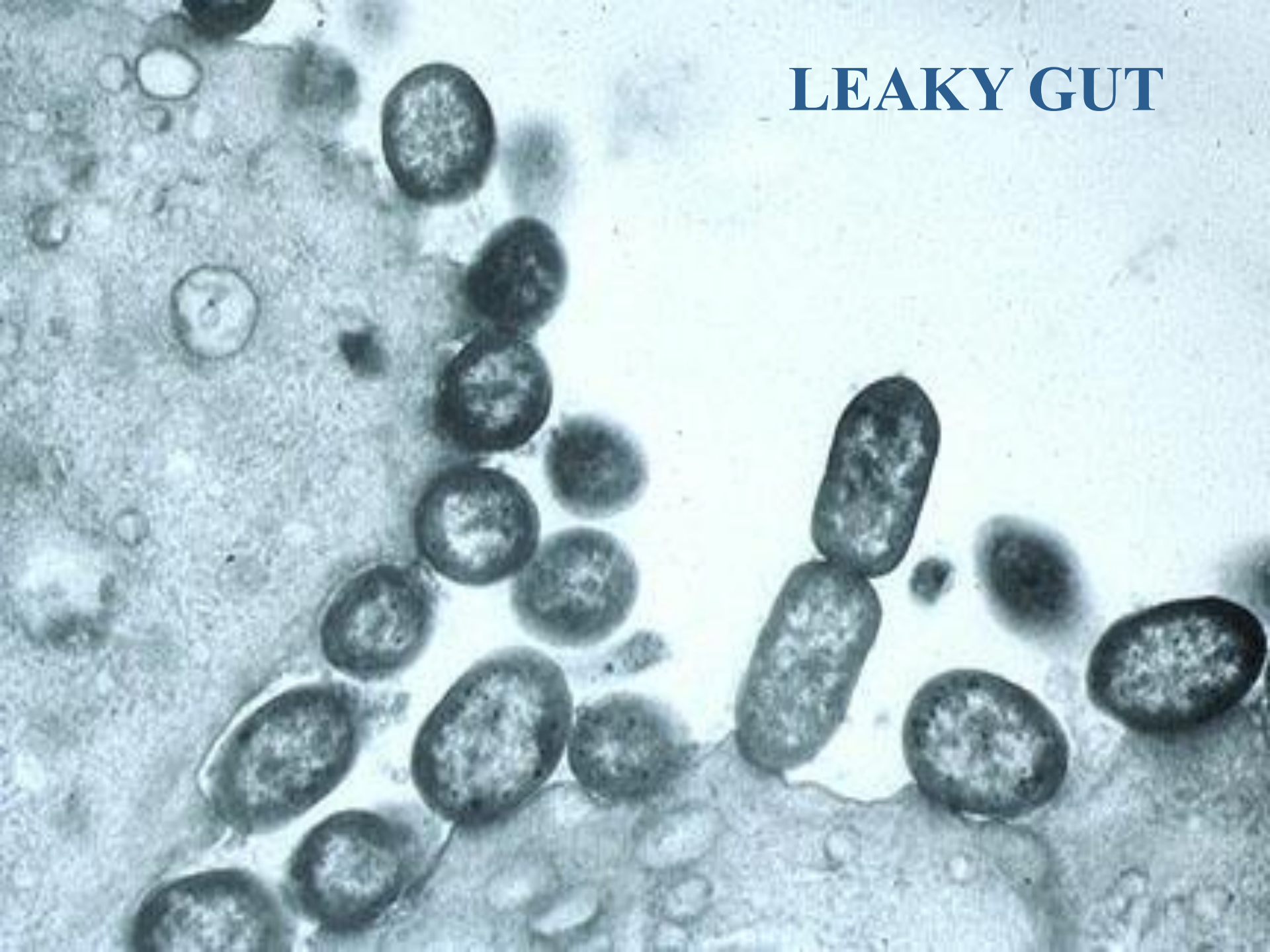


PART 1

BARRIERE INTESTINALE

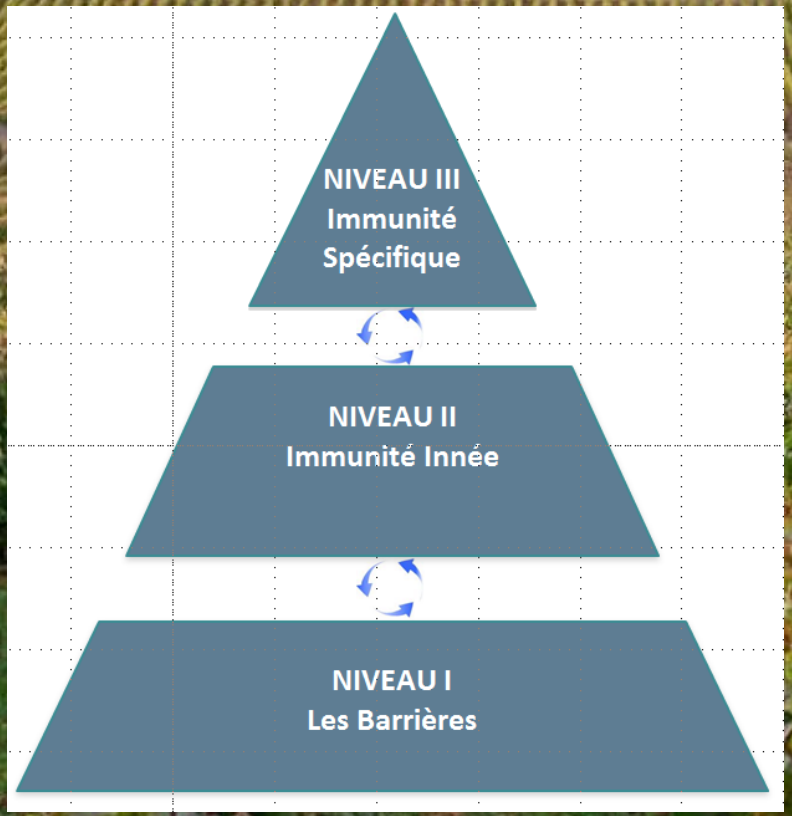


LEAKY GUT



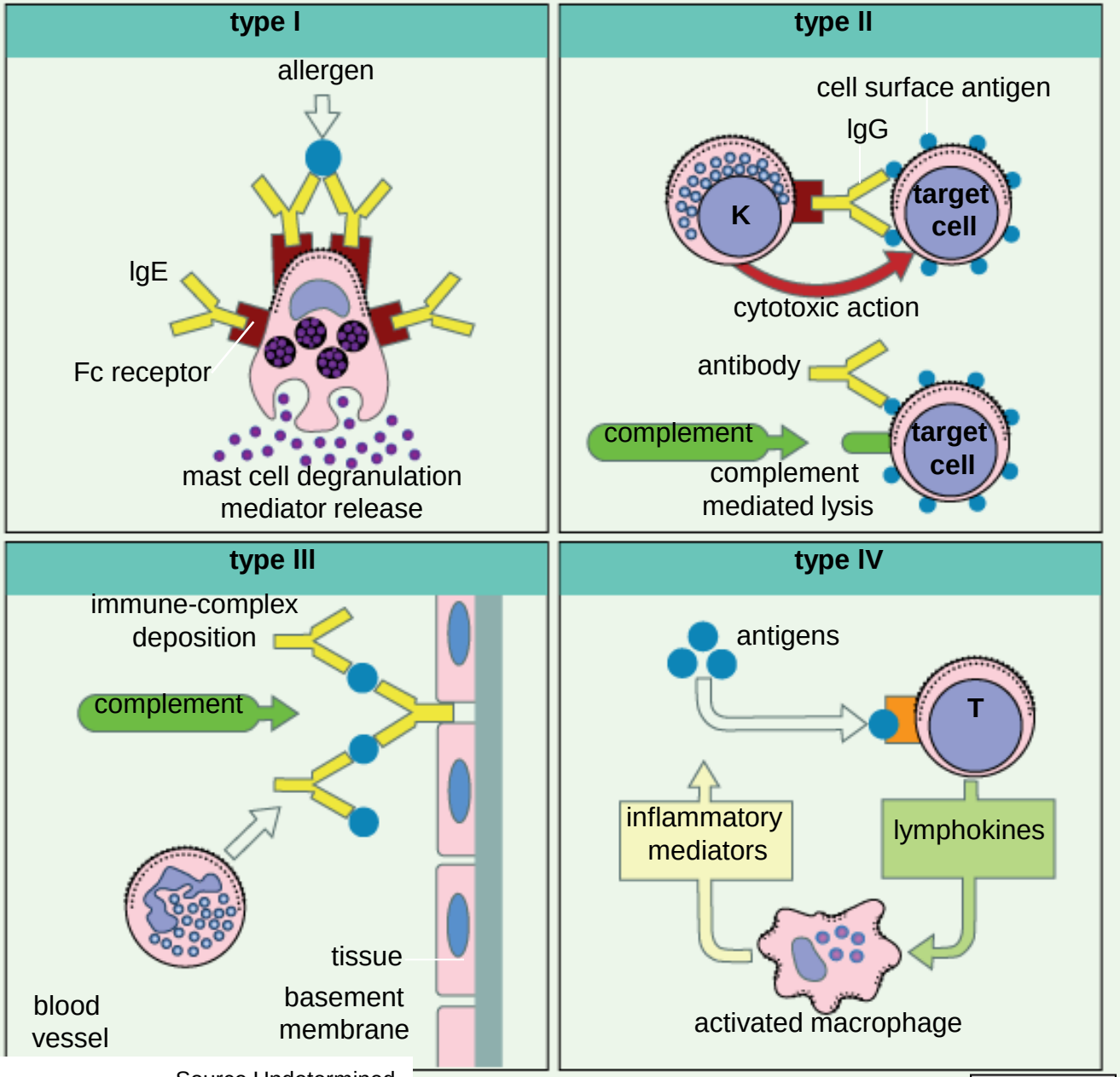
DEFENSES

IMMUNITE



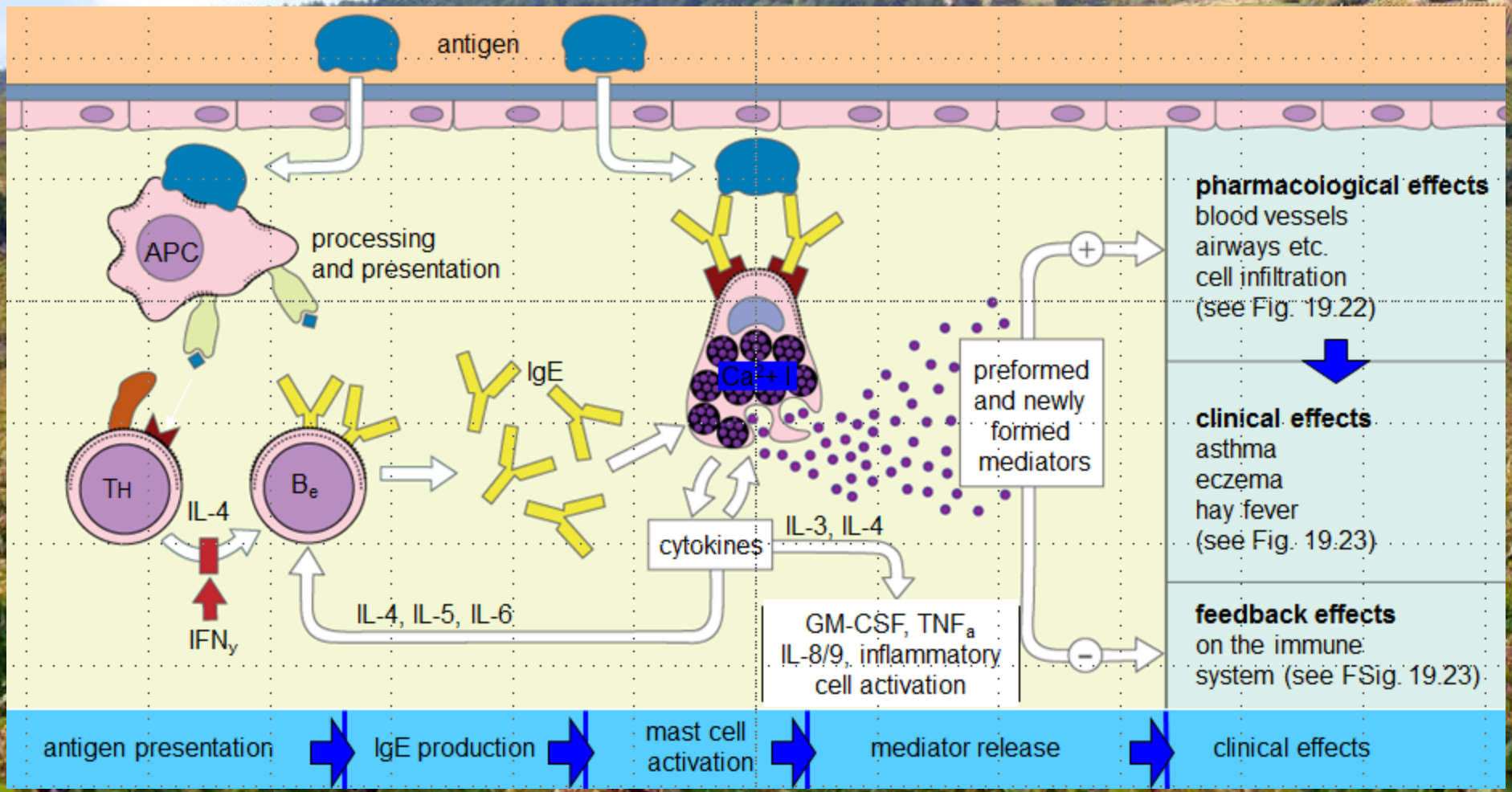
PART 2

The four types of hypersensitivity reaction

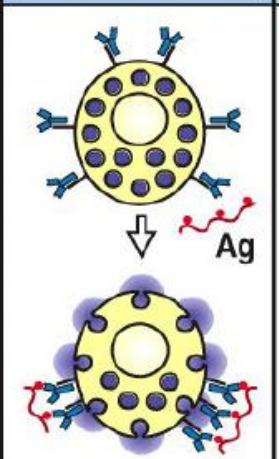
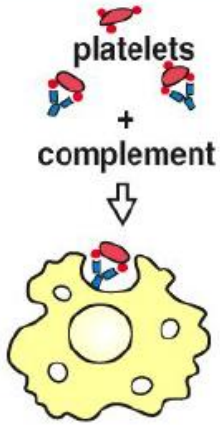
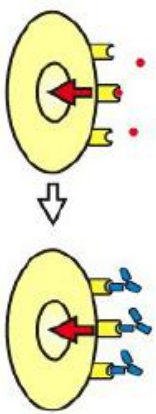
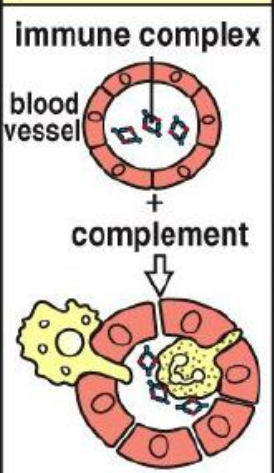
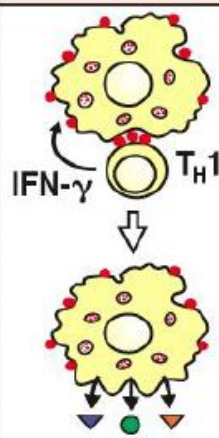
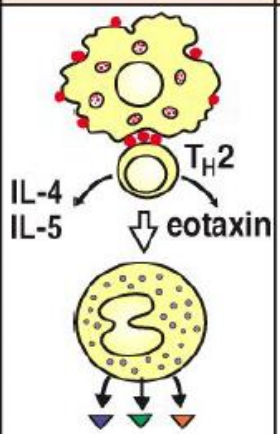
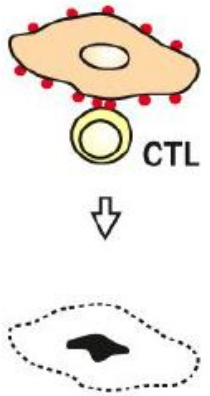


Source Undetermined

Induction and effector mechanisms in Type I Hypersensitivity



Classification of hypersensitivities
Allergic (immunological) HS

Type I	Type II		Type III	Type IV		
IgE	IgG		IgG	T_H1 cells	T_H2 cells	CTL
Soluble antigen	Cell- or matrix-associated antigen	Cell-surface receptor	Soluble antigen	Soluble antigen	Soluble antigen	Cell-associated antigen
Mast-cell activation	Complement, FcR^+ cells (phagocytes, NK cells)	Antibody alters signaling	Complement, Phagocytes	Macrophage activation	IgE production, Eosinophil activation, Mastocytosis	Cytotoxicity
						
° Rhinite allergique ° Asthme, ° Choc anaph. ° Anaphylaxie	° Cytopénies médic. ° Réaction transfus. ° Anémie Hémolytique autoim ° Pemphigus	° Thyroidite ° Myasthénie.	° Réaction d'Arthus ° Maladie sérique ° Lupus érythémateux ° Vasculites immuno.	°IDR tuberculine °Rejet de greffes °Arthrite,Diabète, °Psoriasis	°Asthme chronique °Rhinite chronique °Dermatite atopique	°Dermatite de contact °Rejet de greffes °Diabète type I

Allergy Asthma Proc. 2012 May-Jun

GELL et COOMBS est actuellement inadaptée

Chapter 28: Classification of hypersensitivity reactions.

Uzzaman A[1], Cho SH.

Abstract

The original Gell and Coomb's classification categorizes hypersensitivity reactions into four subtypes according to the type of immune response and the effector mechanism responsible for cell and tissue injury:

type I, immediate or IgE mediated;
type II, cytotoxic or IgG/IgM mediated;
type III, IgG/IgM immune complex mediated;
type IV, delayed-type hypersensitivity or T-cell mediated.

The classification has been improved so that

type IIa is the former type II and

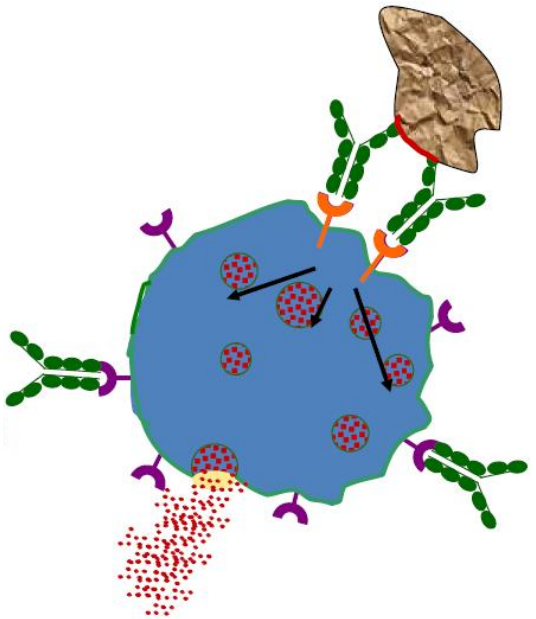
type IIb is antibody-mediated cell stimulating (Graves Disease and the « autoimmune » type of chronic idiopathic urticaria).

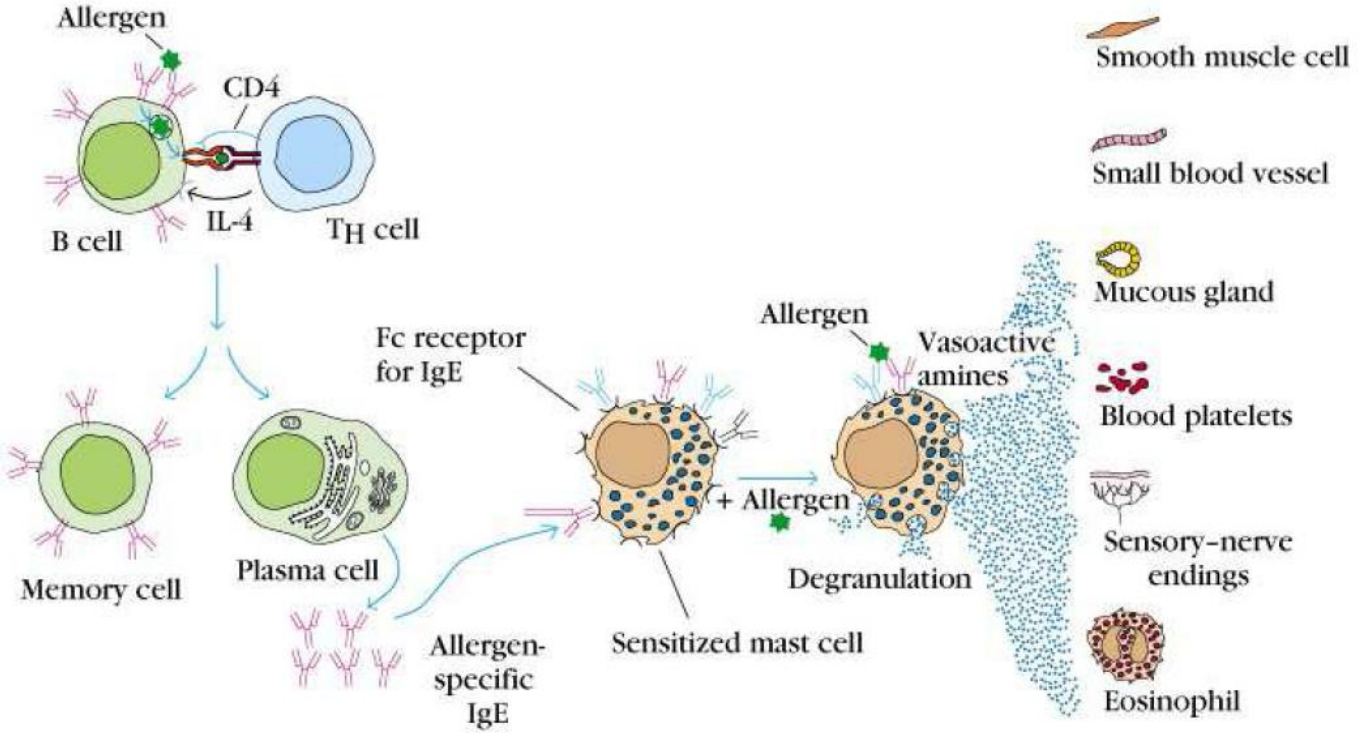
Type IV has four major categories:

type IVa is CD4(+)Th1 lymphocyte mediated with activation of macrophages (granuloma formation and type I diabetes mellitus);

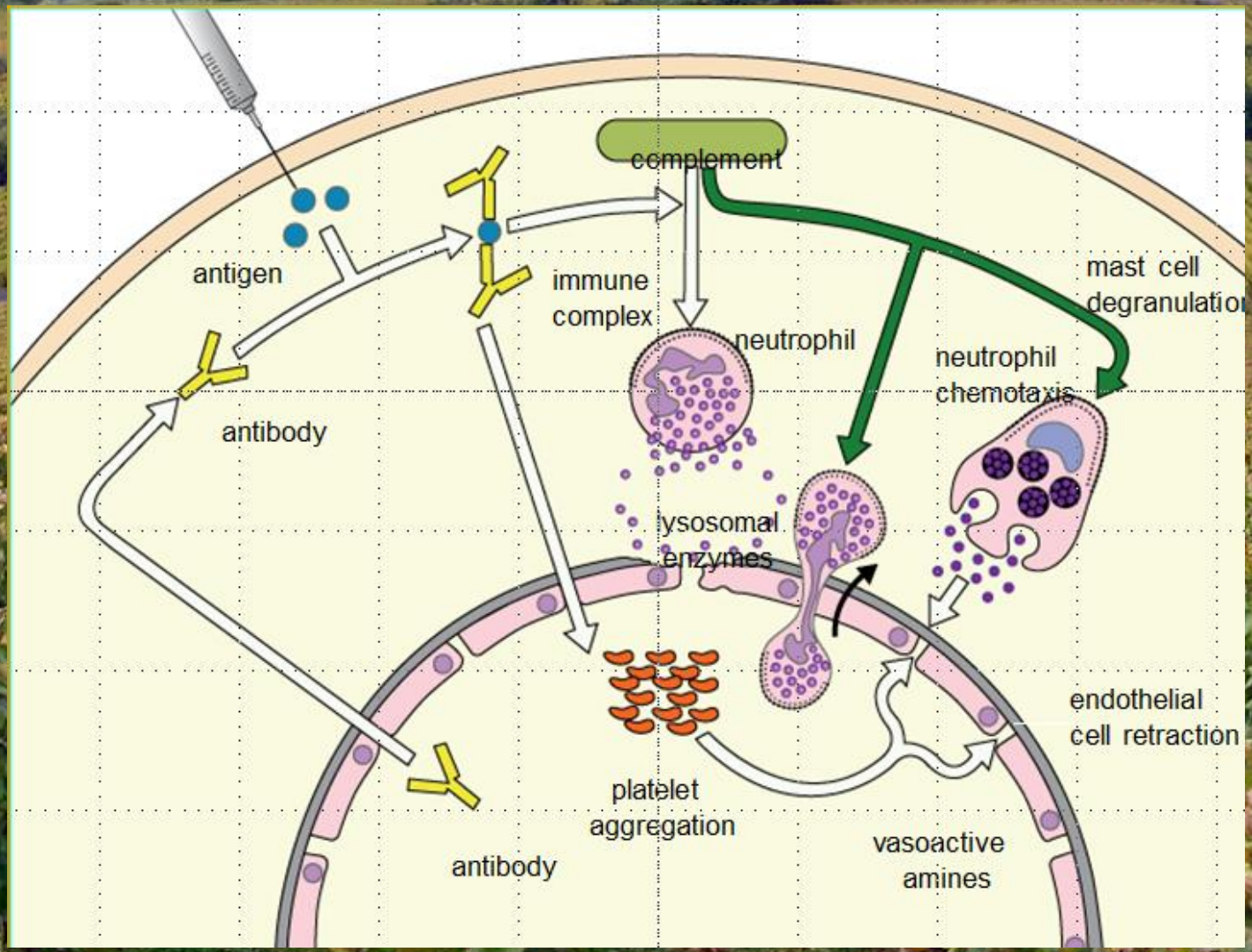
type IVb is CD4(+)Th2 lymphocyte mediated with eosinophilic involvement (persistent asthma and allergic rhinitis);
type IVc is cytotoxic CD8(+) T lymphocyte with involvement of perforin-granzme B in apoptosis (Stevens-Johnson syndrome and toxic epidermal necrolysis);
type IVd is T-lymphocyte-driven neutrophilic inflammation (pustular psoriasis and acute generalized exanthematous pustulosis).

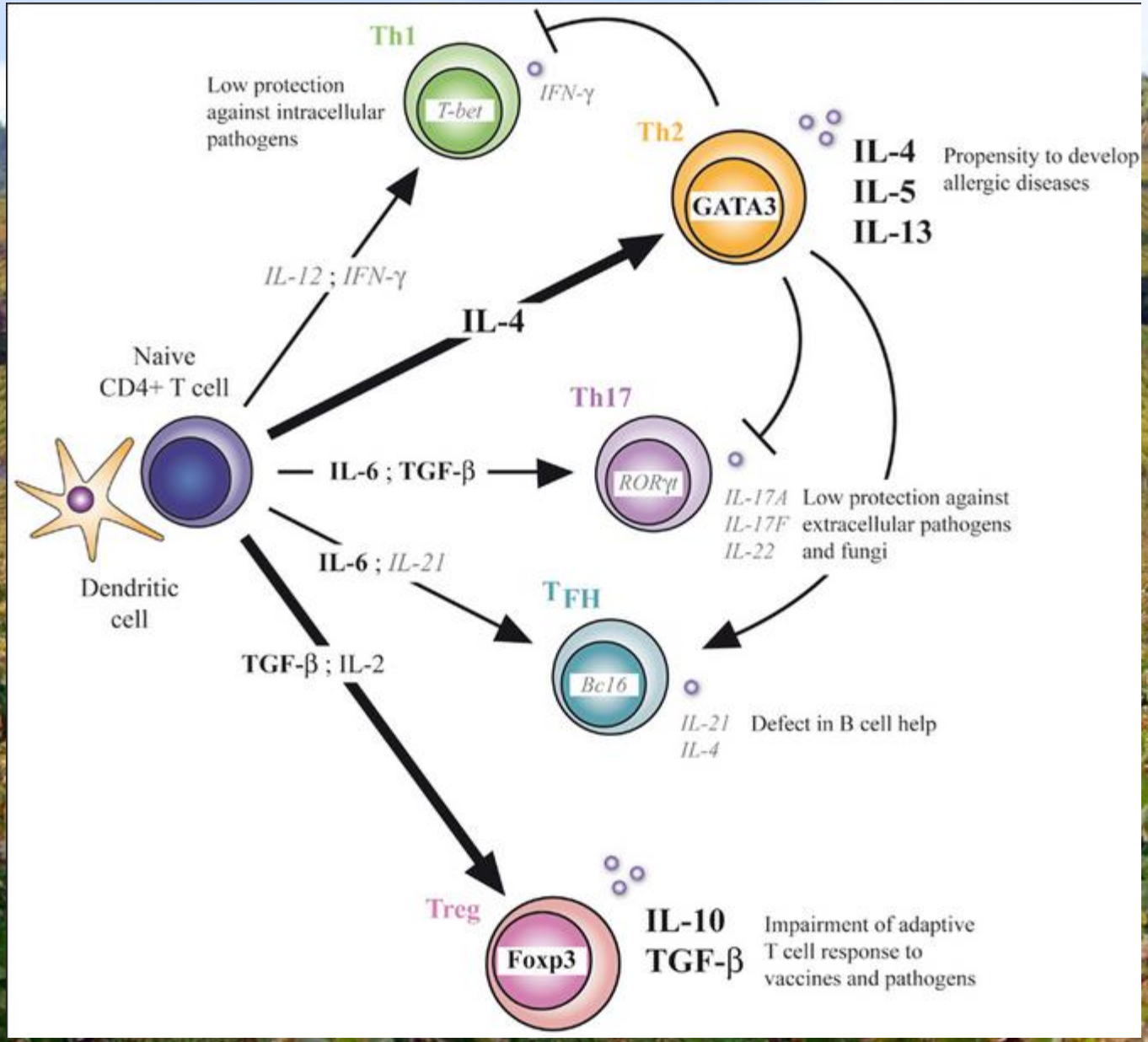
IgE, mastocytes et réactions d'hypersensibilité de type I





Type III Hypersensitivity: Local I.C. Disease




Th1
T-bet
IFN-γ
Low protection against intracellular pathogens
Th2
GATA3
IL-4
IL-5
IL-13
Propensity to develop allergic diseases
IL-12 ; IFN-γ
IL-4
Naive CD4+ T cell
Th17
RORγt
IL-6 ; TGF-β
IL-17A
IL-17F
IL-22
Low protection against extracellular pathogens and fungi
IL-6 ; IL-21
Dendritic cell
TFH
Bc16
TGF-β ; IL-2
IL-21
IL-4
Defect in B cell help
Treg
Foxp3
IL-10
TGF-β
Impairment of adaptive T cell response to vaccines and pathogens

TOLERANCE

Conception ancienne de la tolérance :

1)- Le rôle primordial du système immunitaire est la lutte contre les micro-organismes pathogènes

2)- La tolérance était envisagée comme « l'absence de réaction »

3)- La tolérance est un mécanisme principalement central, reposant sur la délétion des lymphocytes (T & B) autoréactifs

TOLERANCE ORALE

P.A. APOIL – C.H.U de Toulouse - 2013

Conception actuelle :

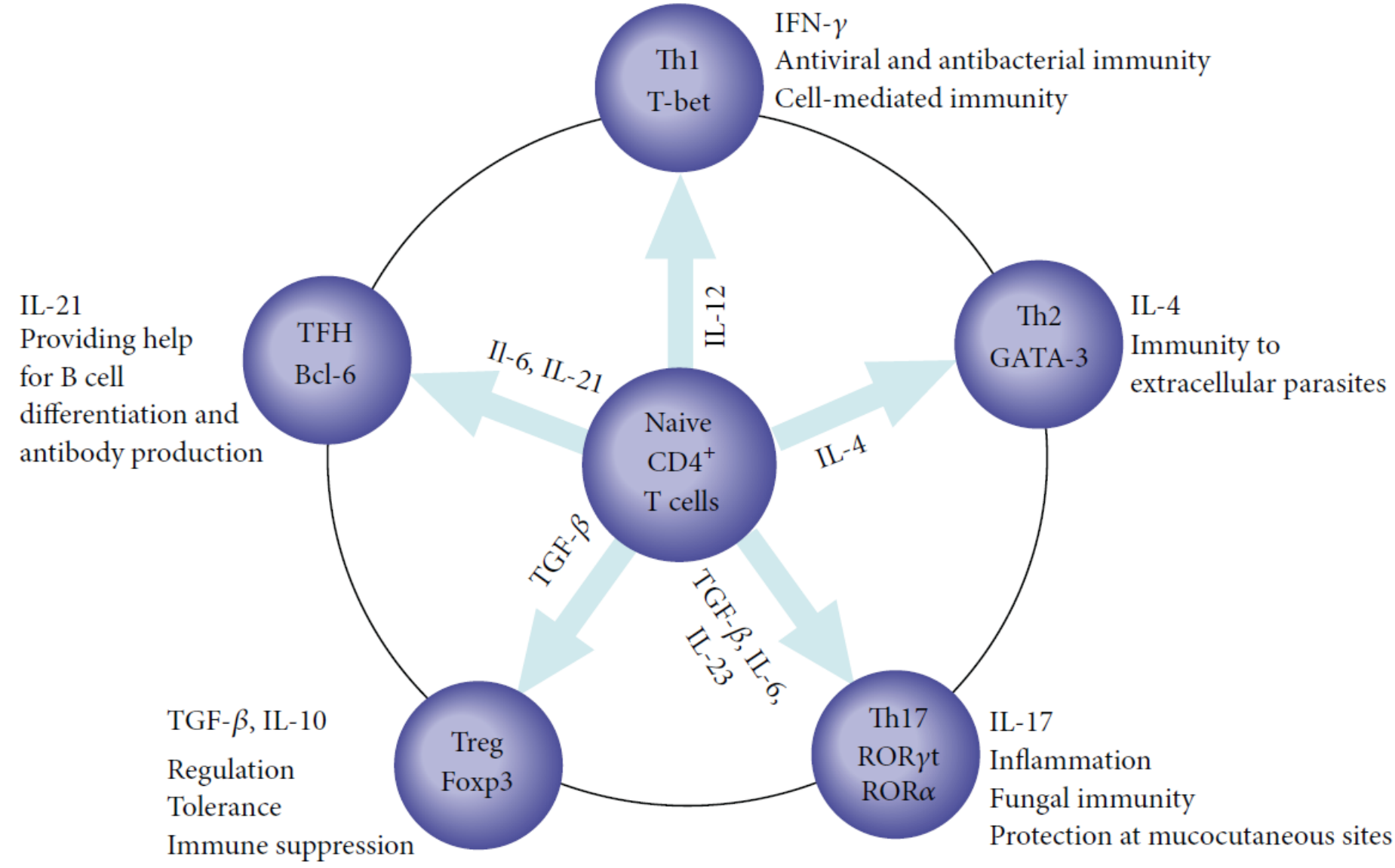
Mécanisme actif & spécifique qui nécessite la présence de l'antigène

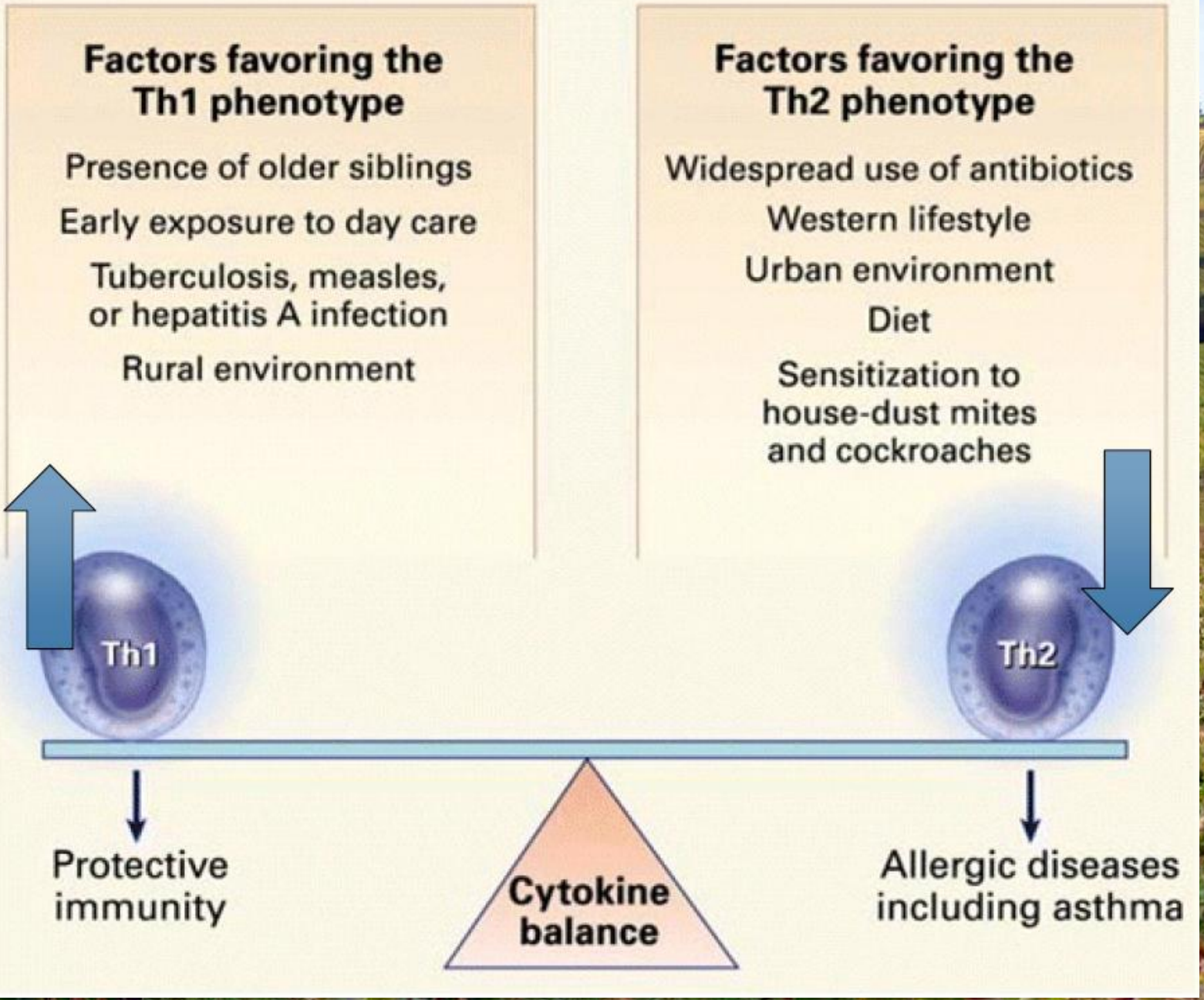
La tolérance est un mécanisme actif, reposant sur de multiples mécanismes, centraux et périphériques…

L'un de ces mécanismes, périphérique, indispensable à la survie de l'individu est la tolérance induite au niveau du tube digestif, ou Tolérance Orale (TO)

La TO est définie par « la suppression des réponses immunitaires systémiques, cellulaire et humorale, dirigées contre un antigène, faisant suite à l'administration de cet antigène par voie orale » *(Chase M.W.– 1946).*

TOUT EST QUESTION D'EQUILIBRE …

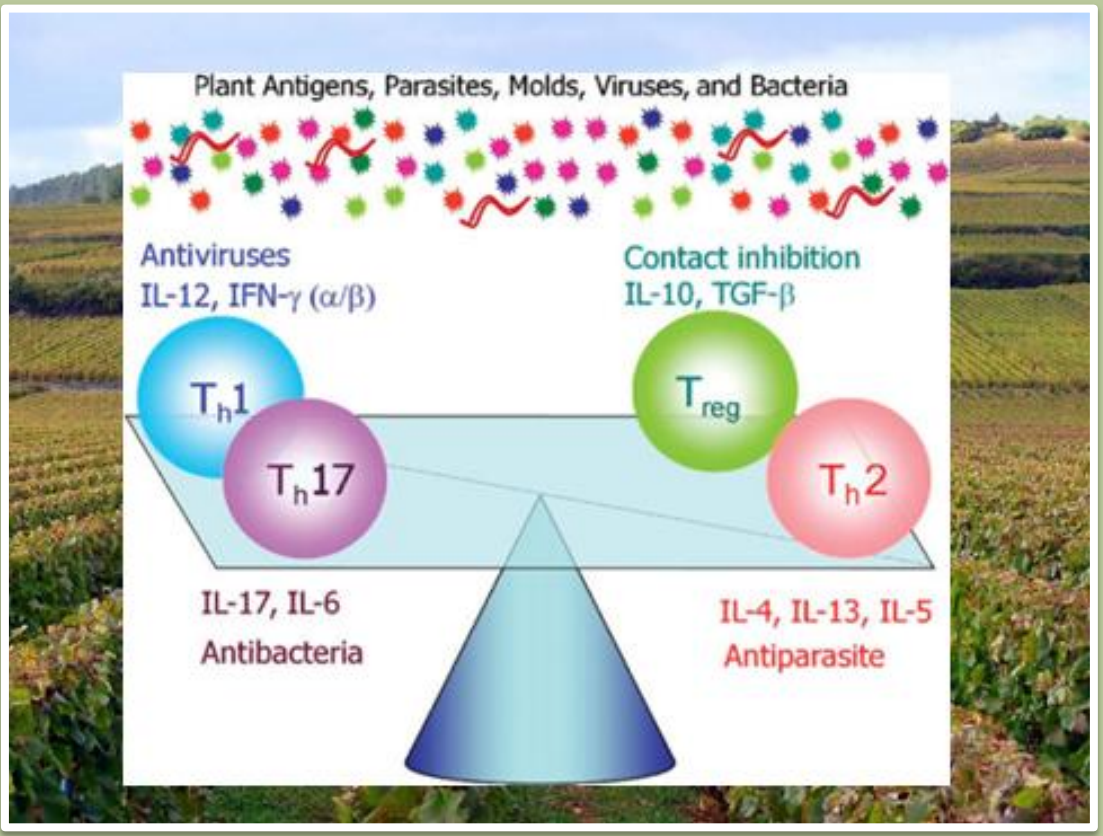


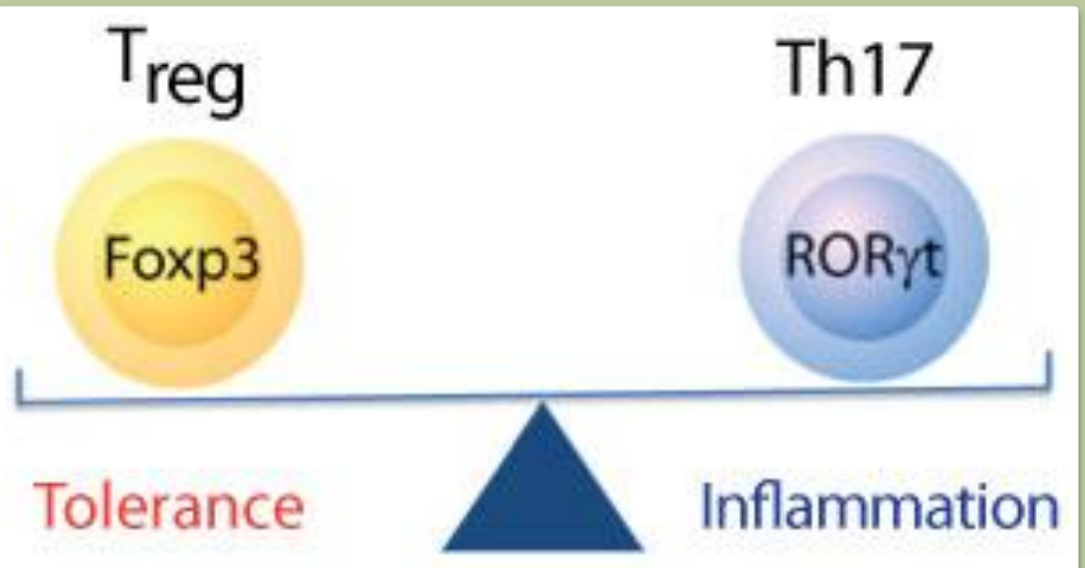


Busse & Lemanske (2001) N Engl J Med ; 344: pg 350

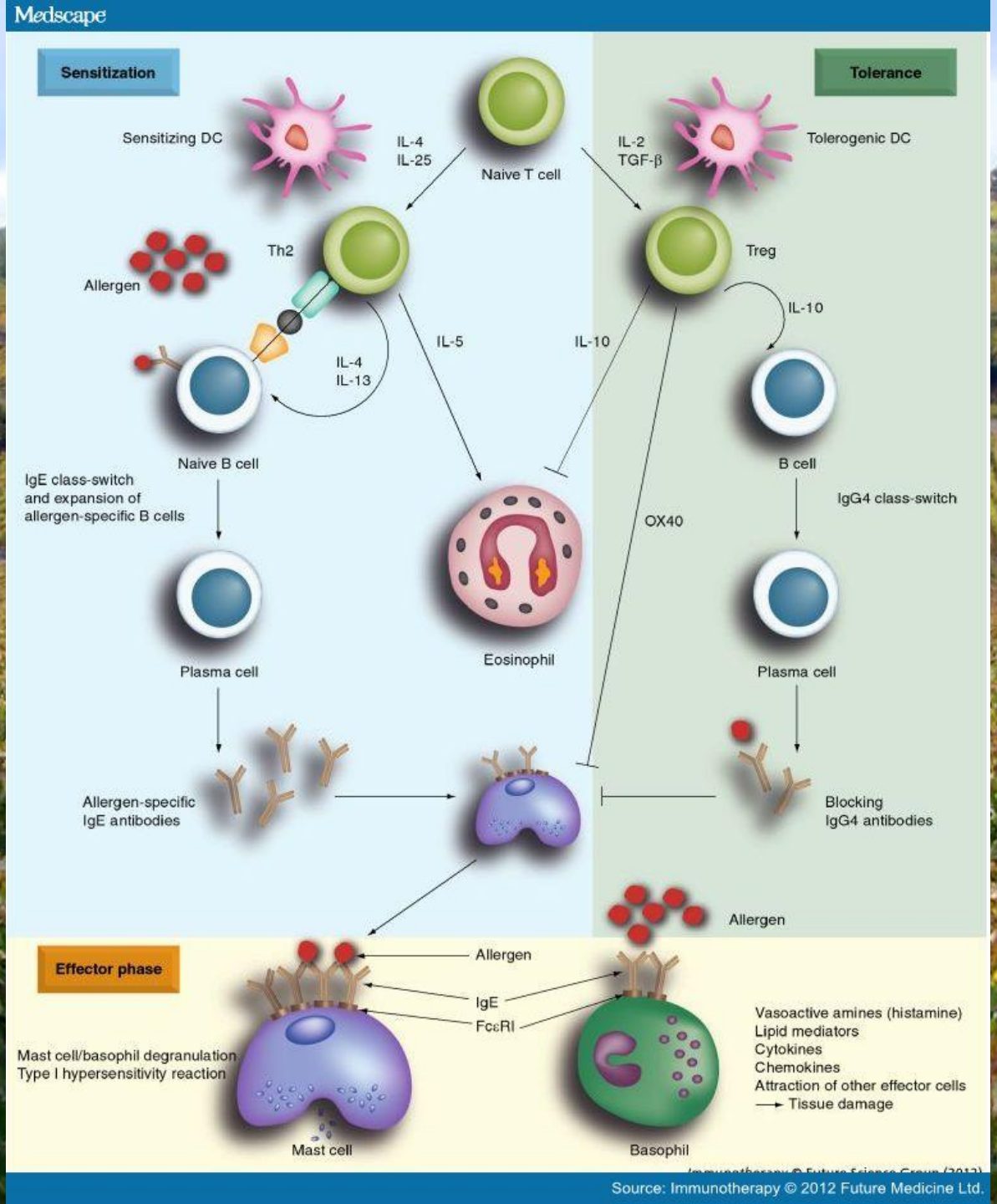
FOXP3 (forkhead box P3) est le marqueur des lymphocytes T régulateurs, codé par le gène forkhead box protein3. Ce gène code lui-même le répresseur de transcription Scurfin.

FoxP3 est essentiel pour l'acquisition de propriétés régulatrices par les lymphocytes TCD4+CD25+, on peut dire que FoxP3 est le "rhéostat de la réponse immunitaire".





EQUILIBRE …



Source: Immunotherapy © 2012 Future Medicine Ltd.

LES DOGMES COMMENCENT A VACILLER …

Revue Française d'Allergologie

Volume 52, Issue 3, April 2012, Pages 218–222

7ème Congrès Francophone d'Allergologie

IgE et IgG, basophiles et neutrophiles : l'arbre et la forêt

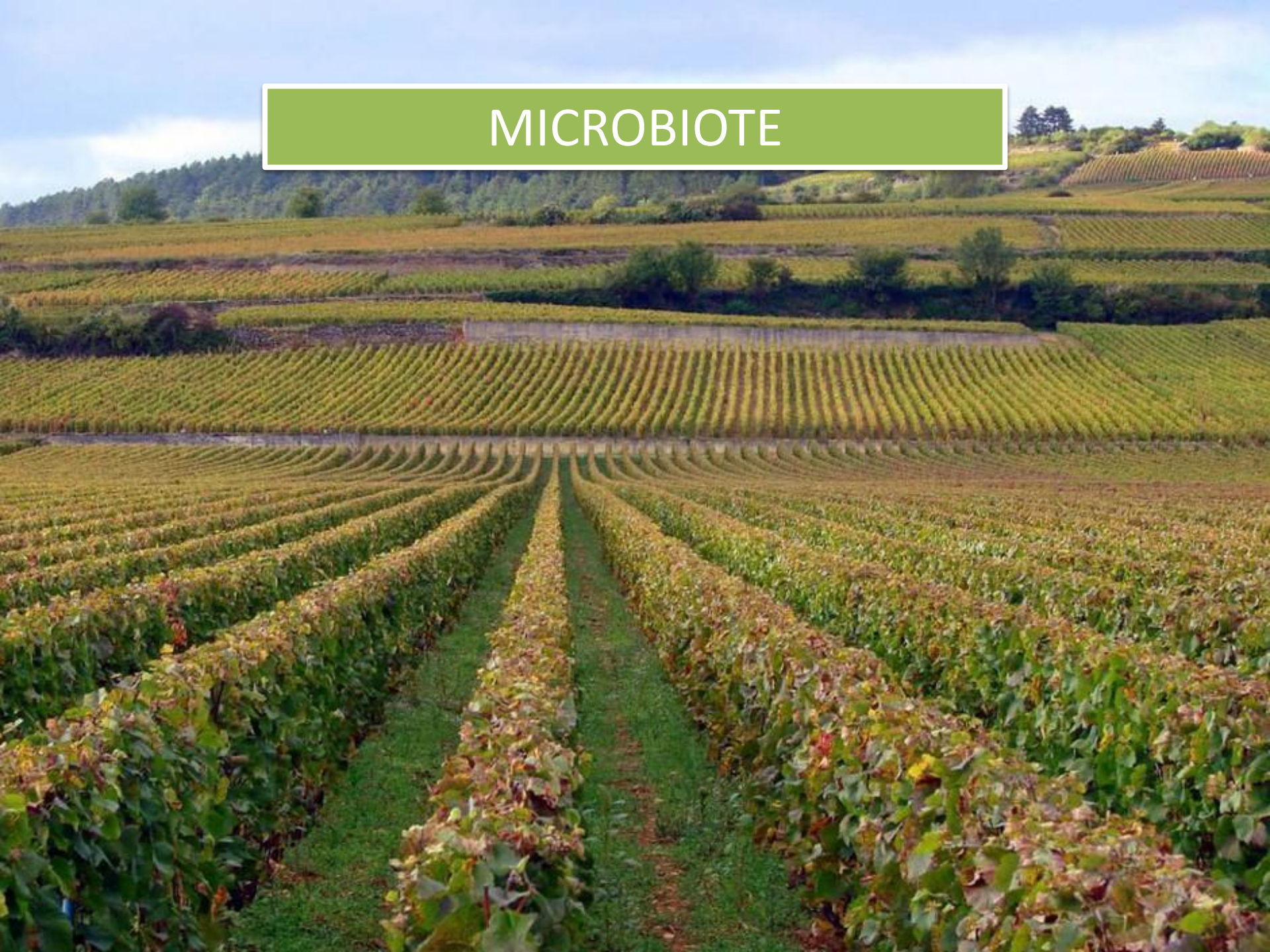
IgE and IgG, basophils and neutrophils: The tree and the forest

M. Daëron

CE SERA LA CONCLUSION … SURPRENANTE ET PROVISOIRE … (patience)

Institut Pasteur

MICROBIOTE



‘NORMAL' or ‘HEALTHY' INTESTINAL MICROBIOME

Key characteristics:

- diversity,
- richness,
- microbial community's resilience and
- ability to resist change.
- age,
- host immune system,
- host genetics,
- diet and
- antibiotic use, appear to modify the intestinal microbiome in the normal state.

The microbiome likely plays a critical role in the healthy human immune system and metabolism.

It is clear that there is a complicated *bidirectional relationship* between the *intestinal microbiota and host* which is vital to health.

An enhanced understanding of this relationship will be critical not only to maximize and maintain human health but also to shape our understanding of disease and to foster new therapeutic approaches.

QUEL RÔLE JOUE LA FLORE INTESTINALE ? - LE MICROBIOTE

	NaCl i.p.	ß-Lg i.p	Groupe test ß-Lg i.p
IgG	--	++++	++
IgE	--	++++	++

The histological scrutiny showed villi atrophy, lymphocyte hyperplasia and a significant chorion detachment in the positive control group. In the group administered with hydrolysates of fermented milk, inflammatory signs were lower, the villi were long and thin and lymphocytes were less dense.

L'allergénicité de la β-lactoglobuline (β-Lg) est étudiée sur un modèle murin allergique à la β-Lg par inj. Intrapéritonéale de β-lactoglobulines.
Un groupe est supplémenté 18 jours per os avec des hydrolysats de lait fermenté pendant 48 h à 37°C avec Enterococcus faecalis DAPTO 512, identifié par analyse de séquence l'ADNr 16 s.
Les β-caséines et β-lactoglobulines étaient dégradées.

Protective effect of *Enterococcus faecalis* DAPTO 512 on the intestinal tract and gut mucosa: milk allergy application . K. Belkaaloul & coll. - Published Online: July 20, 2015

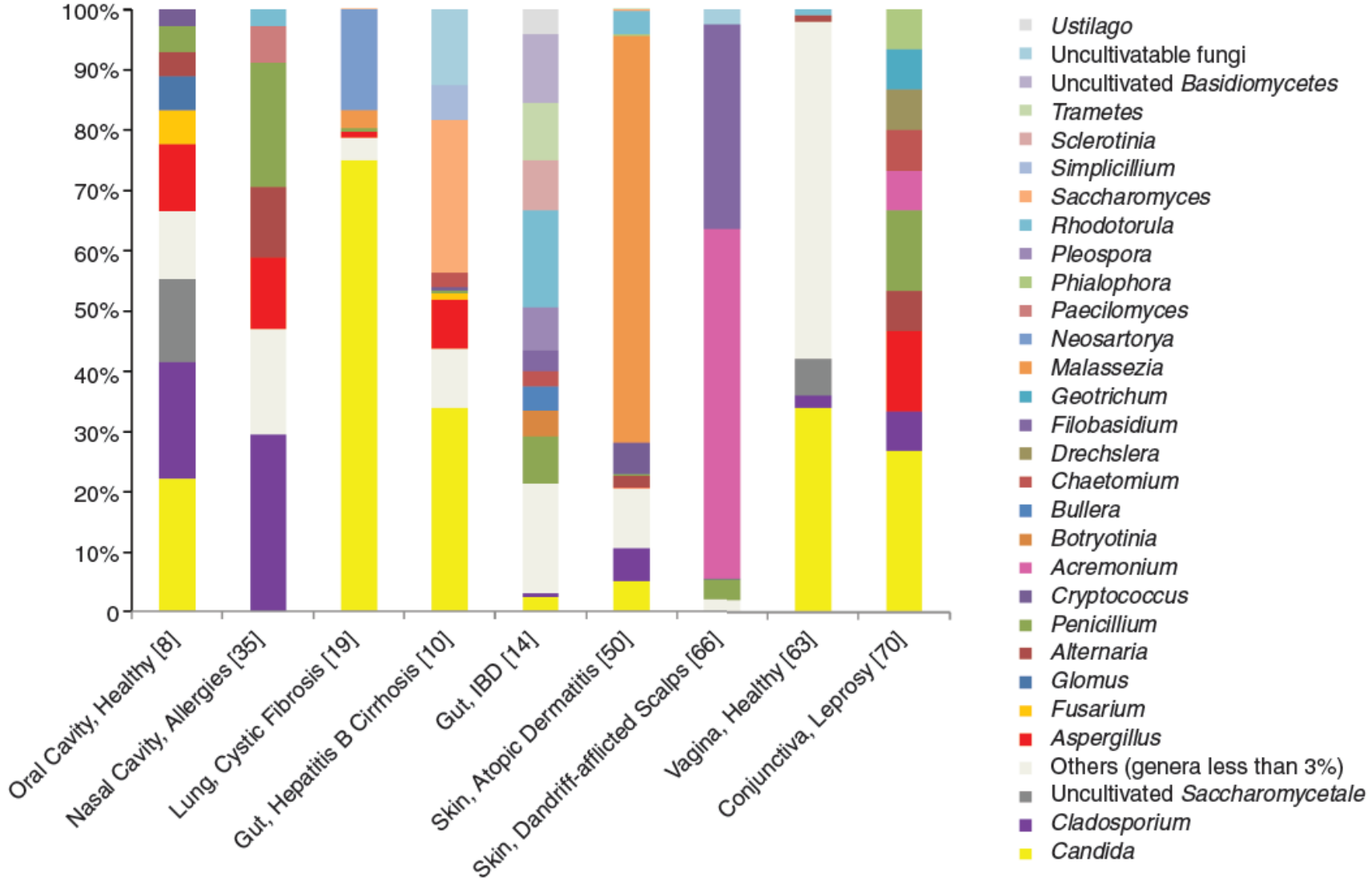
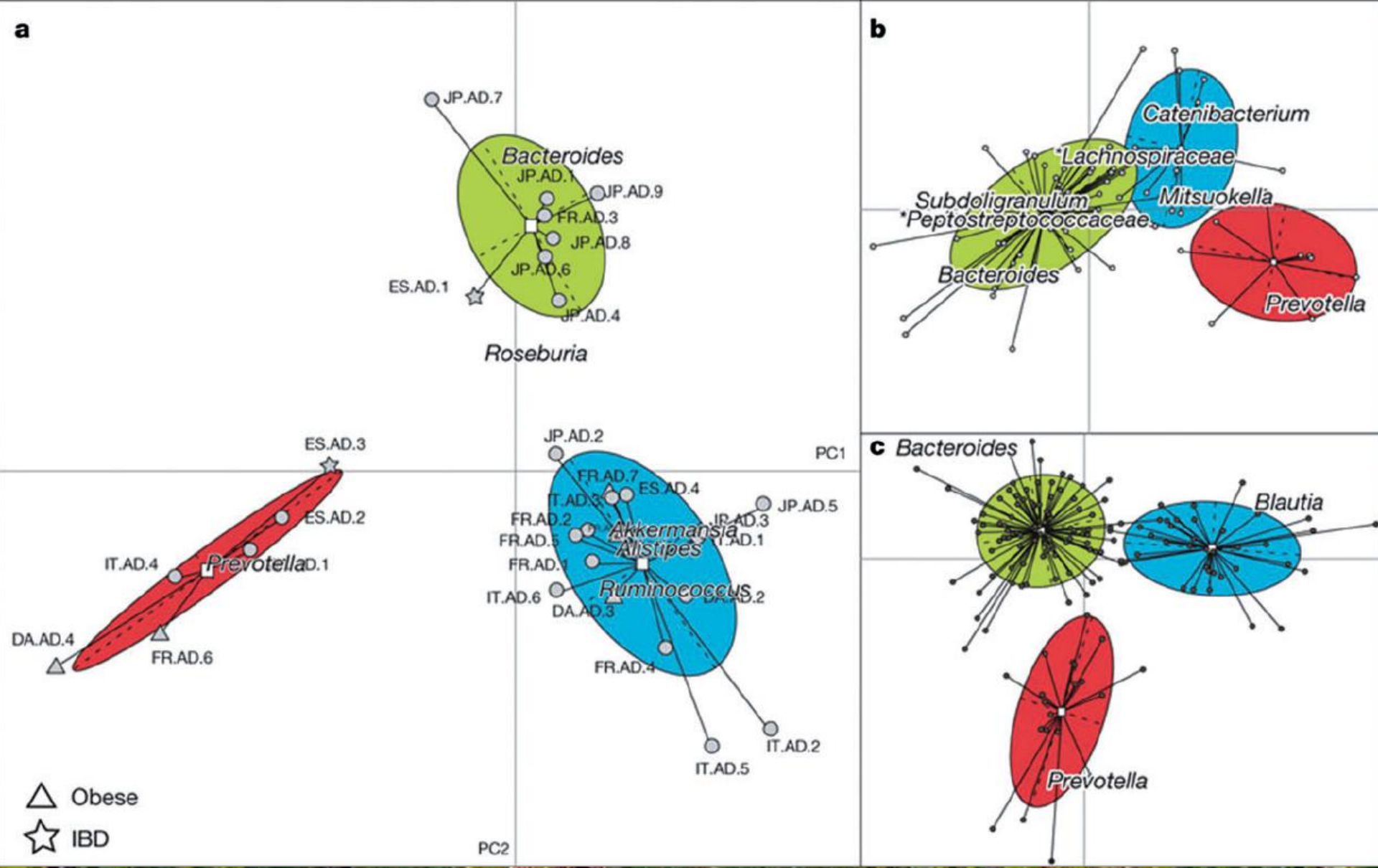
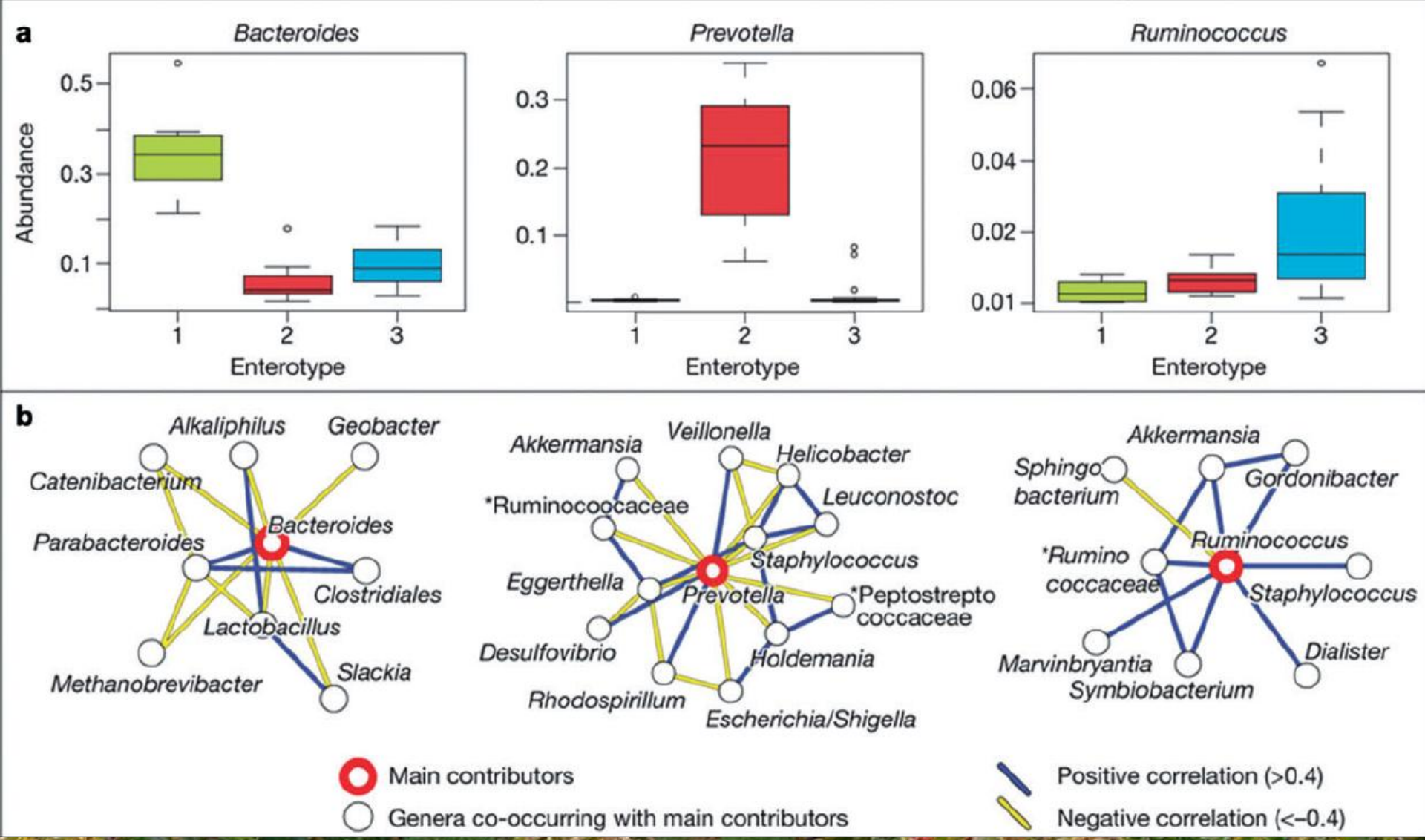


Figure 2. Distribution of fungal genera in different body sites. Fungal distributions differ significantly among distant body sites, whereas similar patterns are found in nearby sites. For example, *Cladosporium* spp., *Aspergillus* spp., and *Penecillium* spp. all dominate other fungal genera in both oral and nasal cavities.

Cui *et al. Genome Medicine* 2013, 5:63
http://genomemedicine.com/content/5/7/63

les Firmicutes (on y trouve notamment les genres : *Ruminococcus*, *Clostridium*, *Lactobacillus* (dont plusieurs souches utilisées comme probiotiques), et des *Eubacterium*, *Faecalibacterium* et *Roseburia* (productrices de butyrate) ;
les Bacteroidetes (dans ce groupe, les *Bacteroides*, *Prevotella* et *Xylanibacter* dégradent une grande variété de molécules complexes de glycanes) ;
les Actinobacteria (ce groupe inclut les genres *Collinsella* et *Bifidobacterium* (dont certaines souches de probiotiques connus) ;
les Proteobacteria (dont communément des *Escherichia* (de la famille des *Enterobacteriaceae* et des bactéries du groupe *Desulfovibrio* (bactéries réductrices de soufre) ;
les Verrucomicrobia (Ce groupe a été récemment découvert, il inclut les *Akkermansia* qui semblent spécialisées dans la dégradation des mucus).
La plupart des genres bactériens cités ci-dessus (*Bacteroides*, *Prevotella*, *Alistipes*, *Akkermansia*, *Oscillibacter*, *Clostridium*, *Faecalibacterium*, *Eubacterium*, *Ruminococcus*, *Roseburia*, et *Bifidobacterium*) font partie du microbiote en dominance. Les genres tel que *Escherichia* et *Lactobacillus* se retrouvent en plus faible quantité. D'autres groupes bactériens rares ont aussi été détectés tel que *Fusobacterium*, *Lentisphaerae*, *Spirochaetes* et TM7[16,17].
Les genres de fungi actuellement connus du microbiote intestinal incluent Candida, *Saccharomyces*, *Aspergillus*, et *Penicillium*. Les archées sont représentées par un seul genre : Methanobrevibacter et plus particulièrement l'espèce *Methanobrevibacter smithii* impliqué dans la méthanogènese intestinale[18].


a
JP.AD.7
Bacteroides
JP.AD.1
JP.AD.9
FR.AD.3
JP.AD.8
JP.AD.6
ES.AD.1
JP.AD.4
Roseburia
ES.AD.3
ES.AD.2
IT.AD.4
Prevotella
D.1
DA.AD.4
FR.AD.6
JP.AD.2
PC1
FR.AD.7
ES.AD.4
IT.AD.3
JP.AD.5
FR.AD.2
JP.AD.3
Akkermansia
T.AD.1
FR.AD.5
Alistipes
FR.AD.1
Ruminococcus
IT.AD.6
DA.AD.3
FR.AD.4
IT.AD.2
IT.AD.5
Obese
IBD
PC2
b
Catenibacterium
Lachnospiraceae
Subdoligranulum
Mitsuokella
Peptostreptococcaceae
Bacteroides
Prevotella
c
Bacteroides
Blautia
Prevotella

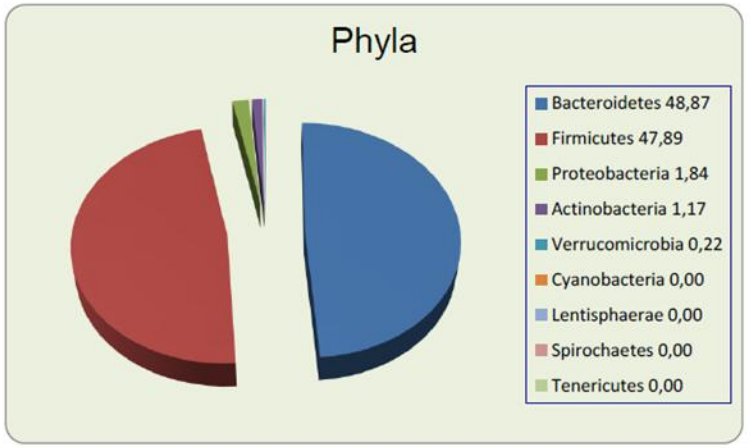

a
Bacteroides
Prevotella
Ruminococcus
Abundance
0.5
0.3
0.1
0.3
0.2
0.1
0.06
0.04
0.02
0.01
1
2
3
Enterotype
b
Alkaliphilus
Geobacter
Catenibacterium
Bacteroides
Parabacteroides
Clostridiales
Lactobacillus
Methanobrevibacter
Slackia
Akkermansia
Veillonella
Helicobacter
*Ruminococcaceae
Leuconostoc
Staphylococcus
Eggerthella
Prevotella
*Peptostrepto
coccaceae
Desulfovibrio
Holdemania
Rhodospirillum
Escherichia/Shigella
Akkermansia
Sphingo
bacterium
Gordonibacter
Ruminococcus
*Rumino
coccaceae
Staphylococcus
Dialister
Marvinbryantia
Symbiobacterium
Main contributors
Genera co-occurring with main contributors
Positive correlation (>0.4)
Negative correlation (<–0.4)

MICROBIOME

Genomic DNA extraction flow from Qiagen which is fully automatable on QIAcube

Résultats microbiote intestinal

Nom : [redacted]



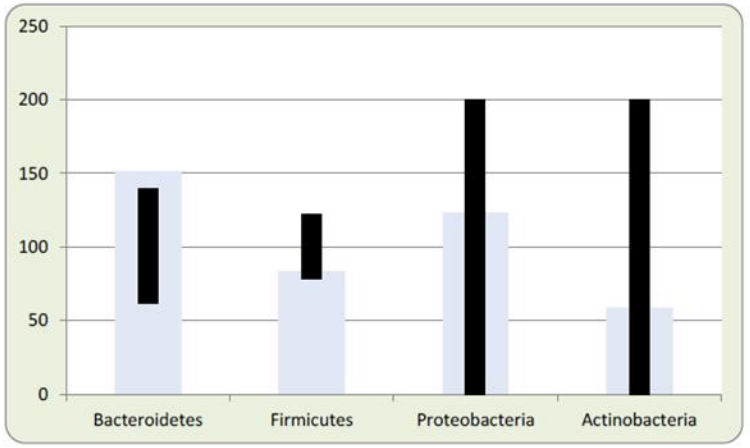


Tableau ratio Firmicutes/Bactéroidetes

Firmicutes	47,89	
Bacteroidetes	48,87	
Ratio Firmicutes/Bacteroidetes	0,98	

Tableau ratio Gram + / Gram -

Gram +	49,06	
Gram -	50,94	
Ratio Gram + / Gram -	0,96	

Tableau indice de diversité

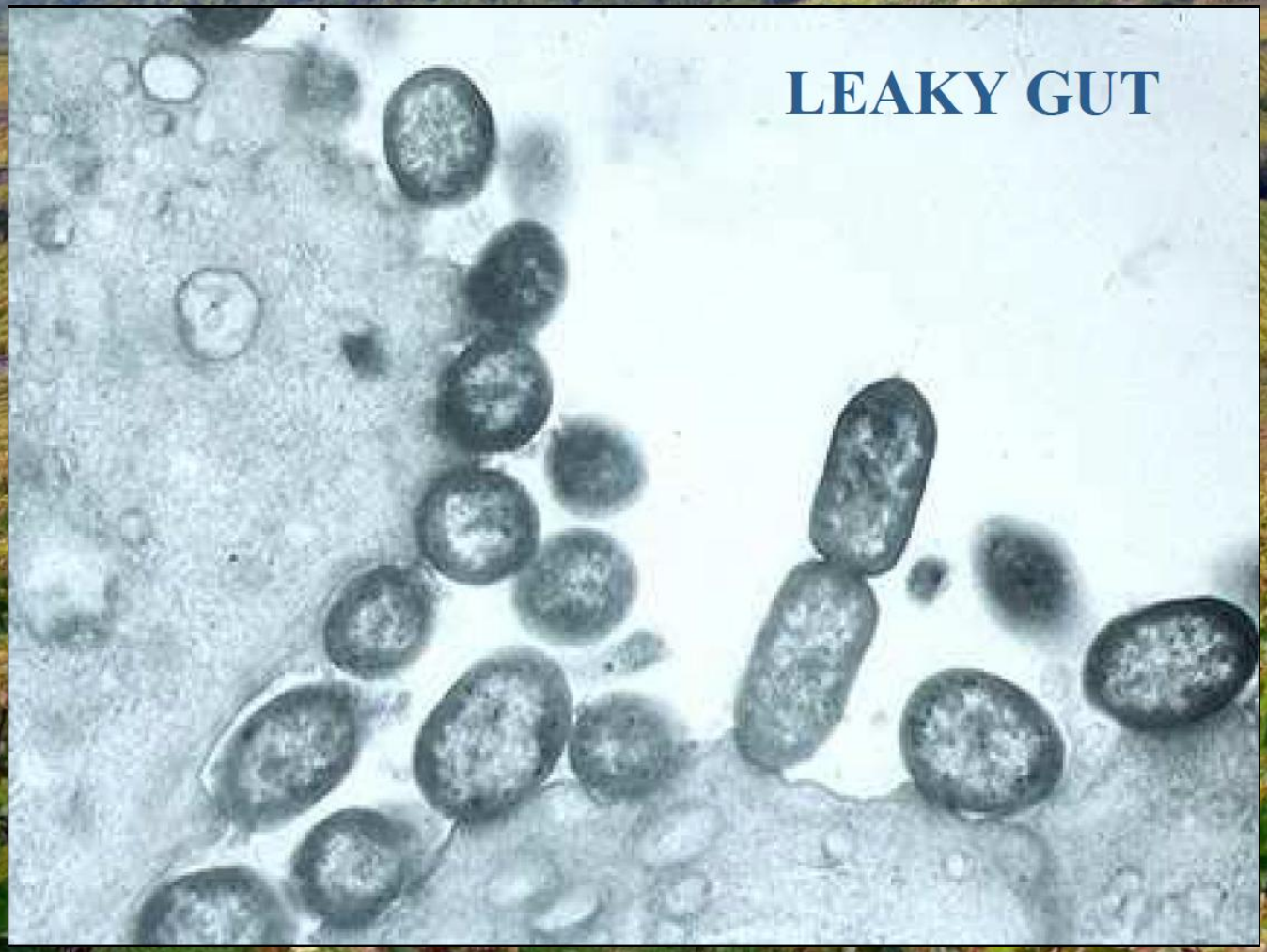
Indice #1	2,66	
Indice #2	70,00	
Indice #3	86,90	

Bactéries productrices d'AGCC

Akkermansia muciniphila	0,22
Faecalibacterium prausnitzii	0,01
Ruminococcus bromii	ND
Butyricicoccus pullicaecorum	ND
Eubacterium rectale	ND
Eubacterium ventriosum	ND
Roseburia cecicola	ND
Roseburia intestinalis	0,09
Bifidobacterium longum	ND
Clostridium leptum	ND
Bacteroides cytophaga	ND
Bacteroides thetaiotaomicron	ND

Espèces d'intérêt

Ruminococcus bromii	ND
Faecalibacterium prausnitzii	0,01
Eubacterium rectale	ND
Roseburia intestinalis	0,09
Clostridium leptum	ND
Akkermansia muciniphila	0,22
Bacteroides vulgatus	ND
Bacteroides fragilis	ND


LEAKY GUT

LABORATOIRE

Nutrition in Clinical Practice
Volume 25 Number 2
April 2010 192-198

10.1177/0884533610362696
http://ncp.sagepub.com
hosted at
http://online.sagepub.com

Testing for Food Reactions: The Good, the Bad, and the Ugly

Gerard E. Mullin, MD[1]; Kathie M. Swift, MS, RD[2]; Liz Lipski, PhD, CCN[3]; Laura K. Turnbull, BS, MSNc[4]; and S. Devi Rampertab, MD[5]

Financial disclosure: none declared.

An increasing number of commercial tests for food allergies are marketed to consumers and healthcare practitioners with tenuous claims. The aim of this article is to provide an evidence-based review of the tests and procedures that currently are used for patients with suspected food allergy. A systematic review of the literature evaluating the validity of tests and procedures used in food reactions was performed using conventional search engines (eg, PubMed, Ovid) as well as consumer sites (eg, Google, Bing). The National Library of Medicine Medical Subject Headings (MeSH) term *food hypersensitivity* was used along with *food allergy testing*, *food sensitivity testing*, *food intolerance testing*, and *adverse food reactions*. Of the results obtained, testing for immunoglobulin E (IgE)–mediated food allergy was best represented in PubMed. IgE-based testing continues to be the gold standard for suspected food allergies. Among modalities used by many conventional and alternative practitioners, immunoglobulin G (IgG)–based testing showed promise, with clinically meaningful results. It has been proven useful as a guide for elimination diets, with clinical impact for a variety of diseases. Mediator release testing and antigen leukocyte cellular antibody testing were only represented on consumer sites. Further investigation into the validity and the clinical application of these tests and procedures is required. Disclosing the basis for food reactions continues to present a diagnostic challenge, and testing for food allergies in the context of an appropriate clinical history is paramount to making the correct diagnosis. (*Nutr Clin Pract.* 2010;25:192-198)

Keywords: food sensitivity; food hypersensitivity; allergy and immunology; immunoglobulin E; immunoglobulin G; skin tests

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- LBP
- IgA
- Vitamine D
- Zinc
- Sélénium

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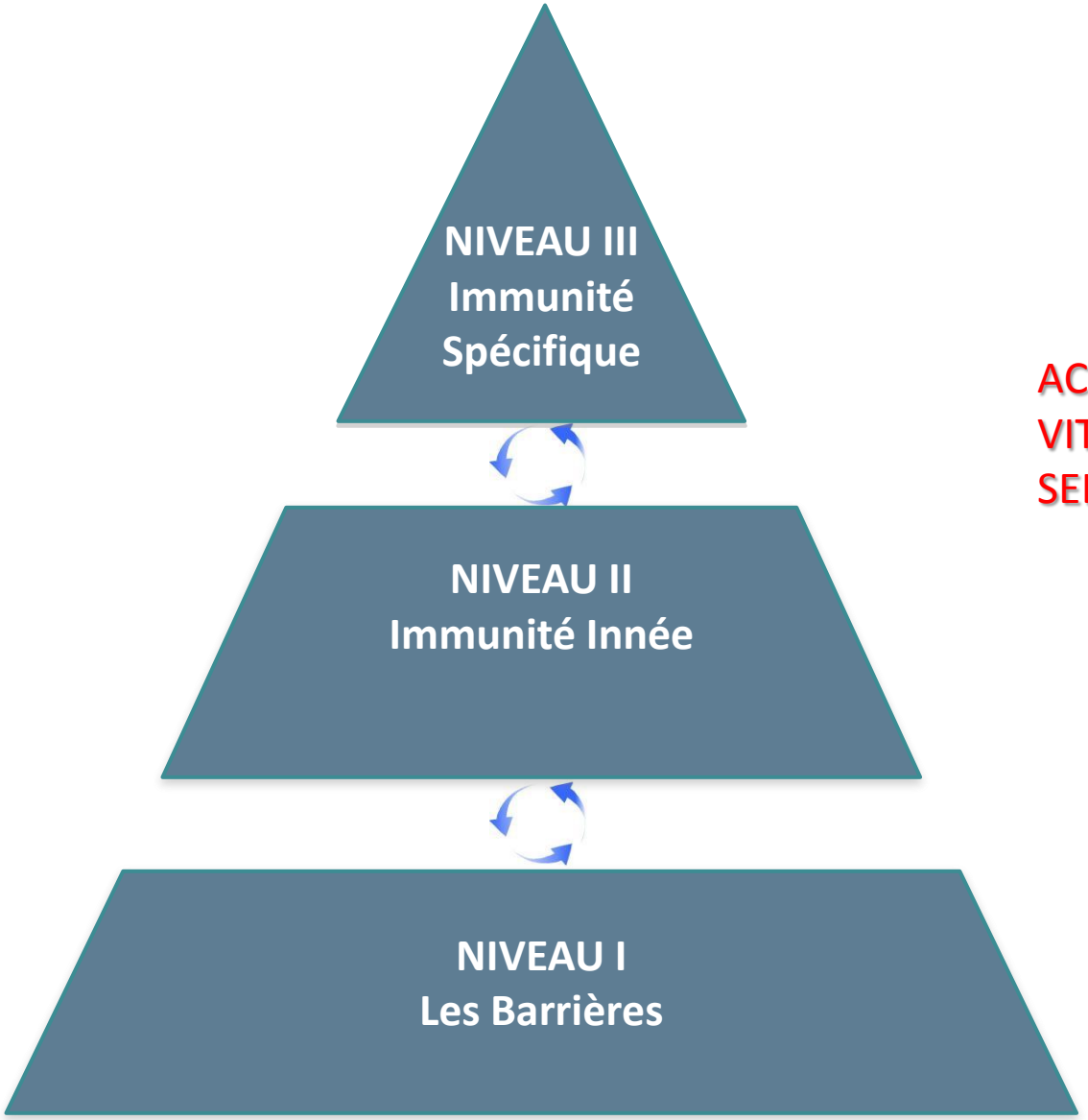
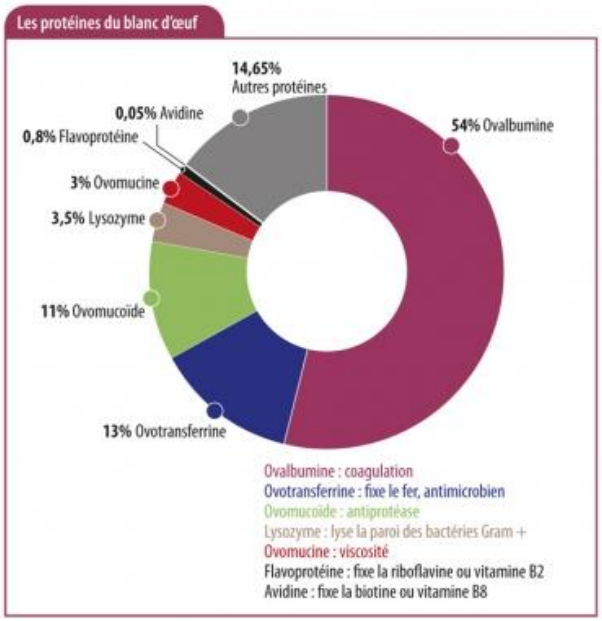


ACIDES GRAS
VITAMINE D
SELENIUM

MOU, LBP, ZINC, IgA
IGG ALIMENTAIRES

> F338-Coquille St.Jacques	<2	mg/L	0 - 5
> F207-Palourde	3.2	mg/L	0 - 5
> F90-Malt	↑↑ 10.5	mg/L	0 - 5
> F86-Persil	<2	mg/L	0 - 5
F96-Avocat	en cours	mg/L	0 - 5
> F214-Epinard	<2	mg/L	0 - 5
> F215-Laitue	<2	mg/L	0 - 5
> F216-Chou	<2	mg/L	0 - 5
> F244-Concombre	<2	mg/L	0 - 5
> F260-Broccoli	<2	mg/L	0 - 5



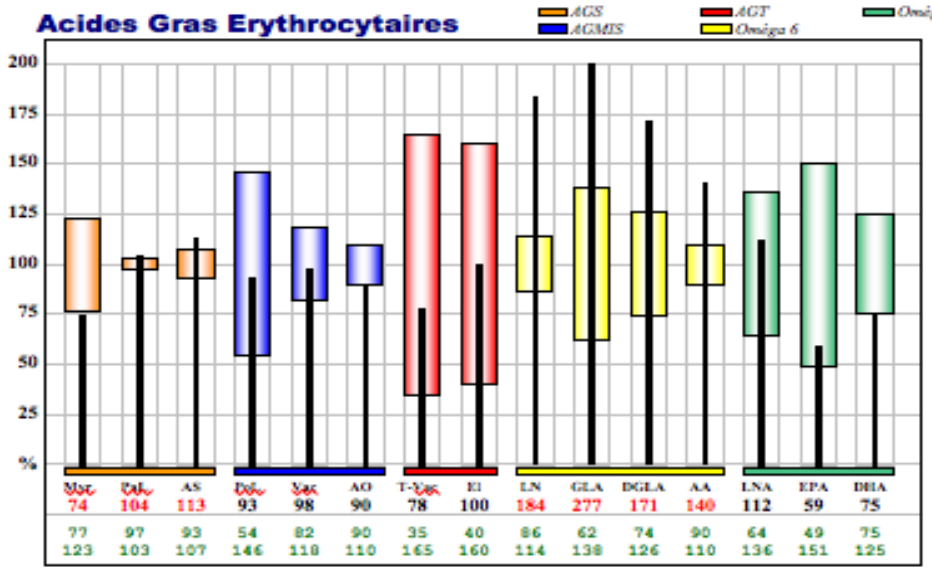
Protein	% of protein	MW	pI	% carb	Function	AA	S-S
Ovalbumin	54	45.0	4.5	3.5	Structural	385	1
Conalbumin	12-13	77.7	6.0	2.6	Iron transport	686	15
Ovomucoïd	11	28.0	4.1	16	Proteinase inibitor	185	9
Ovomucin a Ovomucin b	1.5-3.5	210 720	4.5	13 58	Structural	1276 246	

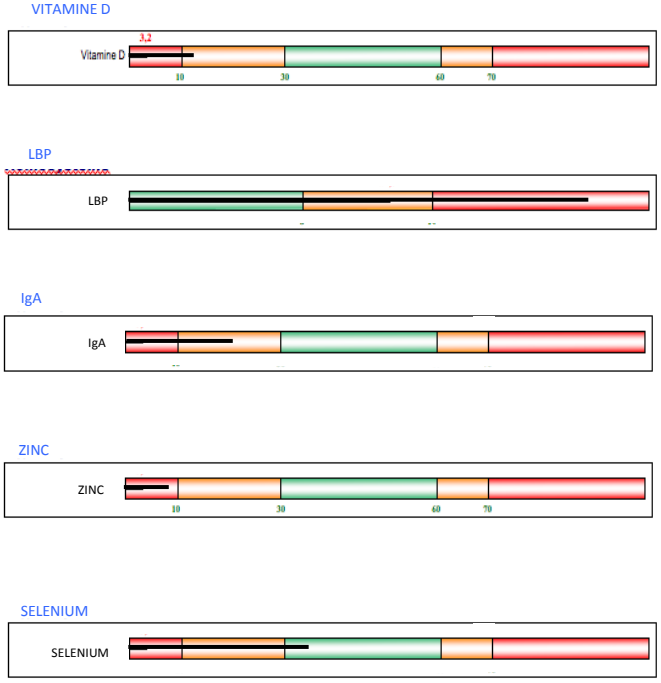
> F87-Melon	<2	mg/L	0 - 5
> F208-Citron	<2	mg/L	0 - 5
> F237-Abricot	<2	mg/L	0 - 5
> F262-Aubergine	2.1	mg/L	0 - 5
> F44-Fraise	2.1	mg/L	0 - 5
> F232-Ovalbumine	↑ 8.8	mg/L	0 - 5
> F212-Champignon	3.9	mg/L	0 - 5
> F50-Maquereau	<2	mg/L	0 - 5
> F291-Chou fleur	<2	mg/L	0 - 5
> F332-Menthe	<2	mg/L	0 - 5
> F300-Lait de chèvre	<2	mg/L	0 - 5
> F328-Figue	2.2	mg/L	0 - 5
> F233-Ovomucoïde	↑ 6.5	mg/L	0 - 5
> F234-Vanille	2.7	mg/L	0 - 5
> F281-Curry	4.7	mg/L	0 - 5
> F269-Basilic	<2	mg/L	0 - 5
> F314-Escargot	3.4	mg/L	0 - 5
> F219-Graine de fenouil	2.5	mg/L	0 - 5
> F263-Poivre vert	<2	mg/L	0 - 5
> F270-Gingembre	<2	mg/L	0 - 5
> F273-Thym	<2	mg/L	0 - 5
> F277-Aneth	<2	mg/L	0 - 5
> F278-Feuille de laurier	<2	mg/L	0 - 5
> F279-Piment rouge	4.5	mg/L	0 - 5
> F294-Fruit de la passion	<2	mg/L	0 - 5
> F217-Chou de Bruxelles	<2	mg/L	0 - 5
F261-Asperge	<2	mg/L	0 - 5
F254-Carrelet (plie)	<2	mg/L	0 - 5

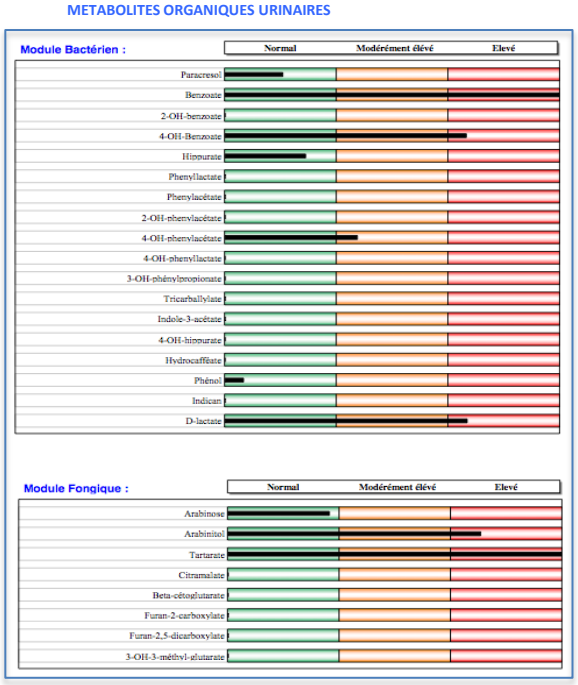
Sexe : Masculin Né(e) le : [illegible] Age : 44 ans

Demande n° : N1 5382 6[illegible]
Réf. Ext. : 835162
Réception : 15/09/15 à 12:38
Prélèvement : 15/09/15

NBT/ALLERGIES®







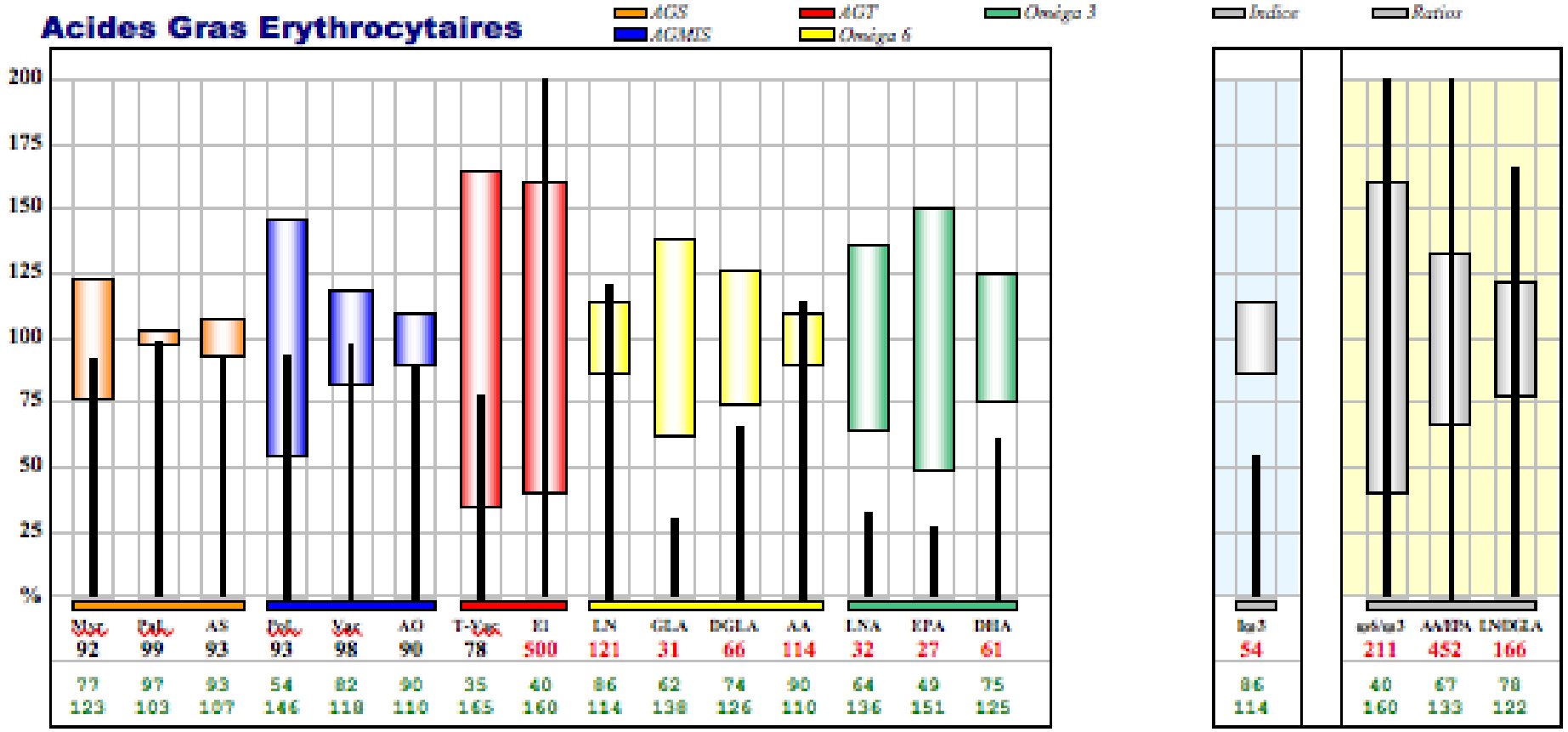
Acides gras Omega-3
Et Allergies

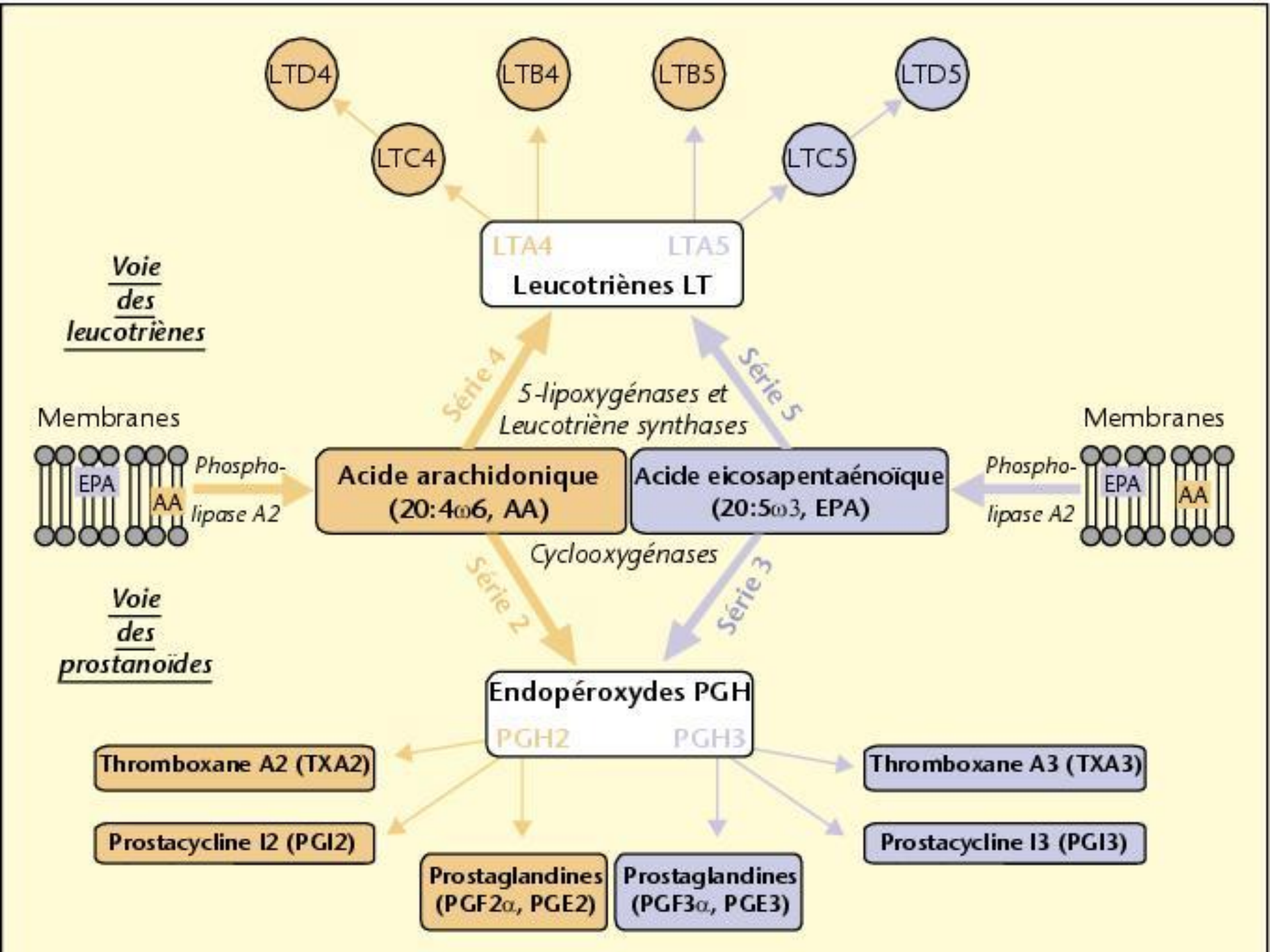
(545 publications)

Acides gras des membranes érythrocytaires

(1381 publications)

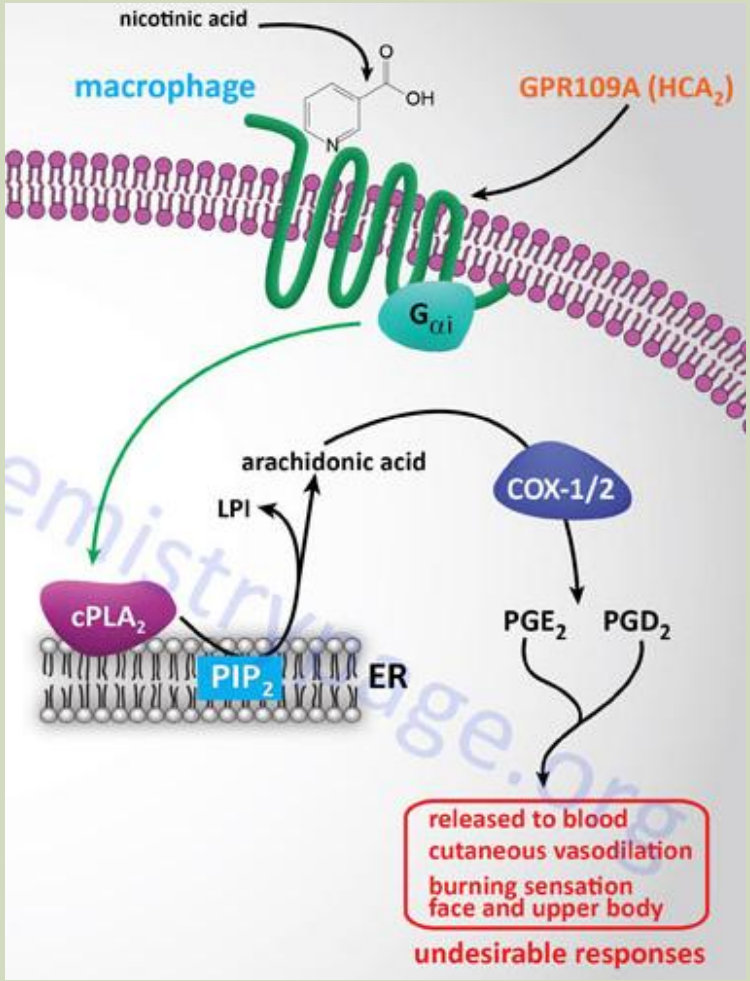
LE PROFIL EN ACIDES GRAS




LTD4
LTB4
LTB5
LTD5
LTC4
LTC5
LTA4
LTA5
Leucotriènes LT
Voie des leucotriènes
Série 4
5-lipoxygénases et Leucotriène synthases
Série 5
Membranes
EPA
AA
Phospho-lipase A2
Acide arachidonique (20:4ω6, AA)
Acide eicosapentaénoïque (20:5ω3, EPA)
Membranes
Phospho-lipase A2
EPA
AA
Cyclooxygénases
Série 2
Série 3
Voie des prostanoïdes
Endopéroxydes PGH
PGH2
PGH3
Thromboxane A2 (TXA2)
Thromboxane A3 (TXA3)
Prostacycline I2 (PGI2)
Prostacycline I3 (PGI3)
Prostaglandines (PGF2α, PGE2)
Prostaglandines (PGF3α, PGE3)

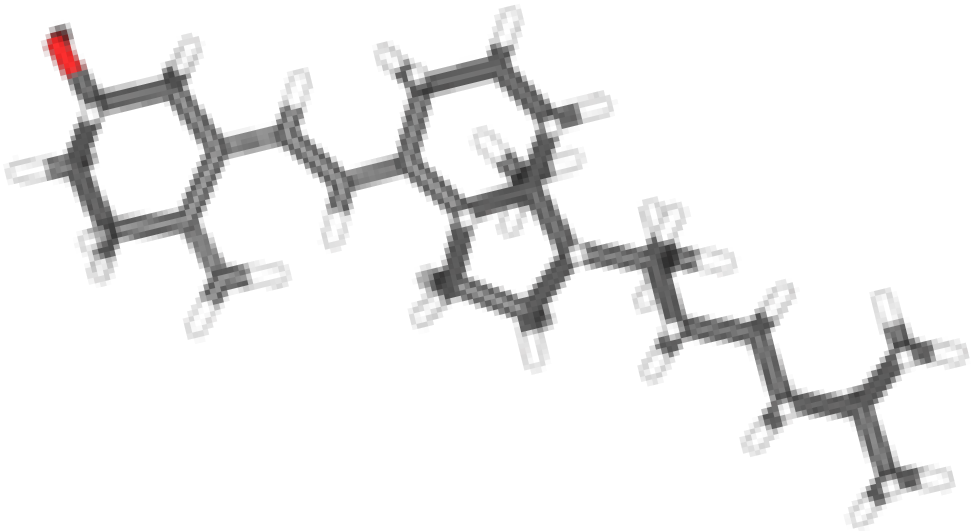
Omega-3 et Allergies

Les PGE2 (dérivées de l'acide arachidonique) modifient le contrôle équilibré du système immunitaire vers la production d'IgE en affectant la génération des cellules T et l'interferon gamma.

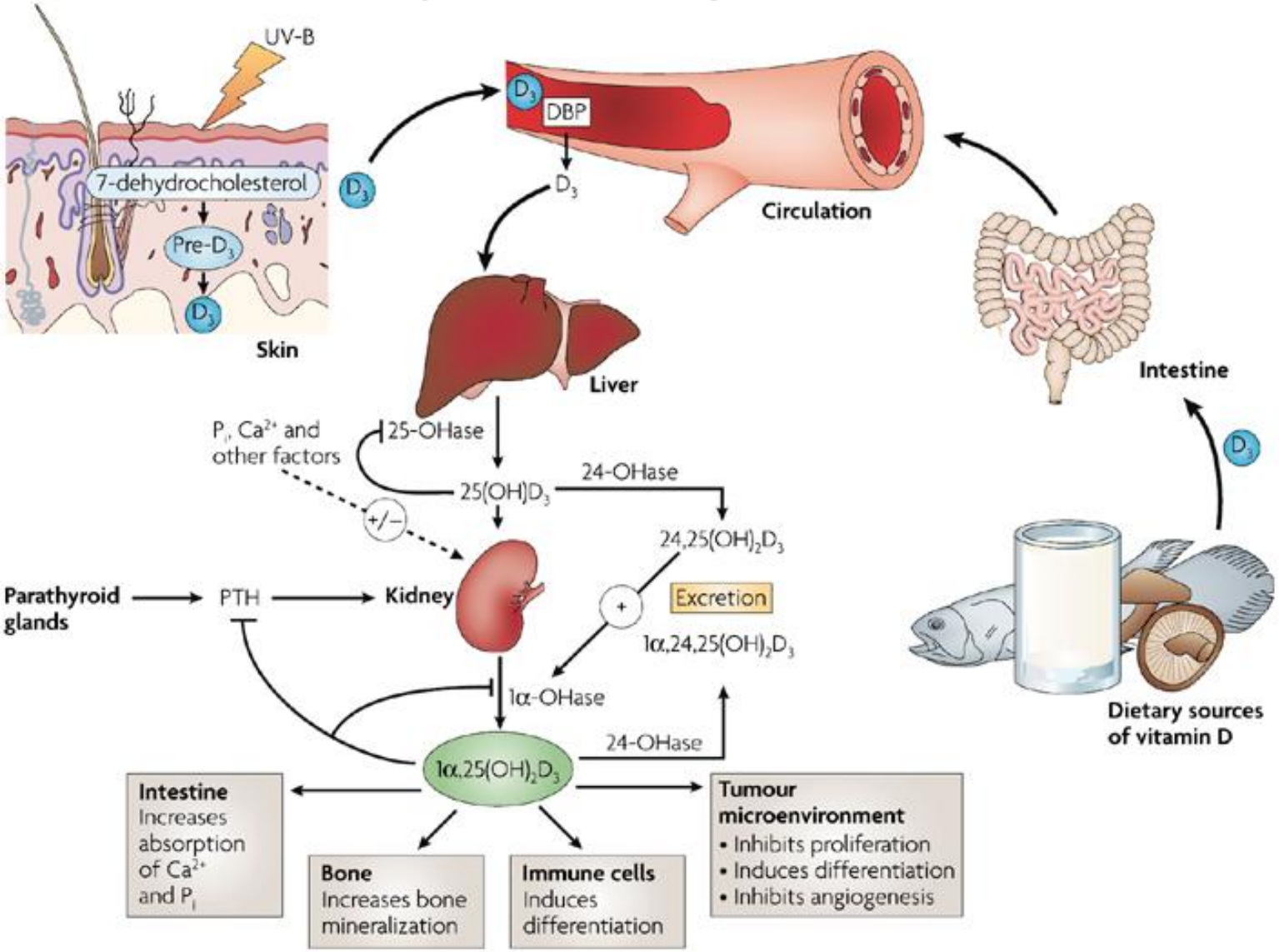


Vitamine D et Allergies

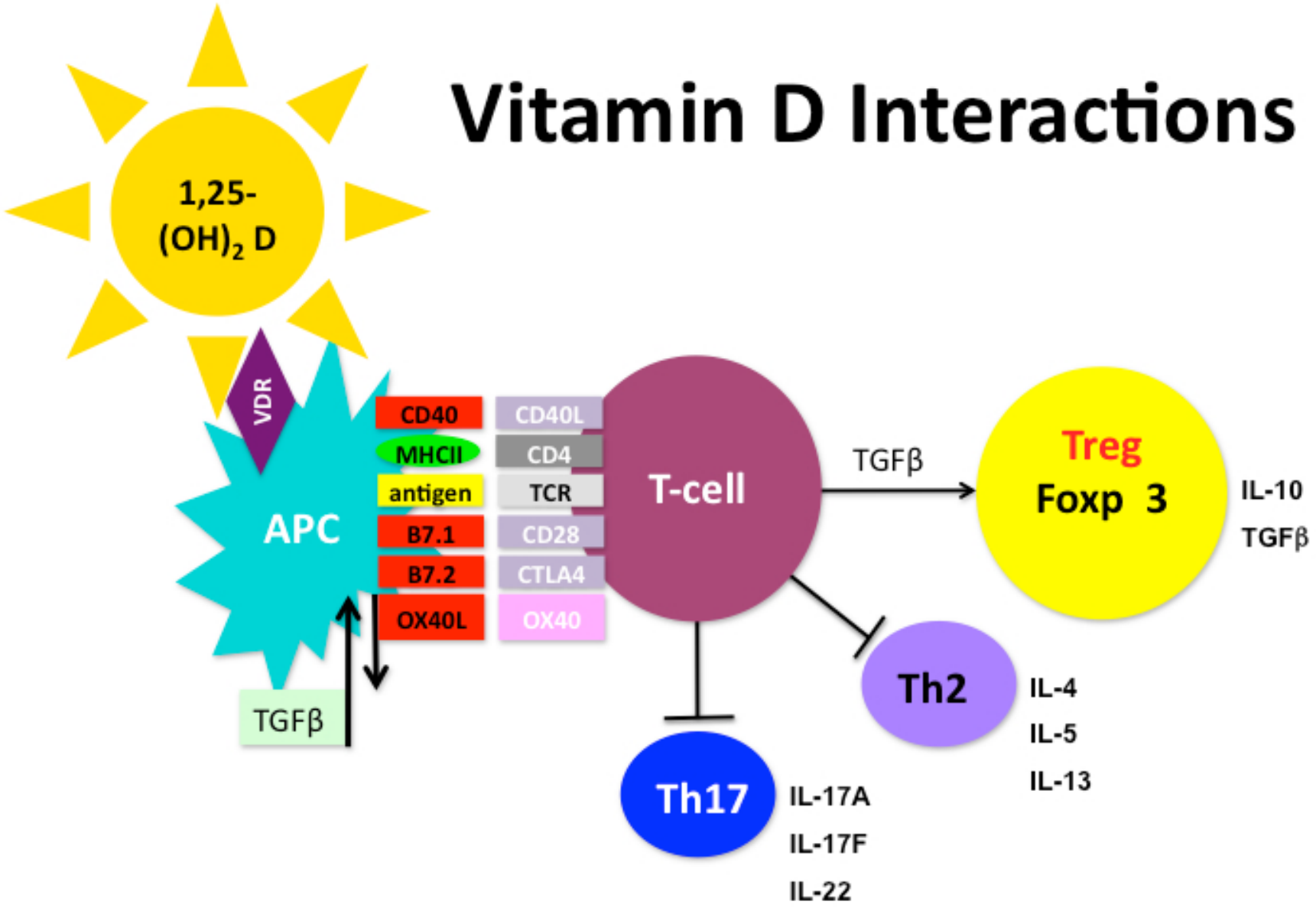
(877 publications)



Vitamine D


UV-B
7-dehydrocholesterol
Pre-D3
D3
Skin
D3
DBP
D3
Circulation
Liver
Intestine
P, Ca2+ and other factors
25-OHase
25(OH)D3
24-OHase
+/−
24,25(OH)2D3
Parathyroid glands
PTH
Kidney
+
Excretion
1α,24,25(OH)2D3
1α-OHase
24-OHase
1α,25(OH)2D3
Intestine
Increases absorption of Ca2+ and P
Bone
Increases bone mineralization
Immune cells
Induces differentiation
Tumour microenvironment
• Inhibits proliferation
• Induces differentiation
• Inhibits angiogenesis
D3
Dietary sources of vitamin D

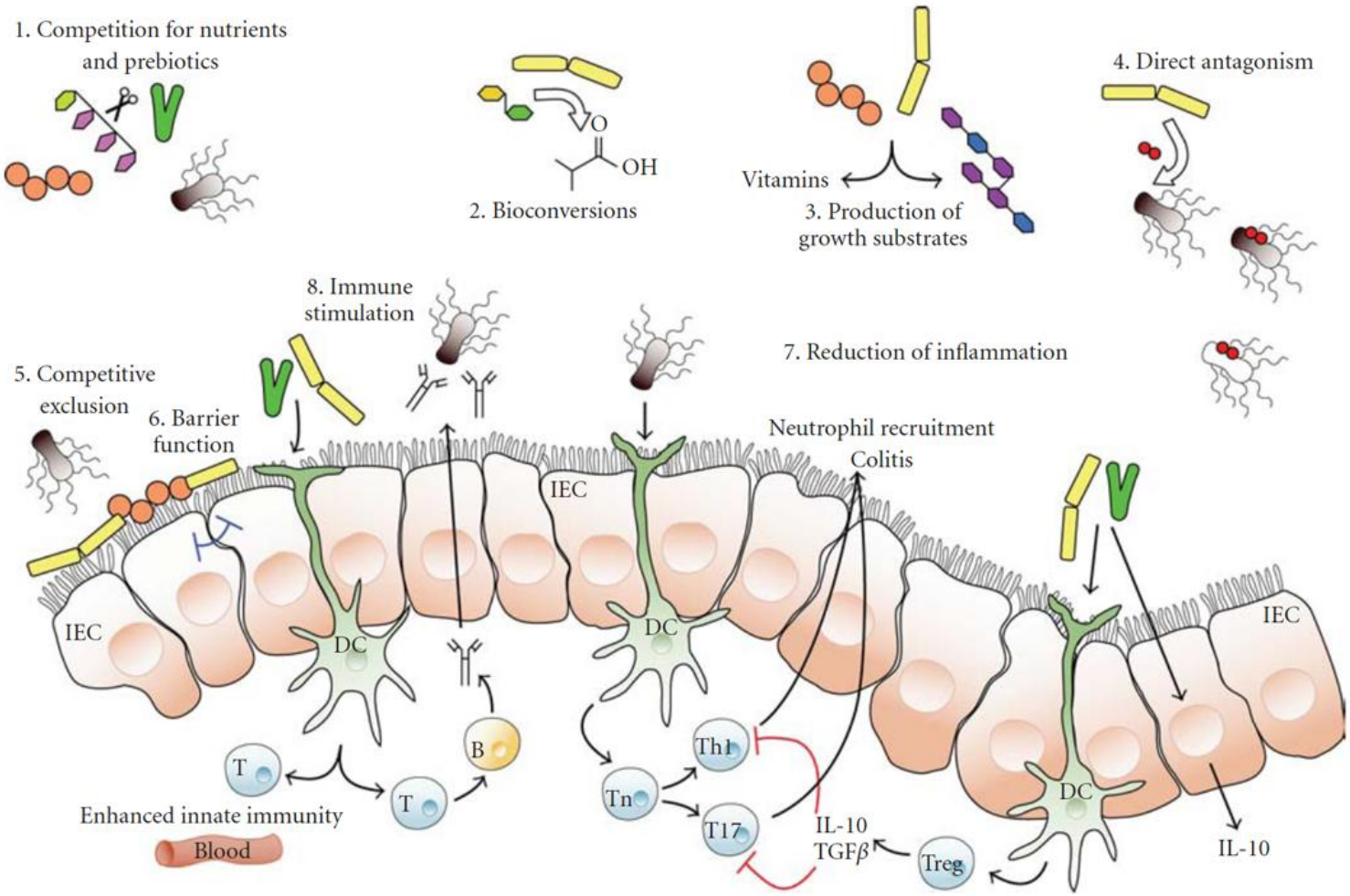
Vitamin D Interactions



Vitamin D acting on APC-T cell interactions, inhibiting Th17 and Th2 proliferation while increasing Treg frequency.
The Richard King Mellon Foundation Institute for Pediatric Research

Dysbiose et Allergies

(840 publications)



European Review for Medical and Pharmacological Sciences 2013; 17(Suppl 2): 11-17

The role of gut microbiota in the pathogenesis and management of allergic diseases

D. COMPARE, G. NARDONE

Department of Clinical Medicine and Surgery, Gastroenterology Unit, Federico II University of Naples, Italy

Abstract. **Allergy is defined as a hypersensitivity reaction due to specific antibody-mediated or cell-mediated immunologic mechanisms. Epidemiological studies are showing a dramatic increase of allergies in industrialized countries in the last few decades, while remaining stable in developing countries.**

In 1989 Strachan, hypothesized that the increase in allergic disorders was the result of a lack of infections in early infancy, and in 1998 Wold suggested that, rather than a decrease in viral or bacterial infections, an altered normal intestinal colonization pattern in infancy, could be responsible for the increase in allergies.

Germ-free mice were shown to mount an exaggerated allergic airway reaction compared with that seen in colonized mice, indicating the important role of microbe-host interactions in the development of allergic diseases.

Infants with food allergies are found to exhibit an imbalance between "beneficial"and potentially harmful bacteria, i.e., decreased *Lactobacilli, Bifidobacteria* and *Enterococcus* species and increased coliforms, Staphylococcus aureus and Clostridium species, suggesting that microbial inhabitants of the human body, may play either a pathogenic or protective role in allergies.

Based on this data, many clinical trial addressing the use of probiotics in the context of allergic disorders, have been conducted in children. However, currently, no conclusive item may be drawn.

Key words:
Gut microbiota, Food allergy, Probiotics.

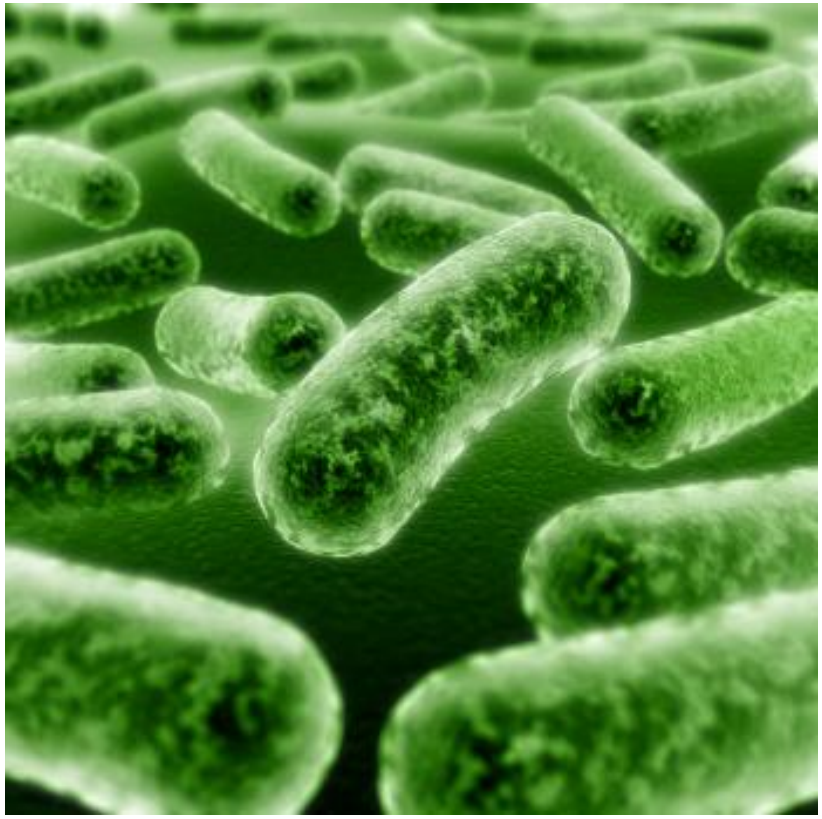
Introduction

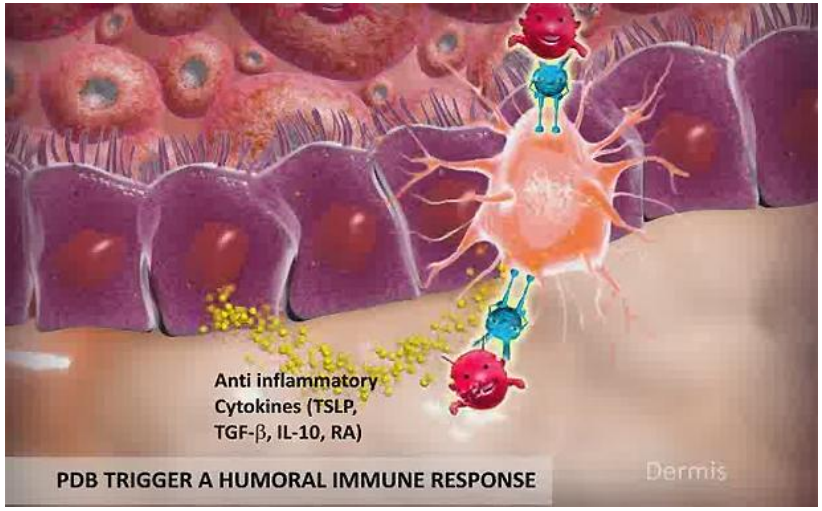
The concept of "allergy" was originally introduced in 1906 by the Viennese pediatrician Clemens von Pirquet, after he noted that some patients were hypersensitive to normally innocuous entities such as dust, pollen, or certain foods. Pirquet called this phenomenon "allergy" from the ancient Greek words αλλος *allos* meaning "other" and εργον *ergon* meaning "work"[1]. A major breakthrough in understanding the mechanisms of allergy was the discovery of the antibody class named immunoglobulin E (IgE), first isolated by Ishizaka and co-workers in the 1960s[2]. One more cornerstone in the history of allergy was the classification designed in 1963 by Philip Gell and Robin Coombs, who described four types of hypersensitivity reactions, known as Type I to Type IV hypersensitivity[3]. With this new classification, the word "allergy" was restricted to type I hypersensitivities (also called immediate hypersensitivity), which are characterized as rapidly developing reactions.

Actually, allergy is defined as a hypersensitivity reaction due to specific antibody-mediated or cell-mediated immunologic mechanisms. The term hypersensitivity describes objectively reproducible symptoms or signs initiated by exposure to a defined stimulus at a dose tolerated by normal (i.e. non-allergic) persons. Sensitization to allergens derived from food, pollen, house dust mite, etc. is thought to be a prerequisite for initiating the allergic march.

Worldwide, sensitization to foreign proteins in the environment is reported in up to 40% of the population. Of note, food allergy prevalence reaches up to 6% among children and 3% among adults. In USA allergic diseases represent the 6th most common chronic disorder, thus making them a major healthcare problem[4]. Overall epidemiological studies are showing a great increase of allergies in industrialized countries in the last few decades, while remaining stable in developing countries[4].

In 1989 Strachan[5] hypothesized that the increase in atopic diseases was the result of a lack of infections in early infancy. This hypothesis was based upon the observation that infants with higher number of siblings were at decreased risk for developing atopy. Although sib-ship size, and other indirect markers of microbial exposure such as rural and farm-living were consistently shown to be associated with a decreased risk of





Prebiotics and probiotics: the prevention and reduction in severity of atopic dermatitis in children less than three years age.

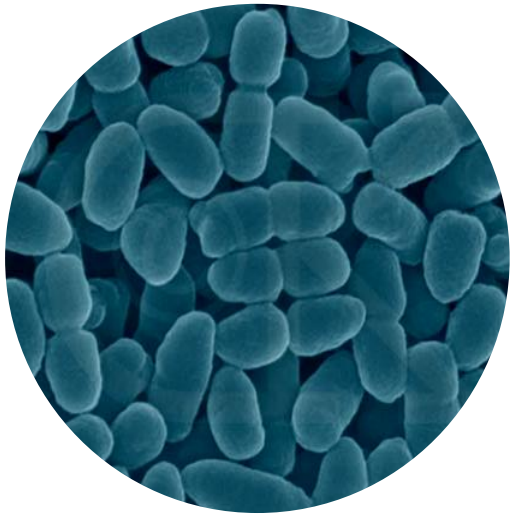
Foolad N, Armstrong AW. - Benef Microbes. 2014 Jan 24:1-10.

- Since 1997, immunostimulatory supplements, such as prebiotics and probiotics, have been investigated. ….
- In this narrative review, we examined 13 key articles on prebiotics and/or probiotics, and their effects on infant atopic dermatitis.
- **Among the selected studies, a total of 3,023 participants received supplements or placebo.**
  - **Eight out of the 13 (61.5%) studies reported a significant effect on the prevention of atopic dermatitis after supplementation with probiotics and/or prebiotics.**
  - **Five out of the 13 (38.5%) studies indicated significant reduction in the severity of atopic dermatitis after supplementation.**

Based on the available studies,

- supplementation with certain probiotics **(Lactobacillus rhamnosus GG)** appears to be an **effective approach for the prevention and reduction in severity of atopic dermatitis**.
- **A mix of specific probiotic strains prevented atopic dermatitis among infants**.
- Based on studies with prebiotics, there was a long-term reduction in the incidence of atopic dermatitis.

Supplementation with prebiotics and probiotics appears useful for the reduction in the severity of atopic dermatitis. Additional interventional studies exploring prebiotics and probiotics are imperative before recommendations can be made.



Probiotics in primary prevention of atopic disease: a randomised placebo-controlled trial.

Kalliomaki M, Salminen S, Arvilommi H, Kero P, Koskinen P, Isolauri E.

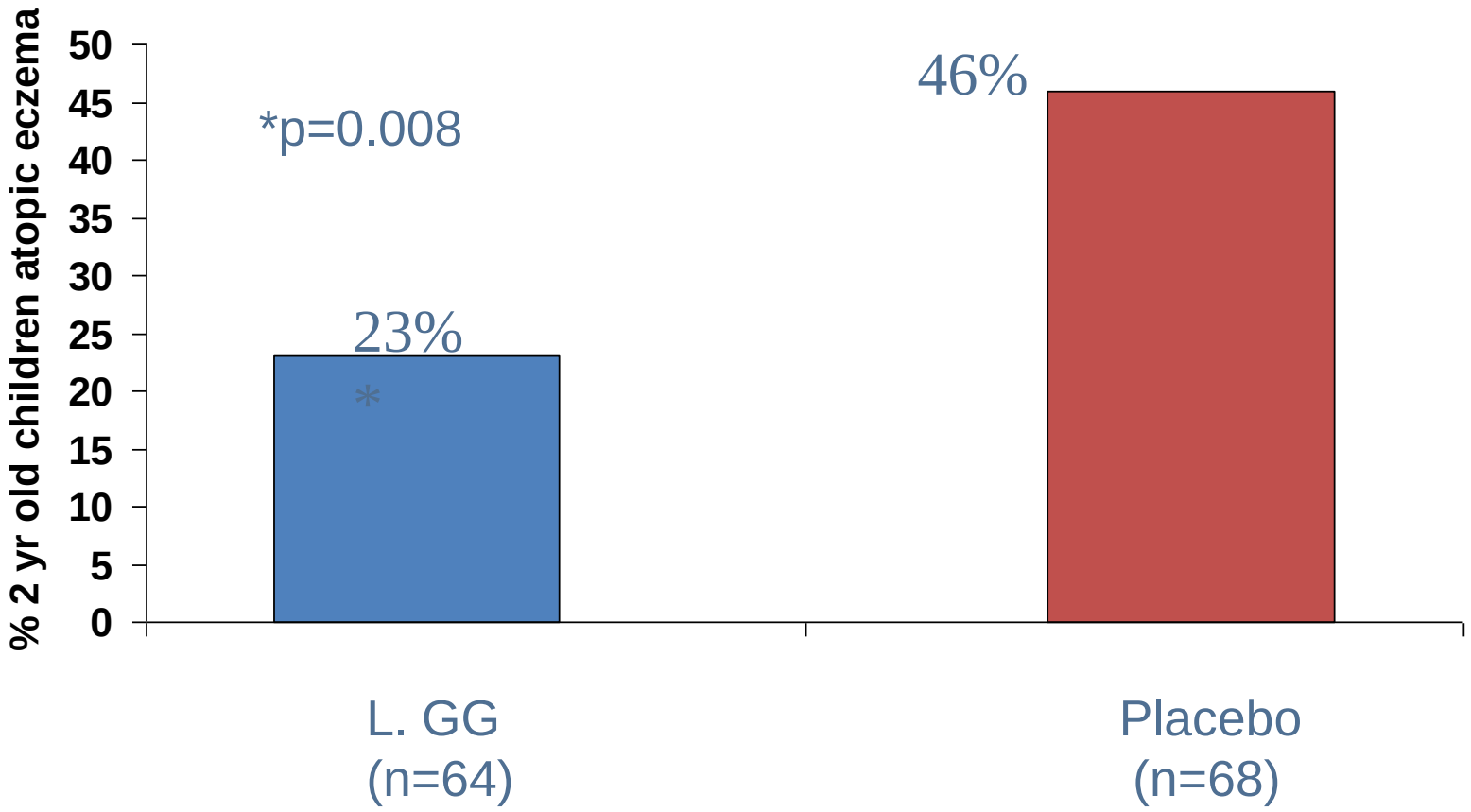
Lancet 2001 Apr 7;357(9262):1076-9

BACKGROUND: Reversal of the progressive increase in frequency of atopic disease would be an important breakthrough for health care and wellbeing in western societies. In the hygiene hypothesis this increase is attributed to reduced microbial exposure in early life. Probiotics are cultures of potentially beneficial bacteria of the healthy gut microflora. We assessed the effect on atopic disease of Lactobacillus GG (which is safe at an early age and effective in treatment of allergic inflammation and food allergy). METHODS: In a double-blind, randomised placebo-controlled trial we

Lactobacillus GG was effective in prevention of early atopic disease in children at high risk. Thus, gut microflora might be a hitherto unexplored source of natural immunomodulators and probiotics, for prevention of atopic disease.

prevention of early atopic disease in children at high risk. Thus, gut microflora might be a hitherto unexplored source of natural immunomodulators and probiotics, for prevention of atopic disease.

Lactobacillus GG and Infantile Atopic Disease [Results]



Kalliomaki M. Lancet 2001;357:1076-9

Specific probiotics alleviate allergic rhinitis during the birch pollen season. (Pollen de bouleau)
Ouwehand AC, Nermes M, Collado MC, Rautonen N, Salminen S, Isolauri E.
World J Gastroenterol. 2009 Jul 14;15(26):3261-8.

AIM: **To investigate whether birch pollen allergy symptoms are linked with gut microbiota changes and whether probiotics have an effect on these**.

Forty seven children with confirmed birch pollen allergy were randomized to receive either a probiotic combination of *Lactobacillus acidophilus (L. acidophilus)* NCFM (ATCC 700396) and *Bifidobacterium lactis (B. lactis)* Bl-04 (ATCC SD5219) or *placebo in a double-blind manner* for 4 mo, starting prior to onset of the birch pollen season.

Blood samples were taken for analysis of cytokines and eosinophils. Fecal samples were analysed for microbiota components, calprotectin and IgA. Nasal swabs were taken for analysis of eosinophils.

RESULTS:
The pollen season induced a reduction in Bifidobacterium, Clostridium and Bacteroides which could not be prevented by the probiotic intervention. During the intervention, significantly higher numbers of B. lactis 11.2 x 10(7) +/- 4.2 x 10(7) vs 0.1 x 10(7) +/- 0.1 x 10(7) bacteria/g feces ($P < 0.0001$) and L. acidophilus NCFM 3.5 x 10(6) +/- 1.3 x 10(6) vs 0.2 x 10(6) +/- 0.1 x 10(6) bacteria/g feces ($P < 0.0001$) were observed in the probiotic group compared to the placebo group. During May, there was a tendency for fewer subjects, (76.2% vs 95.2%, $P = 0.078$) to report runny nose, while during June, fewer subjects, 11.1% vs 33.3%, reported nasal blocking in the probiotics group ($P = 0.101$). Concomitantly, fewer subjects in the probiotic group had infiltration of eosinophils in the nasal mucosa compared to the placebo group, 57.1% vs 95% ($P = 0.013$). Eye symptoms tended to be slightly more frequent in the probiotic group, 12.5 d [interquartile range (IQR) 6-18] vs 7.5 d (IQR 0-11.5) ($P = 0.066$) during May. Fecal IgA was increased in the placebo group during the pollen season; this increase was prevented by the probiotics ($P = 0.028$).

CONCLUSION:

- **Birch pollen allergy was shown to be associated with changes in fecal microbiota composition.**
- **The specific combination of probiotics used was shown to prevent the pollen-induced infiltration of eosinophils into the nasal mucosa, and indicated a trend for reduced nasal symptoms.**

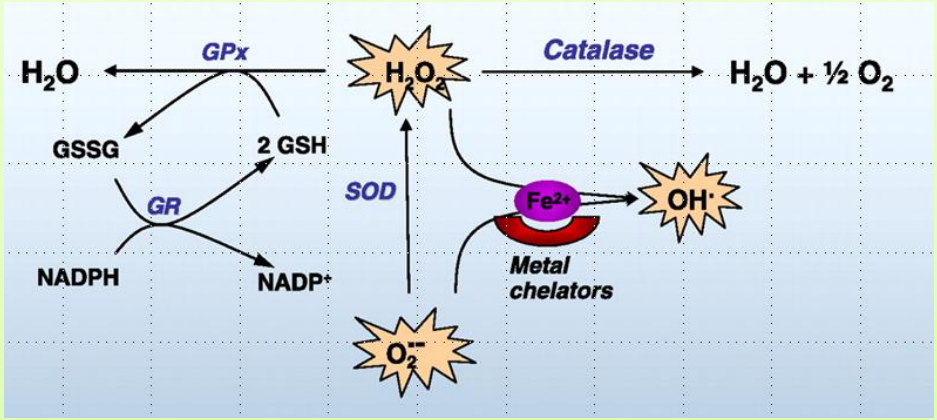
SELENIUM

Selenium and asthma

Robert L. Norton and Peter R. Hoffmann

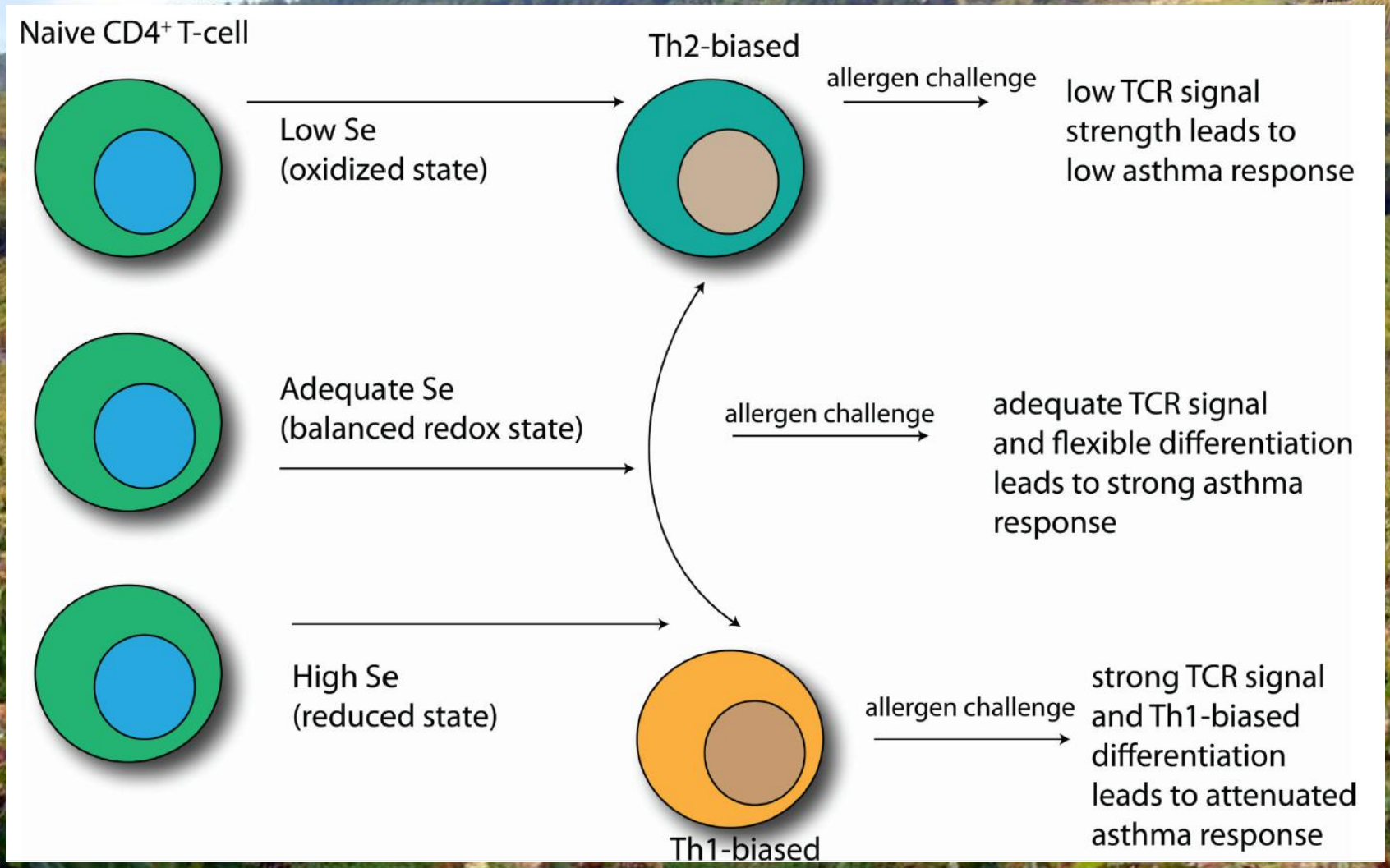
Mol. Aspects Med. 2012 February ; 33(1): 98 – 106

Se is a potent nutritional antioxidant important for various aspects of human health



Because asthma has been demonstrated to involve increased oxidative stress, levels of Se intake have been hypothesized to play an important role in the pathogenesis of asthma …

Effects of dietary Se levels on T helper cells and asthma



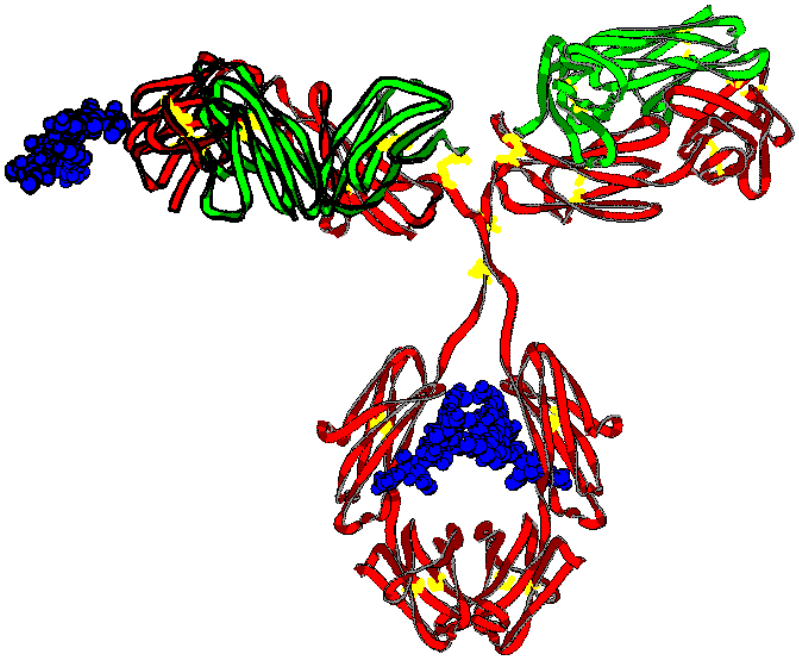
Norton & Hoffman - Mol Aspects Med. 2012 February

BIBLIOGRAPHIE

Quelques commentaires

1. Le nombre de publications journalières est impressionnant.
2. Malheureusement, les « guide lines » semblent paralyser de nombreux auteurs qui résument en disant que les tests (hors IgE) sont déconseillés par les autorités scientifiques, et on reste là.
3. Il faut savoir que la Belgique n'est pas en reste, puisque Jean Duchateau se posait déjà des questions il y a environ 20 ans sur les IgG
4. N'oublions pas non plus que la notion de « probiotiques » née vers 1983 dune publication de Gibson et … Marcel Robertfroid.
5. Nous comptons encore une unité très active dans la recherche (NaThalie Delzenne, Patrice Cani).
6. Nous disposons de modèles animaux permettant des recherches fondamentales très pointues: les souris transgéniques permettent de reconstituer l'équipement cellulaires de l'homme et de tester , comme vu plus haut, les caractéristiques des récepteurs, et ce n'est qu'un exemple.
7. En 2004, Atkinson, dans GUT, lançait les choix des exclusions alimentaires dans les IBD basées sur les tests sériques à IgG avec des résultats positifs.
8. L'Institut Pasteur a lancé un pavé dans la mare et a entamé des recherches dont nous parlerons.

IgG Anti-Aliments et allergies
(782 publications)



Pediatr Allergy Immunol. 2012 Sep;23(6):590-6. doi: 10.1111/j.1399-3038.2012.01277.x. Epub 2012 Mar 22.

Cow's milk and ovalbumin-specific IgG and IgA in children with eczema: low β-lactoglobulin-specific IgG4 levels are associated with cow's milk allergy.

Savilahti EM[1], Viljanen M, Kuitunen M, Savilahti E.

Author information

Abstract

Tolerance to allergens may partly depend on allergen-specific IgG and IgG subclasses and IgA antibodies. We investigated whether specific IgG and IgG subclasses and IgA antibodies to β-lactoglobulin, α-casein, and ovalbumin differed between infants who had verified cow's milk allergy (CMA) and infants with cow's milk (CM)-associated eczema, but negative CM oral challenge. The study population comprised 95 infants with clinical eczema that was by history associated with the consumption of CM. After an elimination period, a double-blind, placebo-controlled (DBPC) CM oral challenge confirmed CMA in 45 infants. Skin prick tests (SPT) were performed with CM and hen's egg. Serum levels of IgE antibodies to CM and hen's egg were measured with UniCAP (Phadia, Uppsala, Sweden), and levels of IgA, IgG, IgG1, and IgG4 antibodies to β-lactoglobulin, α-casein, and ovalbumin were measured with enzyme-linked immunosorbent assay. We observed that infants with CMA had lower IgG4 levels to β-lactoglobulin than infants with negative DBPC CM challenge ($p = 0.004$). Positive CM SPT was associated with lower IgG4 levels to α-casein ($p = 0.04$). The relation of CM IgE to β-lactoglobulin and α-casein IgG4 was higher in CMA than in infants with negative challenge ($p < 0.002$ and 0.0001). Positive egg SPT was associated with elevated levels of specific IgG to ovalbumin, β-lactoglobulin, and α-casein as well as IgA to α-casein ($p < 0.04$). Our study thus shows that low β-lactoglobulin-specific serum IgG4 levels may differentiate eczematous infants with CMA from infants who have eczema with only suspected association with CM.

Clin Exp Allergy. 2011 Oct;41(10):1414-21. doi: 10.1111/j.1365-2222.2011.03821.x. Epub 2011 Jul 19.

Ovalbumin-specific immunoglobulins A and G levels at age 2 years are associated with the occurrence of atopic disorders.

Kukkonen AK[1], Savilahti EM, Haahtela T, Savilahti E, Kuitunen M.

⊕ Author information

Abstract

BACKGROUND: Humoral responses to food antigens may reflect the propensity of a child's immune system to develop tolerance to innocuous antigens. Early nutrition as well as probiotics may influence these immunological responses.

OBJECTIVE: To study the association of humoral responses to early food antigens with the administration of prebiotics and probiotics, with the occurrence of allergy, and with the length of exclusive breastfeeding.

METHODS: In a randomized double-blind allergy prevention trial in high-risk children, 1018 mothers took probiotics or placebo from the 36th week of gestation, and their newborn infants received probiotics and prebiotics or placebo during 6 months. At 2 and 5 years, we evaluated the cumulative incidence of allergic diseases (food allergy, eczema, asthma, rhinitis) and sensitization (skin prick test ≥3 mm or serum antigen-specific IgE>0.7 kU/L). In 688 infants at age 2, we measured in sera-specific IgA, IgG, IgG1, and IgG4 antibody levels to cow's milk (CM), α-casein (CAS), β-lactoglobulin (BLG), and ovalbumin (OVA) with ELISA, and specific IgE levels to CM and hen's egg with UniCap.

RESULTS: Probiotic treatment (n=342) compared with placebo (n=346) showed no effect on serum food-specific IgA, IgG, IgG1, or IgG4 concentrations at age 2. Atopic children had higher OVA-IgA (P<0.001), OVA-IgG (P=0.001), OVA-IgG1 (P<0.001), and egg-IgE but lower OVA-IgG4/egg-IgE ratio (P<0.001) than non-atopic children. Longer duration of exclusive breastfeeding (≥4 vs. <4 months) was associated with reduced CM- and CAS-specific serum IgA (P<0.001) and IgG levels (P<0.001; P=0.003).

CONCLUSION AND CLINICAL RELEVANCE: Allergy was associated with more intense IgA and IgG responses to OVA. Breastfeeding depressed humoral responses, whereas prebiotics and probiotics supplementation showed no immunomodulatory effect. The effect of probiotics on allergies is not mediated through food-specific antibody responses. Furthermore, OVA-specific IgA and IgG antibodies may help in assessing the risk for atopy.

Milk protein IgG and IgA: the association with milk-induced gastrointestinal symptoms in adults.

Anthoni S, Savilahti E, Rautelin H, Kolho KL.
Hospital for Children and Adolescents, University of Helsinki, PO Box 281, FIN-00029 HYKS, Helsinki, Finland.

World J Gastroenterol. 2009 Oct 21;15(39):4915-8.

AIM: To study the association between serum levels of milk protein IgG and IgA antibodies and milk-related gastrointestinal symptoms in adults. METHODS: Milk protein IgG and IgA antibodies were determined in serum samples of 400 subjects from five outpatient clinics in Southern Finland. Subjects were randomly selected from a total of 1900 adults undergoing laboratory investigations in primary care. All 400 participants had completed a questionnaire on abdominal symptoms and dairy consumption while waiting for the laboratory visit. The questionnaire covered the nature and frequency of gastrointestinal problems, the provoking food items, family history and allergies. Twelve serum samples were disqualified due to insufficient amount of sera. The levels of specific milk protein IgG and IgA were measured by using the ELISA technique. The association of the milk protein-specific antibody level was studied in relation to the milk-related gastrointestinal symptoms and dairy consumption. RESULTS: Subjects drinking milk (n = 265) had higher levels of milk protein IgG in their sera than non-milk drinkers (n = 123, $P < 0.001$). Subjects with gastrointestinal problems related to milk drinking (n = 119) consumed less milk but had higher milk protein IgG levels than those with no milk-related gastrointestinal symptoms (n = 198, $P = 0.02$). Among the symptomatic subjects, those reporting dyspeptic symptoms had lower milk protein IgG levels than non-dyspeptics ($P < 0.05$). However, dyspepsia was not associated with milk drinking ($P = 0.5$). The association of high milk protein IgG levels with constipation was close to the level of statistical significance. Diarrhea had no association with milk protein IgG level ($P = 0.5$). With regard to minor symptoms, flatulence and bloating ($P = 0.8$), were not associated with milk protein IgG level. Milk protein IgA levels did not show any association with milk drinking or abdominal symptoms. The levels of milk protein IgA and IgG declined as the age of the subjects increased ($P < 0.004$). CONCLUSION: Milk protein IgG but not milk IgA seems to be associated with self-reported milk-induced gastrointestinal symptoms.

IgG and IgE avidity characteristics of peanut allergic individuals.

El-Khouly F, Lewis SA, Pons L, Burks AW, Hourihane JO.

Pediatr Allergy Immunol. 2007 Nov;18(7):607-13.

The role of antibody avidity in allergy is poorly understood and there is no existing literature describing antibody avidity in food allergy. The main aim of this study was to investigate IgE and IgG avidity to a total peanut protein extract (TPPE) and purified Ara h 2 in a group of well-characterized peanut allergic individuals. Forty peanut allergic patients underwent a double-blind placebo-controlled low-dose peanut challenge, during which the severity of the patients' peanut allergy was scored. Serum peanut-specific IgE (psIgE) and IgG (psIgG) concentrations were measured for 37 individuals and the avidities of the same antibodies to a TPPE and purified Ara h 2 were determined using a thiocyanate ELISA method. Both IgE and IgG avidity to Ara h 2 showed weak positive correlations with challenge score [$r = 0.459$ ($p = 0.012$) and $r = 0.486$ ($p = 0.003$), respectively]. IgE avidity to TPPE showed a weak positive correlation with skin prick test results (SPT), $r = 0.467$ ($p = 0.004$) and there was an inverse relationship between the ratio of total IgE:psIgE and challenge score $r = -0.561$ ($p < 0.001$). No significant relationship was found between the ratios of IgE avidity:IgG avidity and challenge score or SPT. This is the first description of IgE and IgG avidity in peanut allergy, and it appears that the avidities of IgE and IgG antibodies to purified Ara h 2 are weakly related to the severity of peanut allergy (as measured by a challenge score).

Anti-betalactoglobulin IgG antibodies bind to a specific profile of epitopes when patients are allergic to cow's milk proteins.

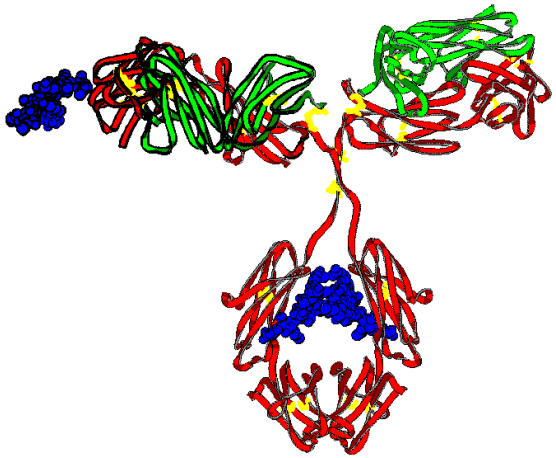
Duchateau J, Michils A, Lambert J, Gossart B, Casimir G.
Immunology Department, Centre Hospitalier Universitaire Brugmann-HUDERF, Université Libre de Bruxelles, Brussels, Belgium.

Clin Exp Allergy. 1998 Jul;28(7):824-33.

BACKGROUND: We demonstrated recently that mite-allergic patients differed from healthy controls in the specificity of their IgG antibodies towards mite antigens. OBJECTIVE: The present study investigates whether these discriminatory IgG responses could be associated with the expression and the evolution of clinical manifestations in allergy to cow's milk proteins. METHODS: Antibody specificity was evaluated by comparing IgG-binding to native bovine beta-lactoglobulin (nBLG) and its products of pepsin hydrolysis (dBLG) using a solid-phase enzyme-linked immunosorbent assay (ELISA). Antibody specificity was further investigated in competitive ELISA using streptavidin-biotin technology with purified IgG fractions from selected subjects and specific mouse monoclonals raised against BLG. RESULTS: IgG antibodies from CM-intolerant or allergic sera (n=222) showed a higher degree of binding to nBLG than to dBLG, while control sera showed similar levels to both nBLG and dBLG (n=99 children/65 adults). Sera from symptomatic patients, wether or not they contained IgE antibodies, demonstrated group-segregating capacities to compete with pooled purified IgG from each clinical class, and with selected murine anti-nBLG monoclonal antibodies for binding to n- and dBLG. Furthermore, this inhibitory capacity shifted dramatically in a small subset (n=14) of children as they developed CM-tolerance. CONCLUSIONS: The IgG responses to BLG of CM-intolerant or allergic patients are very different from those of healthy controls, being characterized not only by increased titres but also similar patterns of modified specificity, including a marked preference for conformational epitopes. Cross-competition experiments confirmed that the restricted specificity was clinically associated, appearing as an immunological signature, which allowed almost complete discrimination between patient groups. This phenomenon is a particularly promising diagnostic feature in this category of young patients where conventional tests usually only document the status of sensitization.j

IgG Anti-Aliments et allergies

Asthme



The effects of exclusion of dietary egg and milk in the management of asthmatic children: a pilot study.

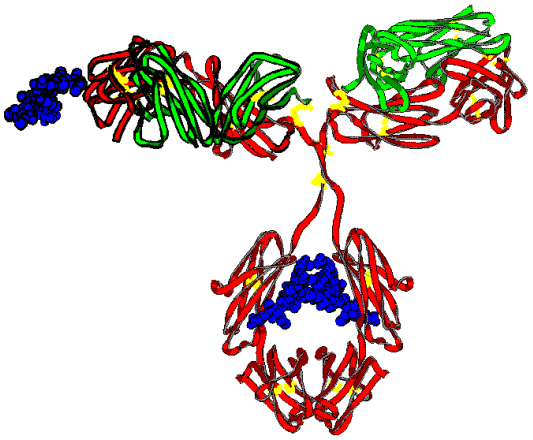
Yusoff NA, Hampton SM, Dickerson JW, Morgan JB.

J R Soc Health. 2004 Mar;124(2):74-80.

Current understanding of the use of exclusion diets in the management of asthma in children is limited and controversial. The aim of this study was to examine the effects of excluding eggs and milk on the occurrence of symptoms in children with asthma and involved 22 children aged between three and 14 years clinically diagnosed as having mild to moderate disease. The investigation was single blind and prospective, and parents were given the option of volunteering to join the 'experiment' group, avoiding eggs, milk and their products for eight weeks, or the 'control' group, who consumed their customary food. Thirteen children were recruited to the experimental group and nine to the control group. A trained paediatrician at the beginning and end of the study period assessed the children. A seven-day assessment of food intake was made before, during and immediately after the period of dietary intervention in both groups. A blood sample was taken from each child for determination of food specific antibodies and in those children who could do so, the peak expiratory flow rate (PEFR) was measured. Based on the recommended nutrient intake (RNI), the mean percentage energy intake of the children in the experimental group was significantly lower ($p < 0.05$) in the experimental group. After the eight-week study period and compared with baseline values, the mean serum anti-ovalbumin IgG and anti-beta lactoglobulin IgG concentrations were statistically significantly reduced ($p < 0.05$) for both in the experimental group. In contrast, the values for anti-ovalbumin IgG in the control group were significantly increased and those for anti-beta lactoglobulin IgG were practically unchanged. The total IgE values were unchanged in both groups. Over the study period, the PEFR in those children in the experimental group able to perform the test was significantly increased, but no such change was noted in the children in the control group who could do the test. These results suggest that even over the short time period of eight weeks, an egg- and milk-free diet can reduce atopic symptoms and improve lung function in asthmatic children.

IgG Anti-Aliments et allergies

Rhinite allergique



ASIAN PACIFIC JOURNAL OF ALLERGY AND IMMUNOLOGY (2001) 19: 7-10

The Relevance of Specific Serum IgG, IgG_4 and IgE in the Determination of Shrimp and Crab Allergies in Malaysian Allergic Rhinitis Patients

Yeoh Sheah-Min and Sam Choon-Kook

SUMMARY The significance of food specific serum IgG_4 antibody in food allergy is unclear and this led us to investigate the relevance of specific IgG_4, along with IgG and IgE antibodies to two common food allergens in Malaysia. Enzyme-linked immunosorbent assay (ELISA) was used to measure the serum antibodies in 143 allergic rhinitis patients' sera, of which 47 were from patients with clinical indication of shrimp allergy, 46 with clinical indication of crab allergy and 50 without indication to either allergy. Clinical indication of allergy was based on answers to a questionnaire or results of the skin prick test. We found that the elevation of specific IgE or IgG_4 is associated with shrimp and crab allergies but elevation of specific IgG is not associated with either allergy. However, the clinical utility of elevated specific IgG and IgG_4 levels is pending further investigation.

NBT/ALLERGIES®

CAS CLINIQUES

PATIENT 1

Julien 9 ans

Fils unique

Parents ensembles

Asthme depuis l'âge de 7 ans

Allergie au pollen bouleau (RAST +++)

TRAITEMENT

Aerius®(en prévention et traitement pdt la saison

Aérosol de Ventolin® lors de bronchospasme

Deux hospitalisation en urgence les deux dernières années.

Pas de prise en charge nutritionnelle ni micro-nutritionnelle

MOTIF CONSULTATION

La Maman vient en consultation car a entendu que la nutrition peut améliorer son enfant au niveau allergie

Julien 9 ans

Anamnèse

Pas d'antécédents familiaux d'allergies
Pas d'allaitement maternel!
Présente des coliques fréquentes et des troubles du transit
Pas de notion d'exacerbation des symptômes suite à la consommation d'un aliment ou groupe d'aliment particulier.
Petites difficultés d'attention à l'école

Bilans prescrits

Biologie classique (y compris statut martial)
Contrôle des RAST pollen bouleau

NBT/allergies
Pas d IgG Alimentaires à ce stade

Julien 9 ans

Biologie classique

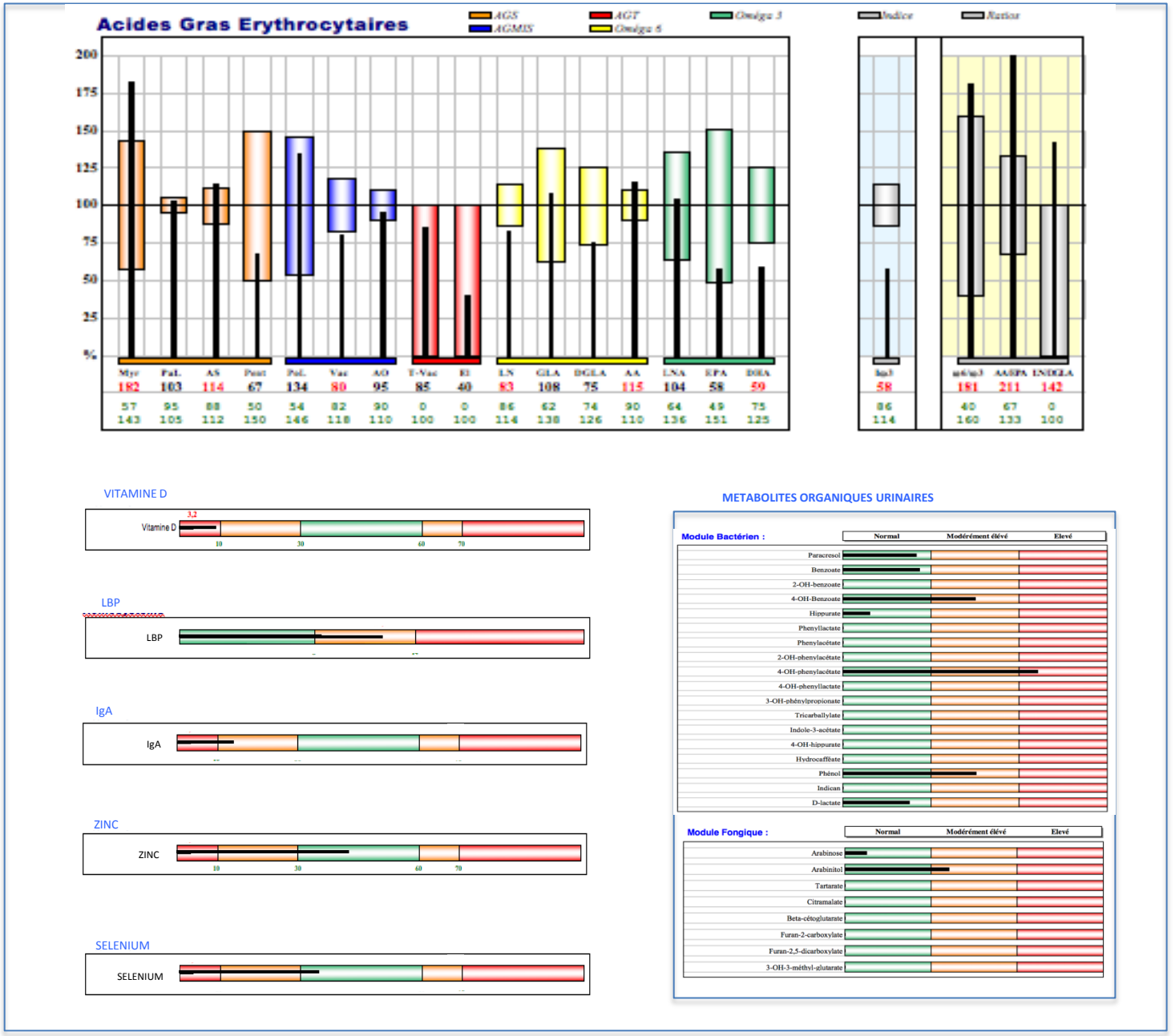
Rien de particulier à part

Une CRPus à 3
Une carence martiale(ferritine normale, transferrine élevée et % de saturation de la transferrine basse

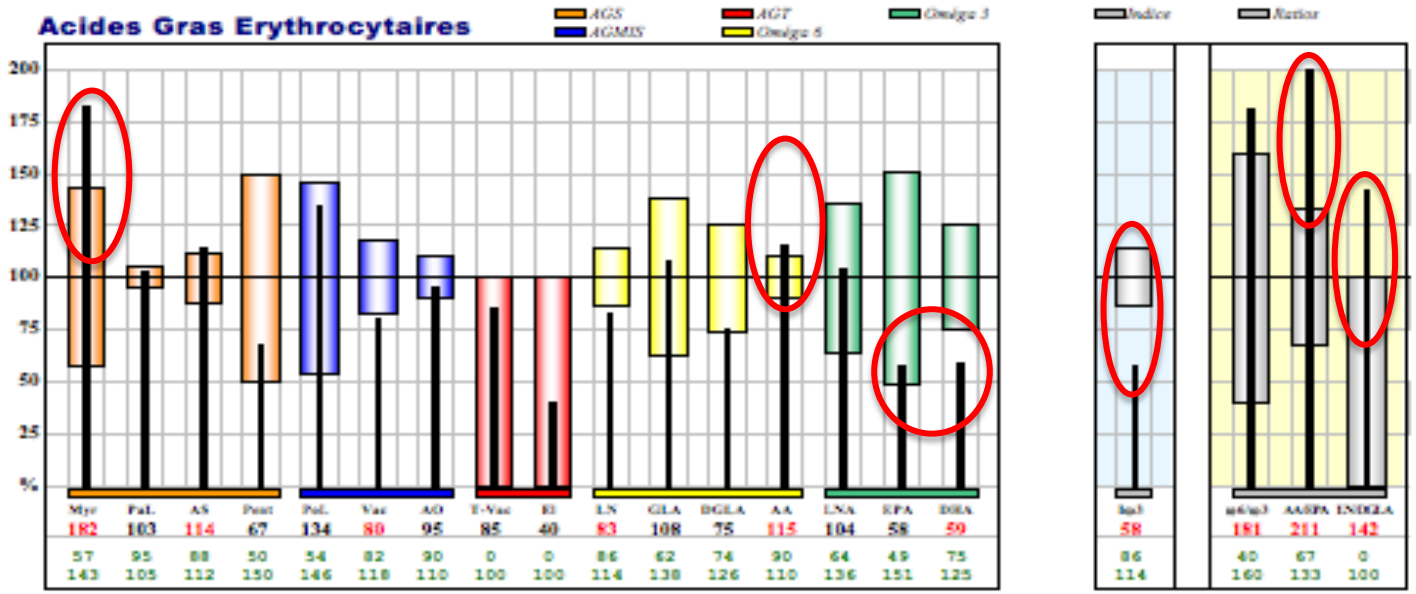
RAST pollen +++

Julien 9 ans

NBT/ALLERGIES®



Profil acide gras



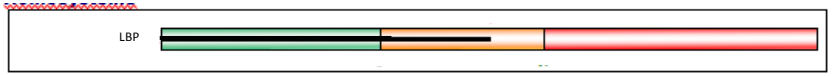
1. **Excès acide myristique** : consommation de sucre rapide, crème…
2. **Excès acide arachidonique** : produits animaux, huiles arachide, mais ou tournesol (olive)
3. **Index omega3**: trop bas
4. **Rapport AA/EPA** > 15
5. **Delta6 désaturase** : pas optimale

NBT/ALLERGIES®

VITAMINE D

Vitamine D : effondrée

LBP

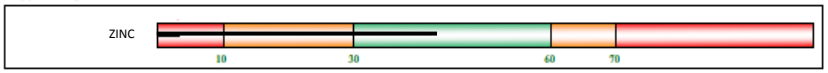


LBP : modérément élevée

IgA

IgA: trop bas

ZINC



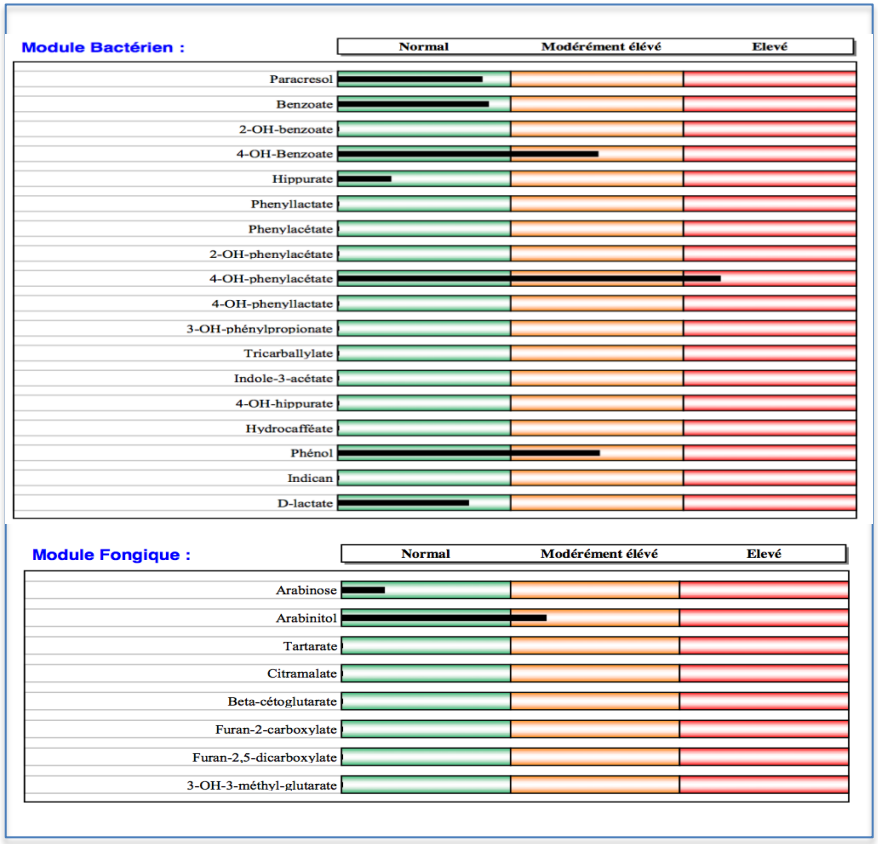
Zinc: normal

SELENIUM

Sélénium: normal bas

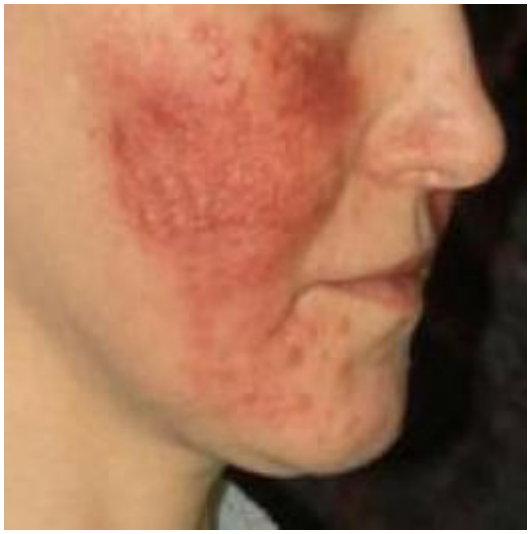
MOU

METABOLITES ORGANIQUES URINAIRES



Legère dysbiose

Pas de mycose

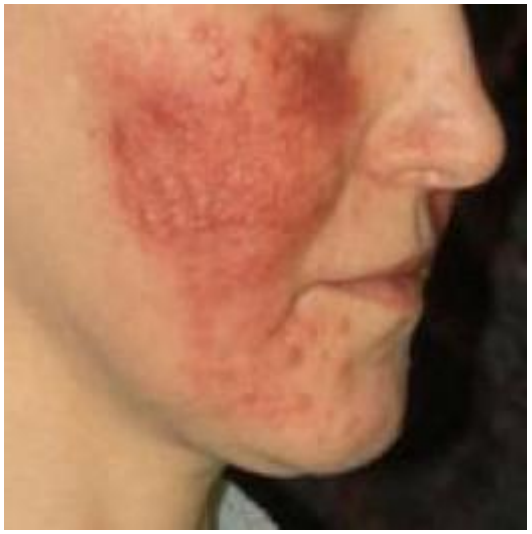


PATIENT 2

FABIENNE 37 ans
Célibataire, sans enfants
Assistante pharmacie
Eczéma surtout facial depuis 31 ans
Exploration immunologique (RASTs, tests cutanés) négatifs

TRAITEMENT
Pommade corticoïdes diverses avec effets passagers peu satisfaisants

MOTIF CONSULTATION
Patiente déprimée par l'aspect esthétique de son affection. Envoyée par son médecin traitant



Fabienne

Anamnèse

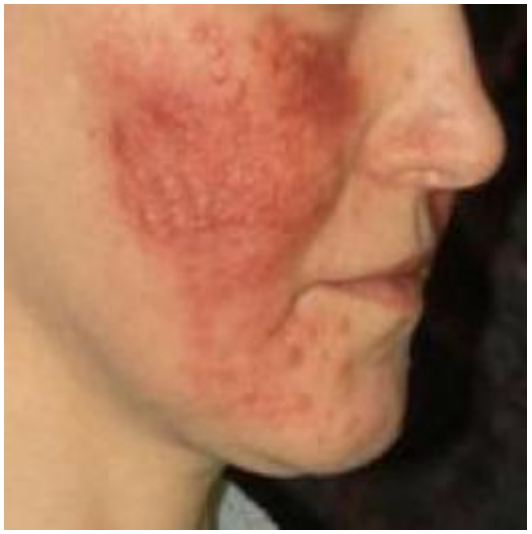
Pas d'antécédents familiaux d'allergies
Allaitement maternel > 6 mois

Ballonnement fréquents et crampes
Gaz putrides
Pas de notion claire d'ecacerbation des symptômes suite à la consommation d'un aliment ou groupe d'aliment particulier.
Légèrement dépressive

Bilans prescrits

Biologie classique (y compris statut martial)

NBT/allergies
Panel de 10 IgG Alimentaires



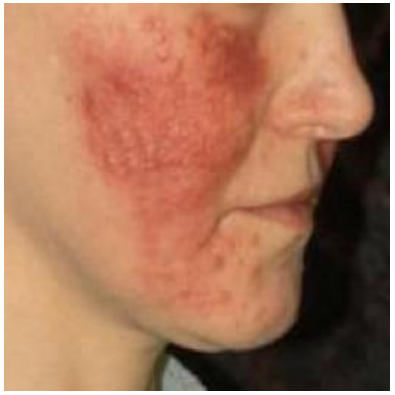
Fabienne

Biologie classique

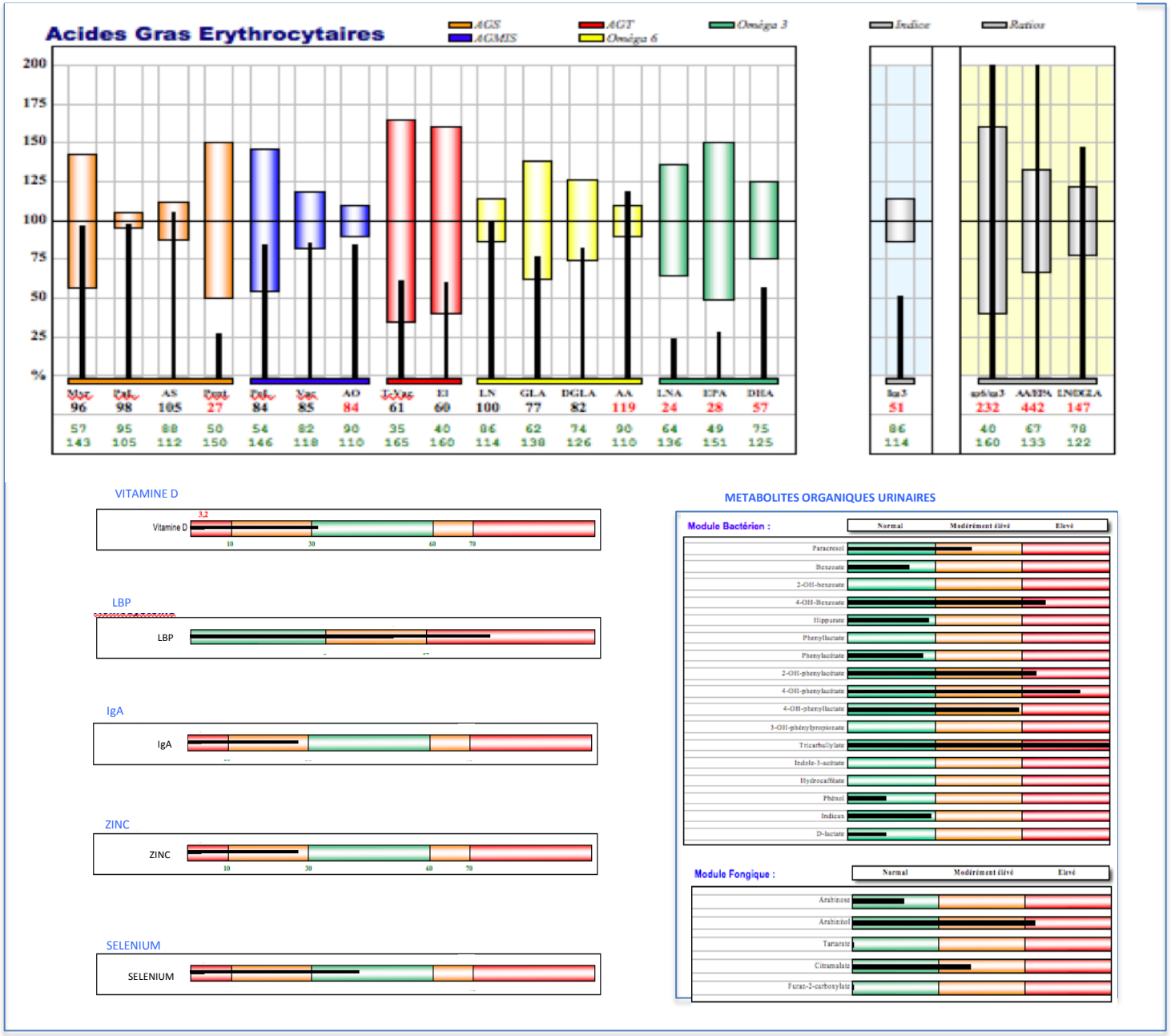
PAS d'anomalies significatives hormis:

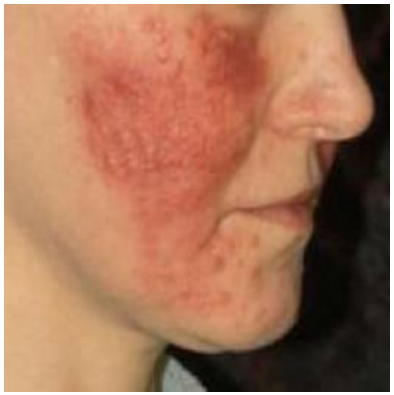
Une CRP à 9

NBT/ALLERGIES®



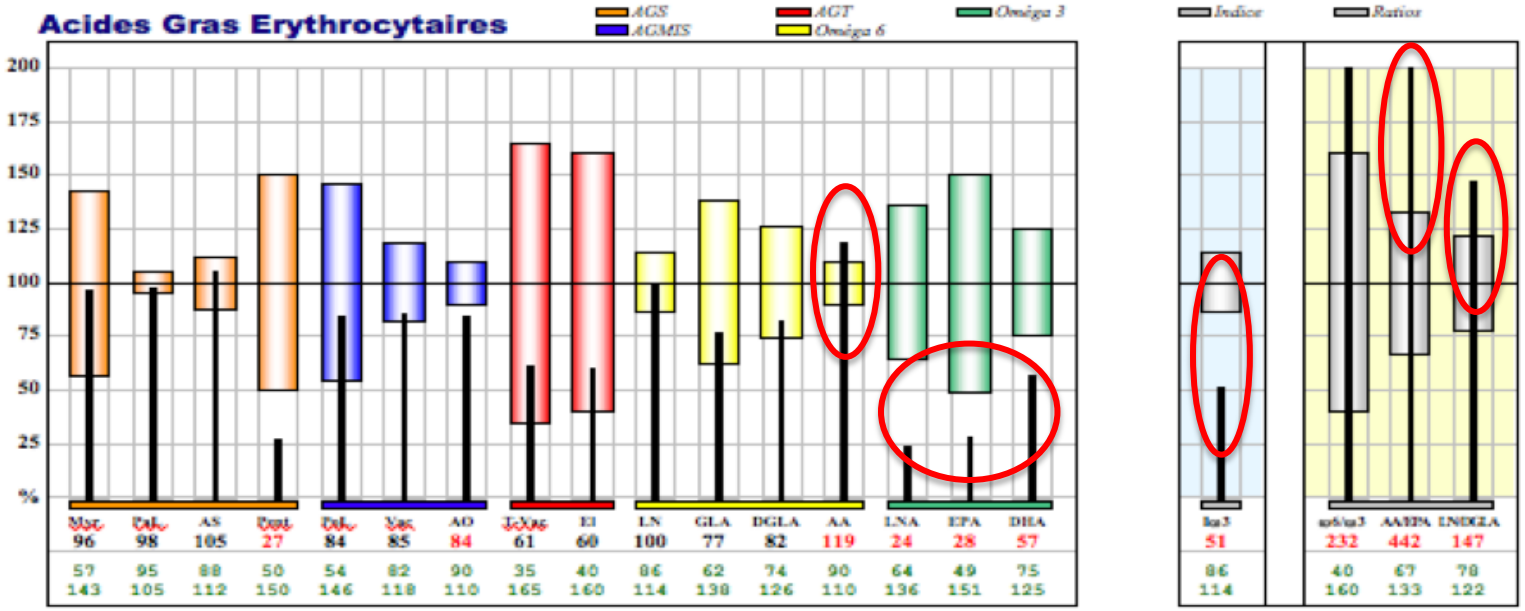
Fabienne



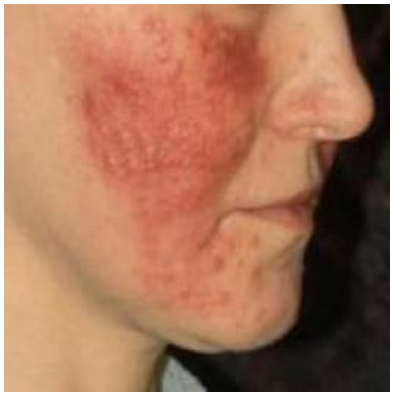


Profil acide gras

Fabienne



1. **Excès acide arachidonique** : produits animaux, huiles arachide, mais ou tournesol (olive)
2. **Index omega3**: très bas
3. **Acide alpha-linolénique**: très bas
4. **Rapport AA/EPA** > 25
5. **Delta6 désaturase** : pas efficace



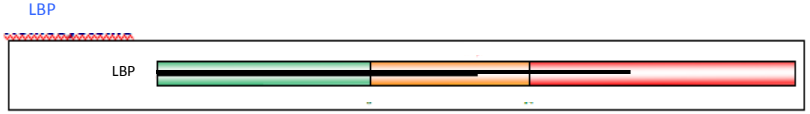
NBT/ALLERGIES®

Fabienne

VITAMINE D

Vitamine D : basse

LBP



LBP : très élevée

IgA

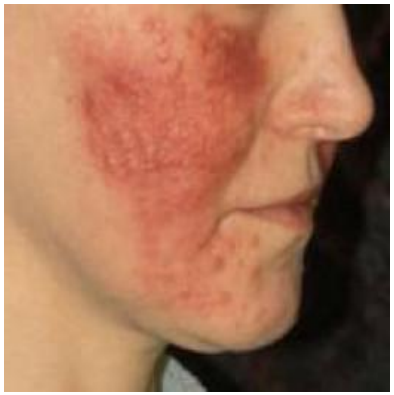
IgA: bas

ZINC

Zinc: carence

SELENIUM

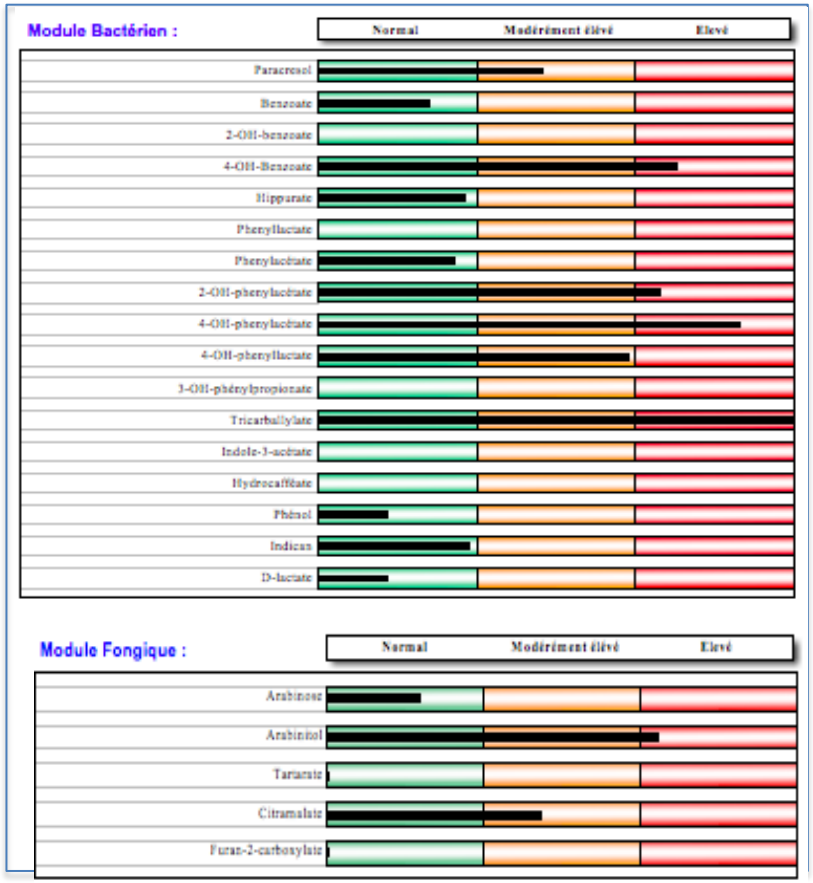
Sélénium: normal



MOU

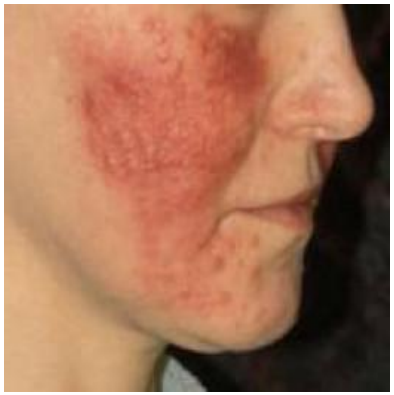
Fabienne

METABOLITES ORGANIQUES URINAIRES



Dysbiose sévère

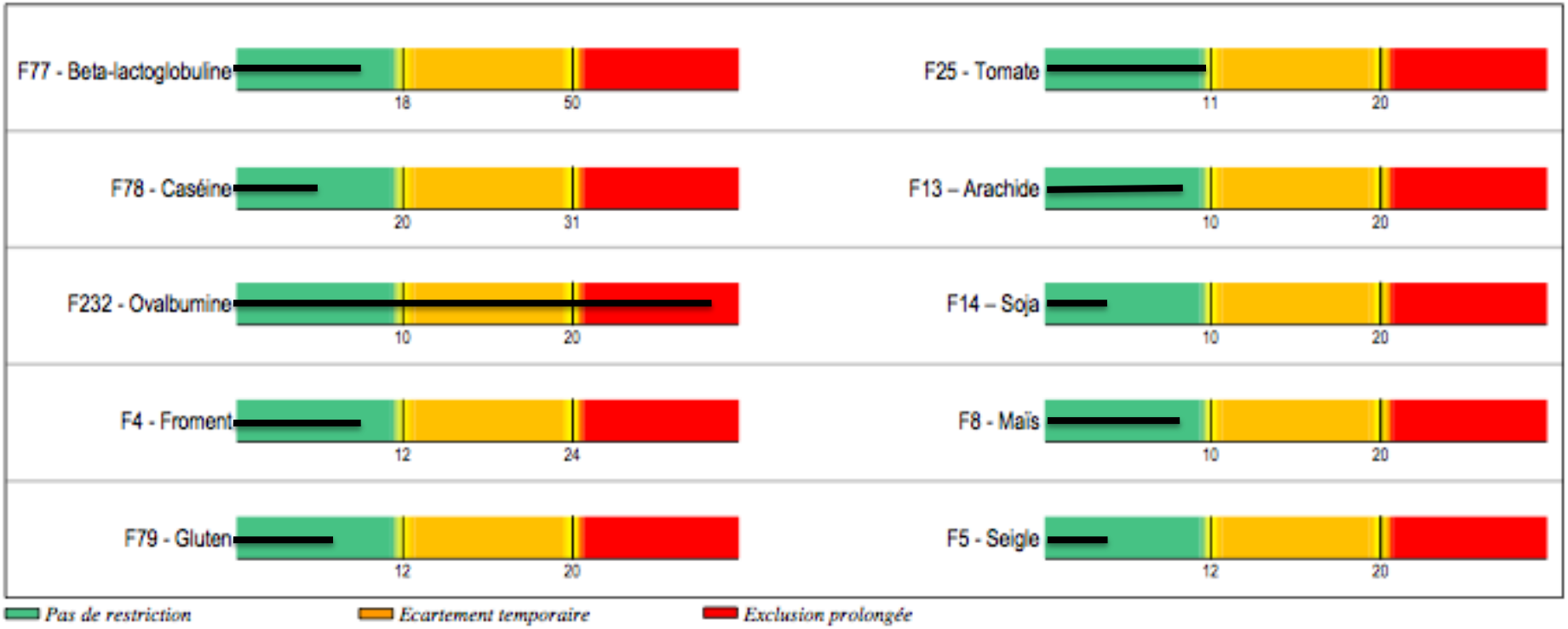
Mycose modérée



IgG Alimentaires

Fabienne

IgG (Méthode par chemiluminescence)



Hypersensibilté au blanc d’oeuf

VOIES D'AVENIR
ET
CONCLUSIONS … PROVISOIRES

POUR ou CONTRE … l'avenir nous le dira

Human FcγRIIA induces anaphylactic and allergic reactions

Friederike Jönsson,[1,2] David A. Mancardi,[1,2] Wei Zhao,[3] Yoshihiro Kita,[4] Bruno Iannascoli,[1,2] Huot Khun,[5] Nico van Rooijen,[6] Takao Shimizu,[4,7] Lawrence B. Schwartz,[8] Marc Daëron,[1,2] and Pierre Bruhns[1,2]

[1]Institut Pasteur, Département d'Immunologie, Unité d'Allergologie Moléculaire et Cellulaire, Paris, France; [2]Inserm, U760, Paris, France; [3]Department of Pediatrics, Division of Rheumatology, Allergy and Immunology, Virginia Commonwealth University, Richmond, VA; [4]Department of Lipidomics, Faculty of Medicine, The University of Tokyo, Tokyo, Japan; [5]Institut Pasteur, Unité d'Histopathologie humaine et modèles animaux, Département Infection et Epidémiologie, Paris, France; [6]Department of Molecular Cell Biology, VU Medical Center, Amsterdam, The Netherlands; [7]Department of Biochemistry and Molecular Biology, Faculty of Medicine, The University of Tokyo, Tokyo, Japan; and [8]Department of Internal Medicine, Division of Rheumatology, Allergy and Immunology, Virginia Commonwealth University, Richmond, VA

IgE and IgE receptors (FcεRI) are well-known inducers of allergy. We recently found in mice that active systemic anaphylaxis depends on IgG and IgG receptors (FcγRIIIA and FcγRIV) expressed by neutrophils, rather than on IgE and FcεRI expressed by mast cells and basophils. In humans, neutrophils, mast cells, basophils, and eosinophils do not express FcγRIIIA or FcγRIV, but FcγRIIA. We therefore investigated the possible role of FcγRIIA in allergy by generating novel FcγRIIA-transgenic mice, in which various models of allergic reactions induced by IgG could be studied. In mice, FcγRIIA was sufficient to trigger active and passive anaphylaxis, and airway inflammation in vivo. Blocking FcγRIIA in vivo abolished these reactions. We identified mast cells to be responsible for FcγRIIA-dependent passive cutaneous anaphylaxis, and monocytes/macrophages and neutrophils to be responsible for FcγRIIA-dependent passive systemic anaphylaxis. Supporting these findings, human mast cells, monocytes and neutrophils produced anaphylactogenic mediators after FcγRIIA engagement. IgG and FcγRIIA may therefore contribute to allergic and anaphylactic reactions in humans. (*Blood*. 2012;119(11):2533-2544)

Inspiré de

Le double jeu des anticorps dans les allergies

Marc Daëron

- Allergies et maladies auto-immunes sont inflammatoires aigües et chroniques
- Fréquence et gravité augmentent exponentiellement depuis 50 ans
- Point commun: des anticorps qui rendent malades au lieu de protéger
- Ces anticorps sont dirigés contre des substances inoffensives de l'environnement ou, pire, contre nos propres constituants
- **Ces réactions apparaissent donc comme des réponses aberrantes du système immunitaire**

- **REMISE EN CAUSE DE CE QUE NOUS CROYIONS AVOIR COMPRIS ???**

Les anticorps peuvent jouer un double rôle dans l'allergie et leurs effets dépendent en premier lieu des cellules impliquées.

Institut Pasteur

Si les allergies sont bien dues à des anticorps,

- Ces anticorps sont extrêmement peu abondants.
- Ils appartiennent à une classe, les IgE, auxquelles on ne reconnaît qu'un rôle pathologique.
- En 1er contact avec un allergène: fixation élevée à des récepteurs d'anticorps uniques, exprimés par des cellules minoritaires dans le sang et les tissus, les basophiles et mastocytes.
- Si l'allergène réapparaît, il déclenche la libération des médiateurs contenus dans les granules de ces cellules et la sécrétion d'autres substances pro-inflammatoires.

« Nous pensons que, pour plusieurs raisons cette façon de voir est réductrice, que l'allergie ne peut être exclue de la réponse immunitaire normale et qu'elle ne se limite pas à ces anticorps, à ces récepteurs et à ces médiateurs ».

« Nous étudions les rôles des IgG, la classe d'anticorps majoritaire, les récepteurs pour ces anticorps, les cellules qui expriment ces récepteurs et les réactions de ces cellules induites par les anticorps en présence d'antigène ».

« Nos travaux les plus récents montrent non seulement que

- ***ces IgG, ces récepteurs et ces cellules participent aux réactions allergiques, mais que***
- ***leurs rôles peuvent être antagonistes ».***

Institut Pasteur

Inspiré de Marc Daëron

- ***Les IgG jouent un rôle prépondérant, bien plus que les IgE, dans le choc anaphylactique.***
- ***Les polynucléaires neutrophiles sont des acteurs majeurs de l'anaphylaxie.***

J. Clin. Invest., 2011;121:1484-1496. Ranked among the top 2% of published articles in biology and medicine by The Faculty of 1000.

Nos résultats ont confirmé que *les IgG sont bien capables d'induire différentes manifestations aiguës de type allergique*,

- **En activant les *neutrophiles*, mais également d'autres cellules qui expriment les mêmes récepteurs :**
- **les *monocytes dans le sang*, et les *mastocytes dans les tissus* comme la peau.**

Ces résultats confirment le rôle des polynucléaires neutrophiles dans l'anaphylaxie, mais démontrent que les *récepteurs* exprimés chez l'homme par ces cellules sont impliqués.

Human FcγRIIA induces anaphylactic and allergic reactions. Blood. 2012, 119: 2533-2544

Les neutrophiles et les monocytes (100 fois plus nombreux que les basophiles dans le sang), peuvent induire des réactions allergiques gravissimes comme le choc anaphylactique lorsqu'ils sont activés par des IgG (1 million de fois plus abondants que les IgE dans le plasma).

Ces résultats posent aussi un problème.

- **Nous produisons tous une grande quantité d'IgG et**
- **Nous possédons tous les neutrophiles responsables.**

Or, si la fréquence des allergies augmente rapidement, les deux tiers d'entre nous ne sont pas allergiques.

Institut Pasteur

LES BASOPHILES

Etude des mécanismes susceptibles de nous protéger des allergies.

- **Les basophiles expriment les mêmes récepteurs pour les IgG que les neutrophiles, mais ils ne sont pas ou très peu activables par ces IgG.**
- **A côté de ces récepteurs capables d'activer les cellules, les basophiles expriment d'autres récepteurs pour les IgG qui inhibent les réponses induites par les premiers**
- **Cette inhibition s'exerce également sur l'activation des basophiles par les IgE. Ils expriment en effet des récepteurs pour les IgE capables de les activer très efficacement, mais leurs récepteurs pour les IgG peuvent inhiber cette activation.**

Les IgG sont donc capables de contrôler les réaction allergiques dues aux IgE.
Les IgG peuvent donc

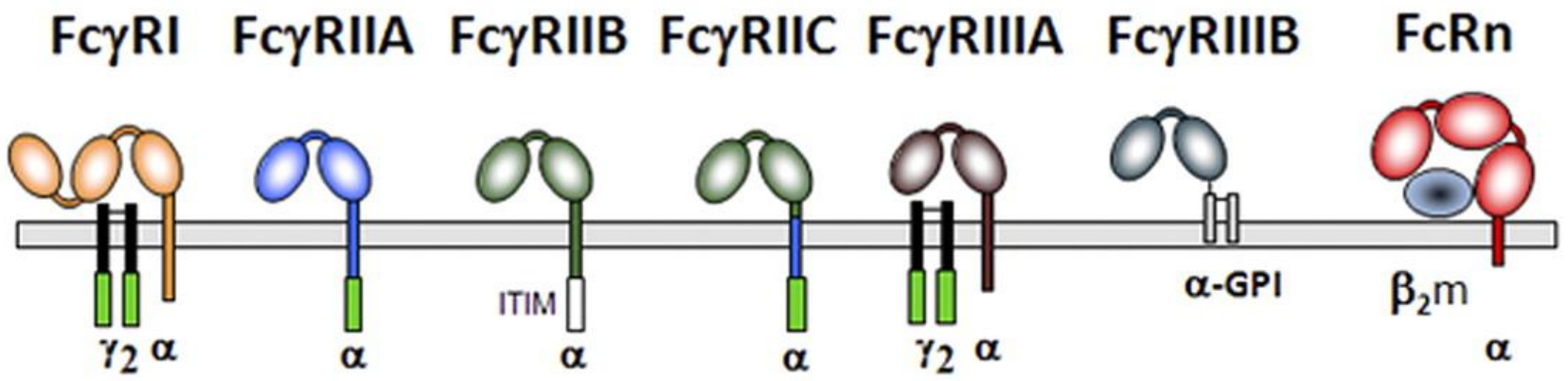
- ***inhiber les réactions allergiques qui dépendent des basophiles***
- ***induire les réactions allergiques qui dépendent des neutrophiles.***

C'est l'expression relative de ces deux catégories de récepteurs aux propriétés antagonistes qui détermine l'effet des anticorps et, en conséquence, la survenue ou non de manifestations pathologiques, allergiques ou autoimmunes

Institut Pasteur

Inspiré de Marc Daëron

IgG



	High affinity		Low affinity		High & Low		Low affinity	High affinity pH<6.5
Function	Activation	Activation	Inhibition	Activation	Activation		?	Recycling Transport Ag uptake…
Variant		*H_{131}*	*R_{131}*		*V_{158}*	*F_{158}*		
IgG subclass binding	**1**	1	1	1	1	1	1	**1**
	-	2	(2)	(2)	(2)	(2)	-	**2**
	3	3	3	3	**3**	3	3	3
	4	4	4	4	4	4	4	**4**

CORATA – Beaune - 2015

Le domaine des hypersensibilités alimentaires est particulièrement étudié, car la réalité fréquemment rencontrée sur le terrain ne s'explique pas dans les « guide lines ».

Si l'on parle d' EBM (Evidence Based Medicine), force est de constater dans la pratique journalière que de nombreux patients voient leurs problèmes se solutionner lorsqu'ils s'adressent à des praticiens rodés à l'anamnèse rigoureuse et à l'interprétation correcte des tests réalisés en labo.

Certes, il y a eu, et il y aura toujours des abus, souvent par incompétence,
mais le rôle du laboratoire et des biologistes est d'informer et non de juger.

Profitez de votre passage en
ces terres Bourguignonnes accueillantes et tellement sympathiques.
A bientôt, pour d'autres aventures ….

Giulia Enders

LE CHARME DISCRET DE L'INTESTIN

TOUT SUR UN ORGANE MAL AIMÉ...

ACTES SUD

LE CHARME DISCRET DE L'INTESTIN

Surpoids, dépression, diabète, maladies de peau… et si tout se jouait dans l'intestin ?

Au fil des pages de son brillant ouvrage, Giulia Enders, jeune doctorante en médecine, plaide avec humour pour cet organe qu'on a tendance à négliger, voire à maltraiter. Après une visite guidée au sein de notre système digestif, elle présente, toujours de façon claire et captivante, les résultats des toutes dernières recherches sur le rôle du "deuxième cerveau" pour notre bien-être. C'est avec des arguments scientifiques qu'elle nous invite à changer de comportement alimentaire, à éviter certains médicaments ainsi qu'à appliquer quelques règles très concrètes en faveur d'une digestion réussie.

Irrésistiblement illustré par Jill Enders, la sœur de l'auteur, voici un livre qui nous réconcilie avec notre ventre.

Succès surprise, *Le Charme discret de l'intestin* s'est vendu à plus de un million d'exemplaires en Allemagne et sera publié dans une trentaine de pays.

Née en 1990, Giulia Enders, passionnée de gastroentérologie, finalise sa thèse à l'université de Francfort. Motivée par la guérison de sa grave maladie de peau grâce à un changement radical de son alimentation, la jeune femme se penche sur les études les plus récentes de ce domaine. Premier prix de la Nuit des sciences de Berlin, où les jeunes chercheurs communiquent de la façon la plus originale le résultat de leurs études, son intervention a eu un succès faramineux sur la Toile. L'illustratrice Jill Enders, graphiste diplômée, participe dès le début au succès des travaux de sa sœur.

Traduit de l'allemand par Isabelle Liber

Giulia et Jill Enders

Illustration de couverture : © Jill Enders

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DIVERS

- L’arbre et la forêt
- CCD et BROMELINE
- GLUTEN
- IgG4 RD
- EURO LINE (tigettes)

Revue Française d'Allergologie
Volume 52, Issue 3, April 2012, Pages 218–222
7ème Congrès Francophone d'Allergologie

IgE et IgG, basophiles et neutrophiles : l'arbre et la forêt

IgE and IgG, basophils and neutrophils: The tree and the forest

M. Daëron, Inserm, unité 760, 25, rue du Docteur-Roux, 75015 Paris, France

Classiquement, l'allergie dépend principalement des IgE et des récepteurs de forte affinité pour les IgE exprimés par les mastocytes et les basophiles.

Des IgG anti-allergène sont néanmoins produits et en beaucoup plus grande quantité que les IgE.

Nous avons démontré dans un modèle murin que:

L'anaphylaxie active dépend principalement des IgG, de récepteurs activateurs pour les IgG et des neutrophiles.

Inversement:

Les récepteurs pour les IgG exprimés par les basophiles murins et humains exercent un effet dominant négatif sur les signaux positifs délivrés par les IgG ou par les IgE.

Les IgG peuvent donc exercer des effets antagonistes dans l'allergie selon les cellules impliquées. Il devient nécessaire de prendre en compte des anticorps 10^5–10^6 fois plus abondants que les IgE et des cellules sanguines 100 fois plus nombreuses que les basophiles comme des acteurs majeurs de l'allergie.

Mise au point
Revue Francaise d'Allergologie 2012/52-4 pg 333-339

Mise au point Les IgG, leurs récepteurs et les neutrophiles : acteurs de la réaction anaphylactique ? (1)

L'anaphylaxie est une réaction allergique hyper-aigüe qui se développe en quelques minutes après rencontre avec l'allergène chez l'homme.

- Les modèles animaux d' anaphylaxie passive proposent que l'anaphylaxie dépende des ***IgE***, de récepteurs activateurs pour les IgE (FcεRI), des mastocytes et de l'histamine.

- Cependant, l'injection d'anticorps ***IgG1*** et d'antigène induit également l'anaphylaxie passive qui dépend d'un récepteur activateur pour les IgG (FcγRIIIA) et, probablement, des basophiles.

- Néanmoins, l'injection d'antigène dans des animaux immunisés ne requiert ni les IgE, ni le FcεRI, ni les FcγRIIIA, ni les mastocytes, ni les basophiles.
  C'est l'anaphylaxie active.

Mise au point
Revue Francaise d'Allergologie 2012/52-4 pg 333-339

Mise au point Les IgG, leurs récepteurs et les neutrophiles : acteurs de la réaction anaphylactique ? (2)

Nous avons montré récemment que l' anaphylaxie active implique

- les IgG, les récepteurs activateurs pour les IgG FcγRIIIA et FcγRIV, le Platelet-Activating Factor, les neutrophiles (et les basophiles).
- La déplétion de neutrophiles inhibe l'anaphylaxie, alors que le transfert de neutrophiles humains restaure l'anaphylaxie chez des souris résistantes.
- Des récepteurs pour les IgG exprimés sur les neutrophiles humains pourraient donc contribuer à l'anaphylaxie.

Mise au point
Revue Francaise d'Allergologie 2012/52-4 pg 333-339

Les IgG, leurs récepteurs et les neutrophiles : acteurs de la réaction anaphylactique ? (3)

Chez l'homme, les neutrophiles, n'expriment ni FcγRIIIA ni FcγRIV, mais le récepteur activateur pour les IgG FcγRIIA.

Nous avons étudié le rôle du FcγRIIA humain dans l'anaphylaxie en créant de nouvelles souris transgéniques pour ce récepteur.

Dans ces souris, le ***FcγRIIA est suffisant pour induire l'anaphylaxie active et passive, qui requiert les monocytes/macrophages et les neutrophiles***.

Nos résultats dévoilent un rôle inattendu des IgG, de leurs récepteurs et des neutrophiles dans l'anaphylaxie, et suggèrent que les neutrophiles (et monocytes) activés par le FcγRIIA contribuent à l'anaphylaxie humaine.

Le polynucléaire basophile: nouveautés en physiopathologie et implications diagnostiques

Octavie Rostan, Karin Tarte, Patricia Amé-Thomas

Revue Francophone des Laboratoires > 2014 > 2014 > 462 > 95-105

- Les polynucléaires basophiles = 1 % des leucocytes sanguins
- Jusqu'à ce jour, rôle similaire à celui des mastocytes tissulaires dans leur fonctionnalité.
- Il a été démontré que les ***polynucléaires basophiles*** avaient des ***fonctions non redondantes avec les mastocytes***,
- Ils peuvent être divisés en sous-populations fonctionnelles différentes.

Il est maintenant ***acquis*** que les polynucléaires basophiles peuvent:

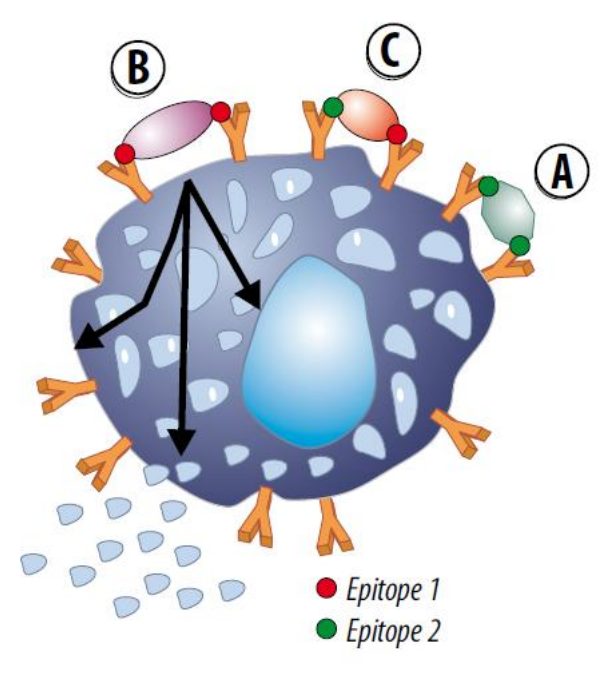
- ***réguler l'immunité innée et adaptative***, (protection contre les parasites),
- développer et maintenir des désordres immunologiques comme les ***réactions allergiques et les maladies auto-immunes***.

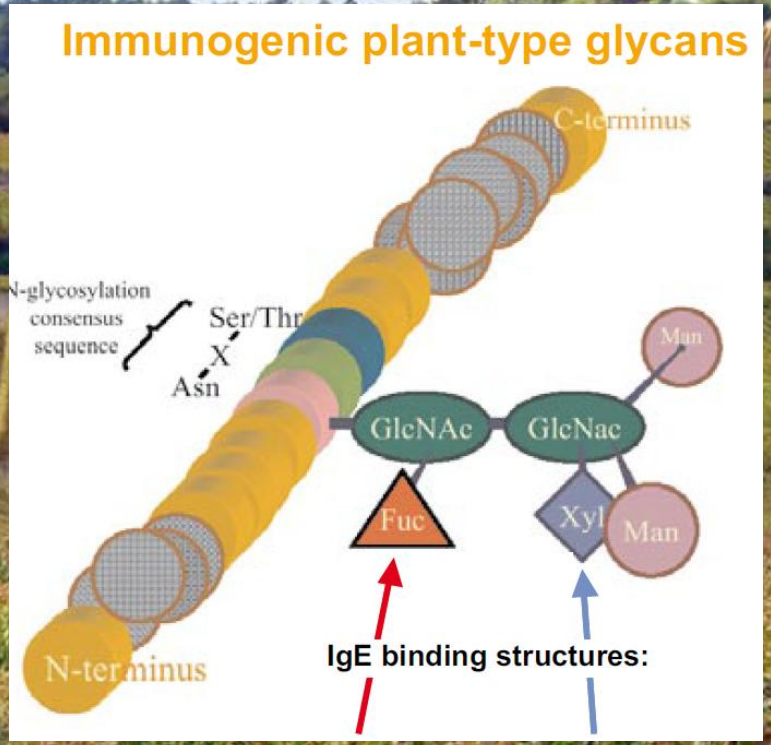
- Malgré leurs multiples fonctions, l'exploration biologique de ces cellules n'est à ce jour essentiellement réalisée que dans le cadre du ***diagnostic des réactions allergiques, par la mise en évidence de leur activation ou leur sécrétion d'histamine après stimulation par les allergènes.***

CCD et BROMELINE

Les CCD (Cross-reactive Carbohydrates Determinants)

- In glycoproteins in *plants* and *invertebrate animals* (e.g. insects such as honey bees and wasps) carrying glycans with carbohydrate determinants that *do not exist in mammals*.





From: van Ree (2002) Int Arch Allergy Immunol 129:189-97

- Since these determinants function as foreign epitopes in humans, CCDs are highly immunogenic and give rise to antibodies such as IgE.

CCDs are present in all in vitro tests based on natural allergen proteins.

CCDs are frequently important for the correct structure of the peptide epitopes in an allergen. General elimination of CCDs from allergen extracts may in some cases give rise to false-negative test results.

If CCDs are not detectable, the amount of allergen protein is not present in sufficient amount , which will result in lower sensitivity. In a sub-group of patients, IgE antibodies to CCDs are likely to have clinical relevance..

A CCD test could be useful when in vitro results do not match the clinical picture (e.g. symptoms, skin tests, etc.), especially when numerous positive results to natural extract allergens are found without obvious clinical symptoms to all of them.

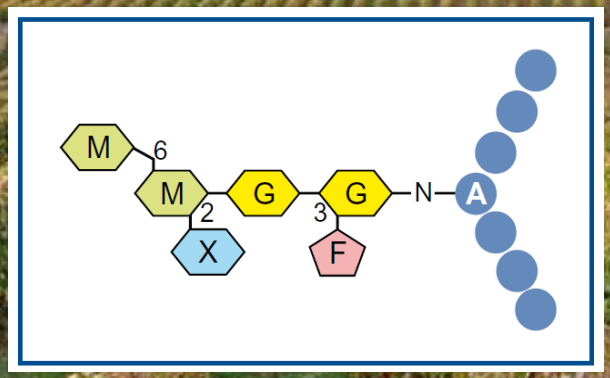
A positive specific IgE (/G) result is a demonstration of sensitization, not a diagnosis of allergy.
Specific IgE (/G) results should always be interpreted in the context of case history and clinical observations.

Ces 3 diapos concernant les CCD's sont largement inspirées des FAQ de Phadia

LE TEST « BROMELINE »

Investigating the presence of antibodies to CCD can be done routinely. ImmunoCAP® Allergen, o214 CCD; MUXF3 from **BROMELIN** is a pure CCD reagent containing only the MUXF3 carbohydrate epitope, thus avoiding IgE antibody binding to other bromelin epitopes.

The MUXF3 carbohydrate epitope is purified from digested bromelin.



GLUTEN

WHEAT-RELATED DISORDERS

TABLE I: MAIN WHEAT ALLERGEN COMPONENTS AND THEIR ASSOCIATIONS

Ω 5 GLIADIN Tri a 19	αβW GLIADINS	ALPHA AMYLASE/TI	PROFILIN	PR-10	LTP Tri a 14	CCD
Risk marker for systemic reactions. Associated with wheat allergy persistence. Associated with wheat dependent exercise induced anaphylaxis.	Marker of severe reactions. Marker of wheat allergy persistence.	Baker's asthma	Cross-reaction with other pollens.	Cross-reaction with other pollens.	Wheat dependent exercise induced anaphylaxis.	Cross-reaction with other pollens.

Review Article

WHEAT-RELATED DISORDERS: MAKING SENSE OF COELIAC DISEASE AND OTHER REACTIONS TO WHEAT AND GLUTEN

C van Rooyen[1] | MBChB, MMed(Path)(Virol), FRCPath
S Van den Berg[2] | MBChB, MMed(Clin)(Path), FCPath(Clin), DTM&H

1. Allergy, Immunology and Virology Pathologist, Ampath Pathology, National Reference Laboratory (Immunology) and Allergy Clinic

2. Allergy, Immunology and Microbiology Pathologist, Ampath Pathology, National Reference Laboratory (Immunology) and Allergy Clinic

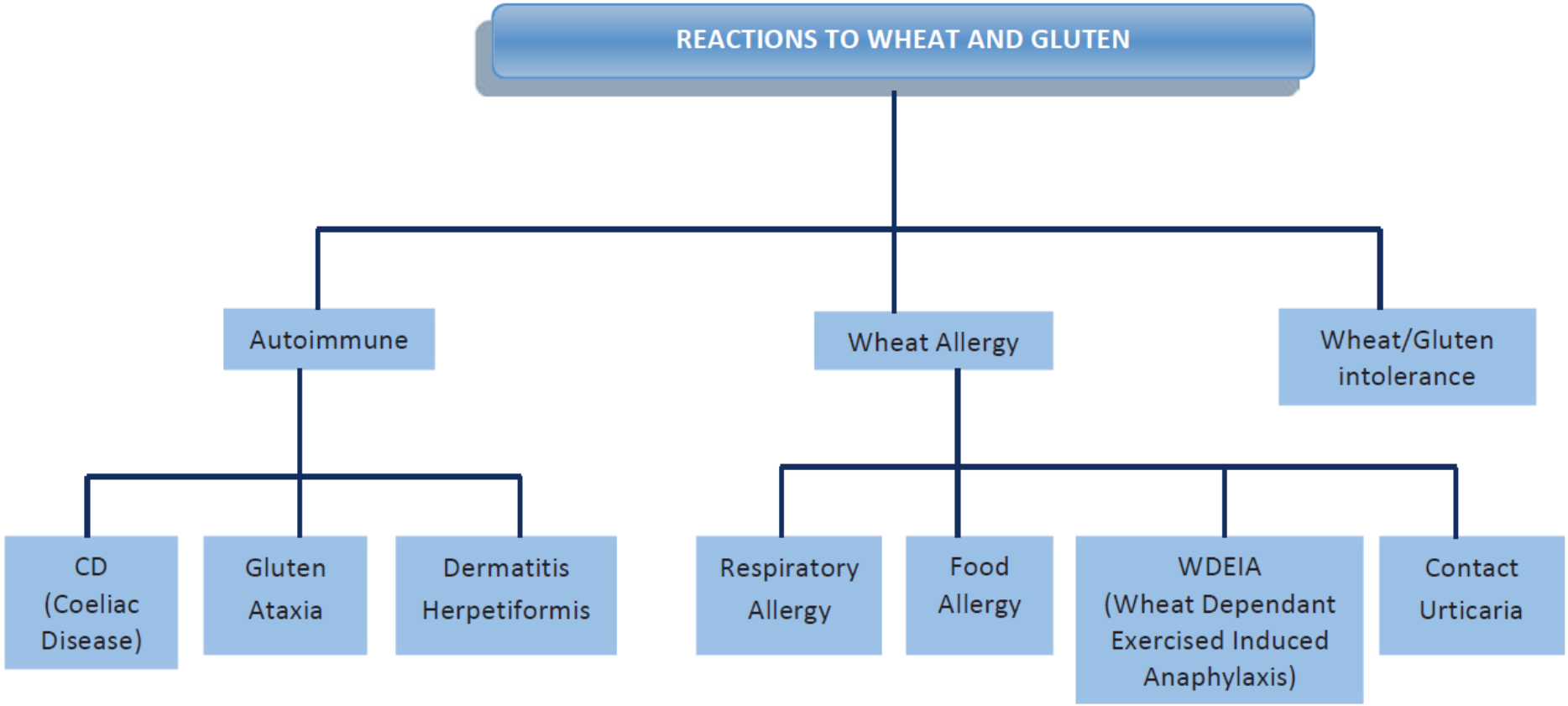


Figure 1: Proposed classifications of immunological reactions to wheat and gluten[1]
(Adapted from Sapone A et al. Spectrum of gluten-related disorders: consensus on new nomenclature and classification. BMC Med 2012;10:3)

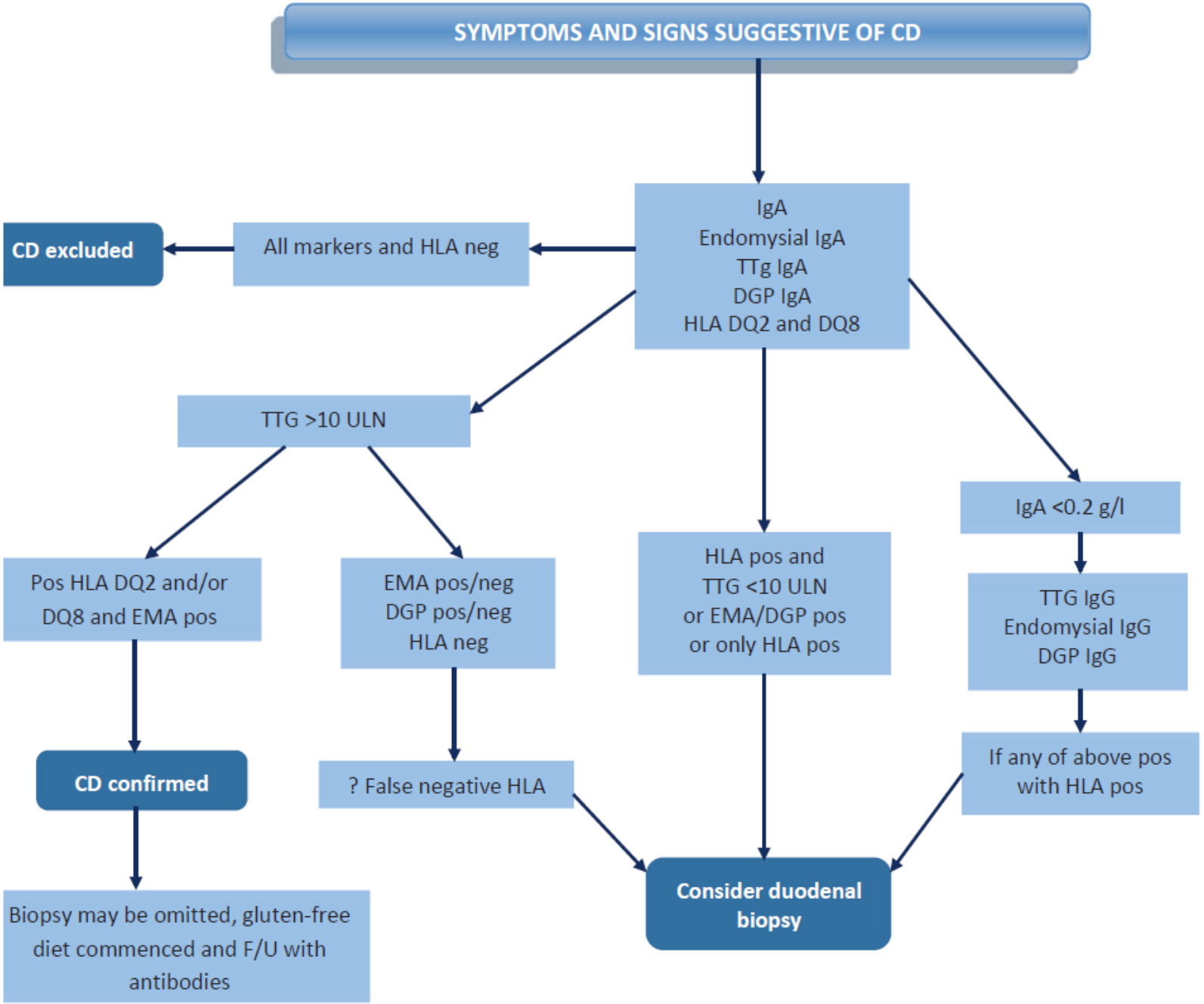


Figure 2: Diagnostic approach to Coeliac Disease in a symptomatic patient

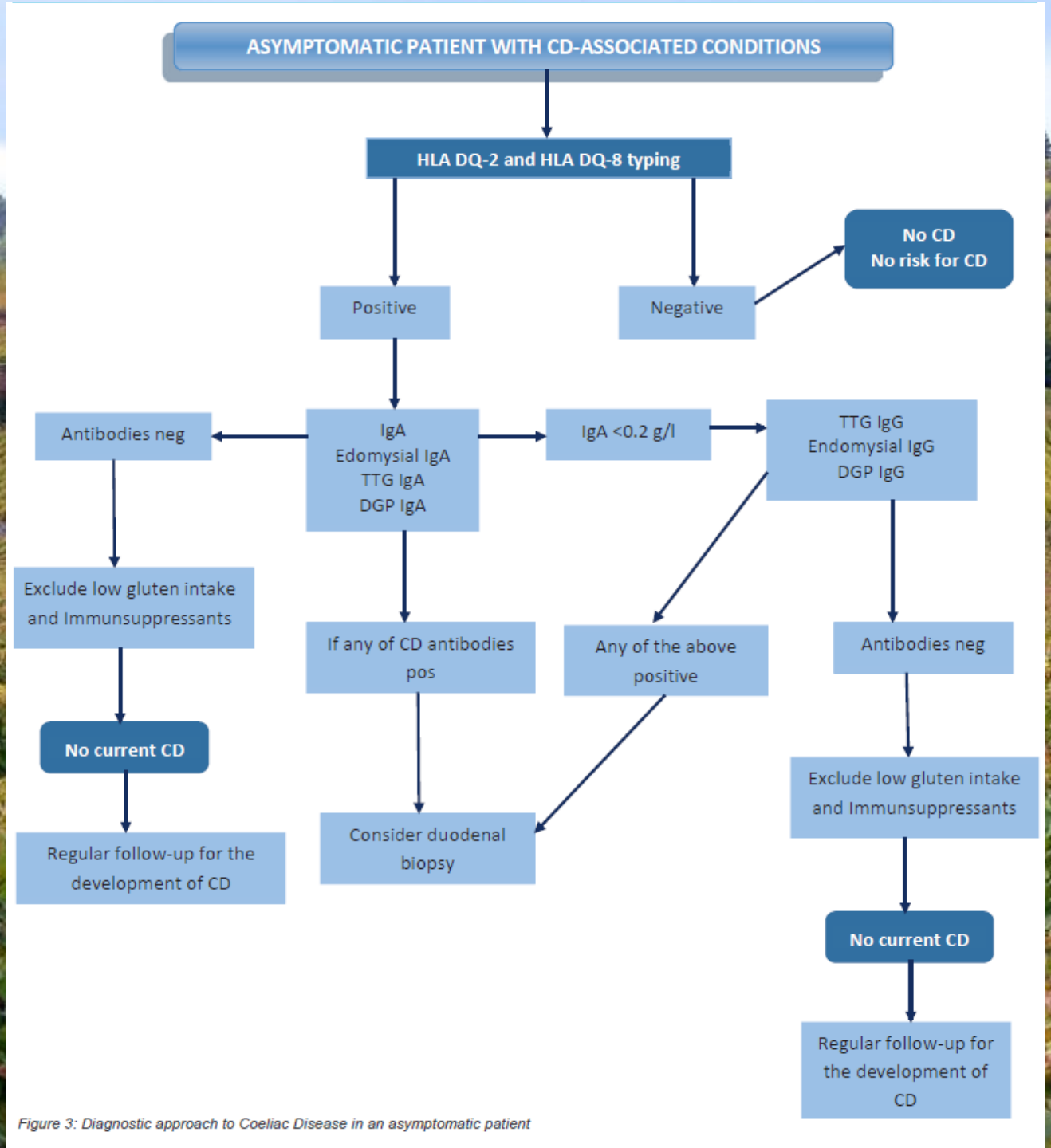


Figure 3: Diagnostic approach to Coeliac Disease in an asymptomatic patient

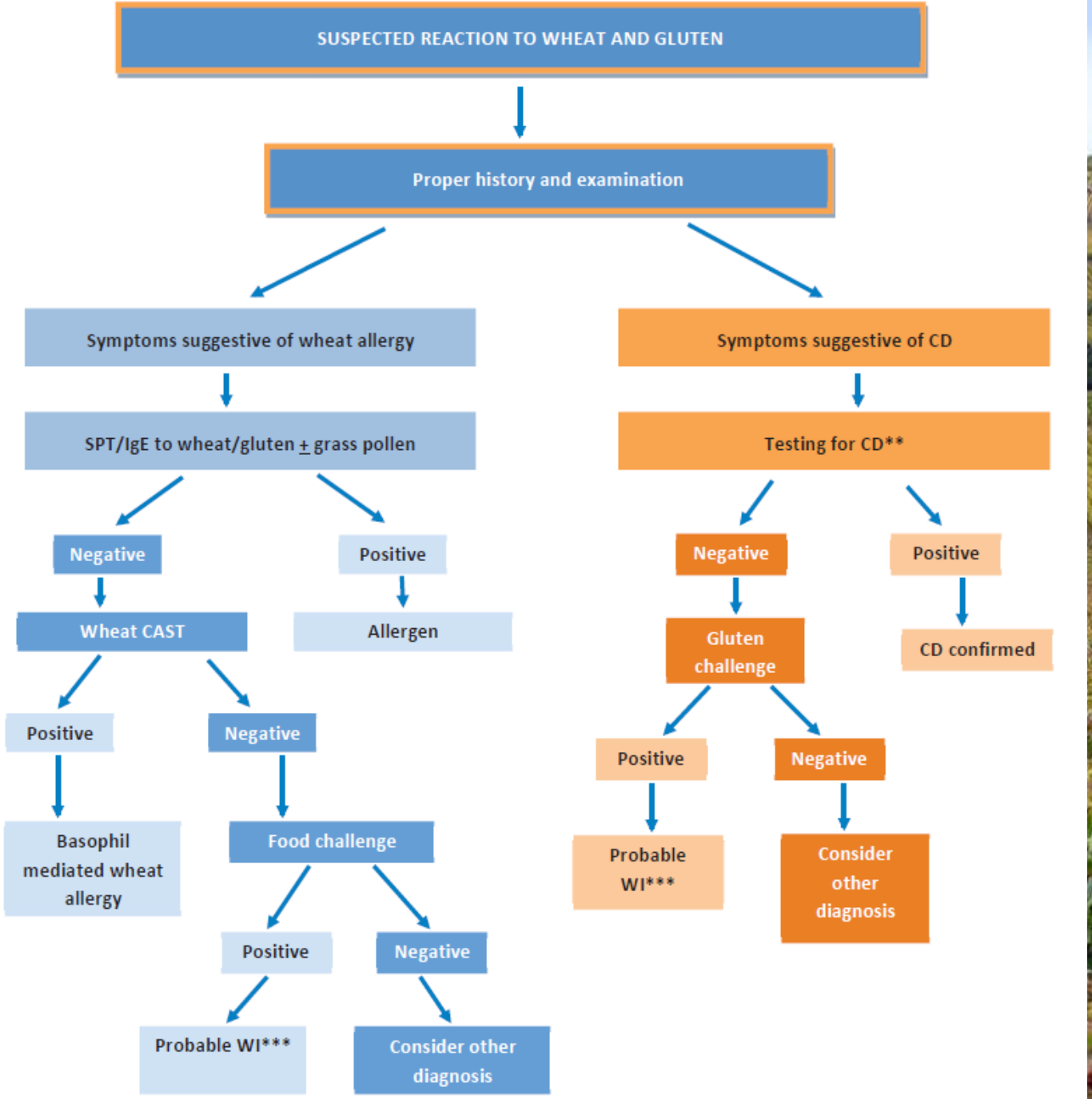
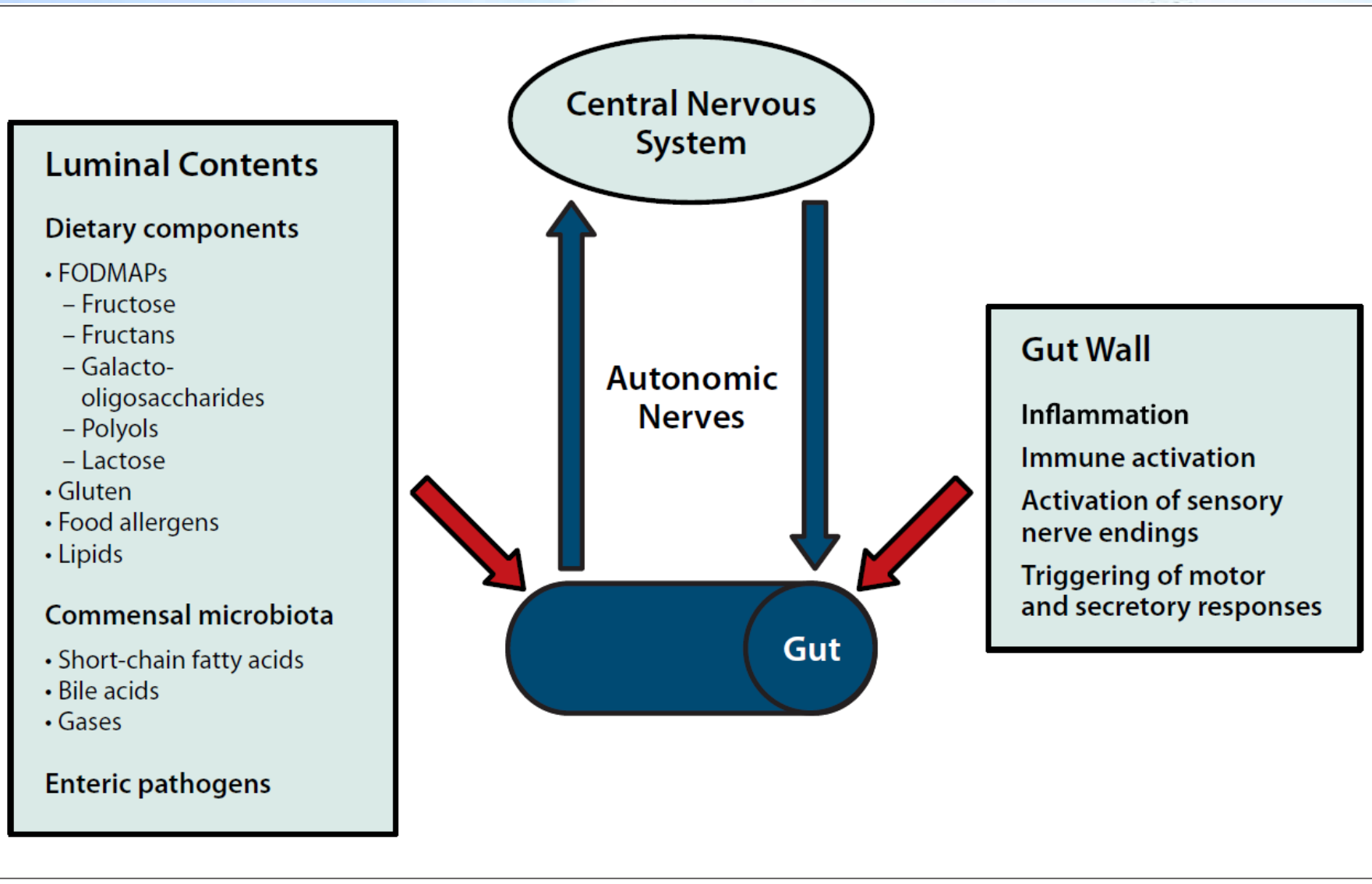


Figure 4: Proposed diagnostic approach to the patient presenting with suspected reactions to wheat and gluten

GLUTEN

IBS – FOODMAP - NCGS ….


Luminal Contents
Dietary components
• FODMAPs
– Fructose
– Fructans
– Galacto-oligosaccharides
– Polyols
– Lactose
• Gluten
• Food allergens
• Lipids
Commensal microbiota
• Short-chain fatty acids
• Bile acids
• Gases
Enteric pathogens
Central Nervous System
Autonomic Nerves
Gut
Gut Wall
Inflammation
Immune activation
Activation of sensory nerve endings
Triggering of motor and secretory responses

Drug Ther Bull.

2015 Aug;53(8):93-6. Epub 2015 Aug 6.

Does a low FODMAP diet help IBS?

[No authors listed]

Abstract

Irritable bowel syndrome (IBS) is a common condition that can have a significant impact on a person's quality of life.

(1) The cause of IBS is unknown but several mechanisms have been proposed including visceral hypersensitivity, central sensitisation, abnormal gut motility and altered gut microbiota.

IBS is challenging to manage and many patients report insufficient symptomatic relief from treatment.

(1) Approximately 60% of patients identify food as a trigger for their symptoms, and there has been interest in exclusion diets for managing IBS.

(2) Dietary adaptation is a common self-management strategy for patients with IBS, with many self-diagnosing intolerance to specific foods. This may lead to patients adopting over-restrictive or inappropriate diets.

(3) In recent years, a diet low in poorly absorbed short-chain carbohydrates, known collectively as **FODMAPs (fermentable oligosaccharides, disaccharides, monosaccharides and polyols), has been advocated for the treatment of IBS.**

Here, we discuss the background to the FODMAP diet and review the evidence supporting its use for people with IBS.

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PMID: 26251411

Wheat-Dependent Exercise-Induced Anaphylaxis

Katharina Anne Scherf, Knut Brockow, Tilo Biedermann, Peter Koehler, Herbert Wieser

Accepted manuscript online: 18 September 2015 Full publication history

DOI: 10.1111/cea.12640 View/save citation

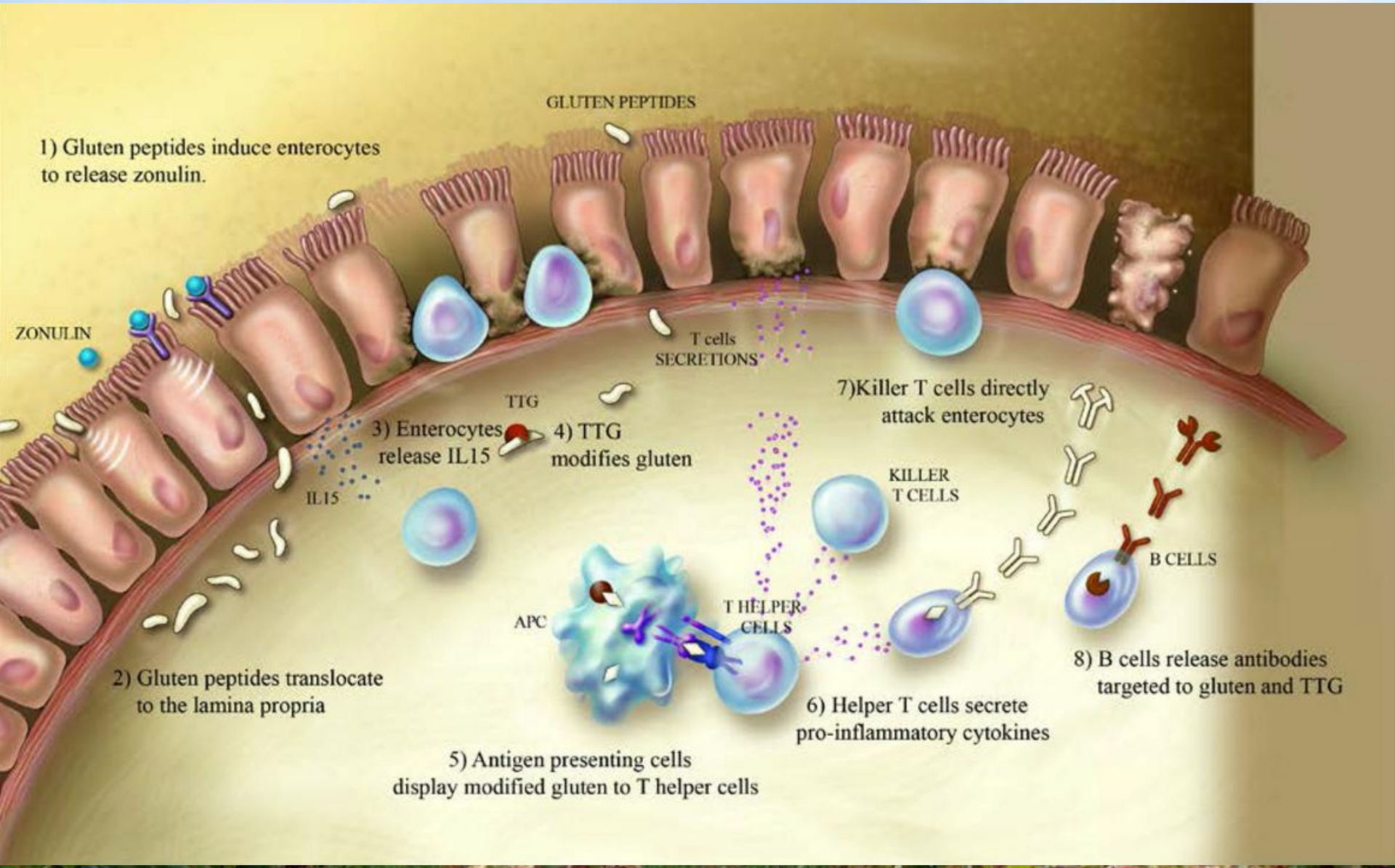
Cited by: 0 articles Check for new citations

Am score 4

Clinical & Experimental Allergy

Abstract

Wheat-dependent exercise-induced anaphylaxis (WDEIA) is a rare, but potentially severe food allergy exclusively occurring when wheat ingestion is accompanied by augmenting cofactors. It is clinically characterized by anaphylactic reactions ranging from urticaria and angioedema to dyspnea, hypotension, collapse, and shock. WDEIA usually develops after ingestion of wheat products followed by physical exercise. Other cofactors are acetylsalicylic acid and other nonsteroidal anti-inflammatory drugs, alcohol, and infections. The precise mechanisms of WDEIA remain unclear; exercise and other cofactors might increase gastrointestinal allergen permeability and osmolality, redistribute blood flow, or lower the threshold for IgE-mediated mast cell degranulation. Among wheat proteins, ω5-gliadin and high-molecular-weight glutenin subunits have been reported to be the major allergens. In some patients, WDEIA has been discussed to be caused by epicutaneous sensitization with hydrolyzed wheat gluten included in cosmetics. Diagnosis is made based on the patient's history in combination with allergy skin testing, determination of wheat-specific IgE serum antibodies, basophil activation test, histamine release test, and/or exercise challenge test. Acute treatment includes application of epinephrine or antihistamines. The most reliable prophylaxis of WDEIA is a gluten-free diet. In less severe cases, a strict limitation of wheat ingestion before exercise and avoidance of other cofactors may be sufficient.



Gloria Serena, Nutrients **2015**, *7*(9), 7143-7162

IgG4 RD (related diseases)

Clin Neuropathol. 2015 Aug 26. [Epub ahead of print]

A case report of meningeal Rosai-Dorfman disease associated with IgG4-related disease.

Tauziede-Espariat A, Polivka M, Chabriat H, Bouazza S, Sene D, Adle-Biassette H.

Abstract

AIMS:

Rosai-Dorfman disease is a rare entity that has been described as **lymphadenopathy in young patients**. Extranodal forms of this disease have been previously observed. The etiology of Rosai-Dorfman disease remains unknown, relationships with the IgG4-related sclerotic disease have been detected. Herein, a **rare case of Rosai-Dorfman disease with meningeal involvement and IgG4-related sclerotic disease** is reported.

MATERIAL:

A **meningeal biopsy** in a 35-year-old woman who had a 6-month history of intermittent headache was performed after MRI examination showing diffuse leptomeningeal enhancement without cerebral parenchymal involvement.

RESULTS:

A mixed infiltration of lymphocytes, plasma cells, and histiocytes exhibiting emperipolesis was identified. The stroma was fibrous. Immunohistochemical analysis revealed a high number of IgG4-positive plasma cells and a rate of IgG4/IgG-positive plasma cells higher than 50%.

CONCLUSION:

The pathological results in this patient with meningeal infiltration are suggestive of Rosai-Dorman disease associated with IgG4-related disease. This observation further confirms the link between these two entities.

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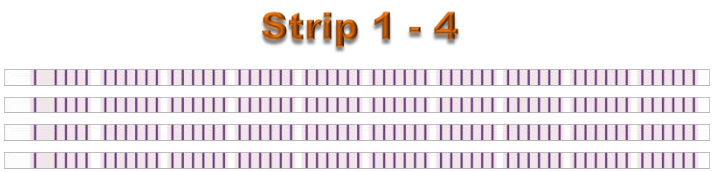

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