TSPCCM Post-ATS Symposium

Treating asthma in patients with obesity : the need for a new approach

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ATS INTERNATIONAL CONFERENCE May 17-May 22, 2019 dallas tx

BASIC • BEHAVIORAL • CLINICAL • TRANSLATIONAL

SCIENTIFIC SYMPOSIUM

CME Credits Available: 2

MOC Points Available: 2

A10 TREATING ASTHMA IN PATIENTS WITH OBESITY: THE NEED FOR A NEW APPROACH

Assemblies on Respiratory Structure and Function; Allergy, Immunology and Inflammation; Behavioral Science and Health Services Research; Clinical Problems; Environmental, Occupational and Population Health; Sleep and Respiratory Neurobiology

9:15 a.m. - 11:15 a.m. **KBHCCD**

Room D221/D225/D226 (Level 2)

Target Audience
Clinicians taking care of obese patients, translational investigators working in basic science, epidemiology and behavioral science

Objectives
At the conclusion of this session, the participant will be able to:

- understand the effects of obesity on respiratory physiology and immune function;
- develop a rationale approach to treating obese patients with asthma;
- explain how comorbidities complicate treatment of asthma in obesity.

Obesity is a major risk factor for asthma, and nearly 60% of patients with severe asthma are obese. Obese patients do not respond as well to standard therapies; this represents a major challenge to clinicians and a public health crisis. This session will discuss the pathophysiology of the different phenotypes of obese asthma, and how this affects treatment responses. The role of medications, life-style interventions,and

co-morbidities will be discussed, along with a discussion of future therapies being developed to address this challenging new patient population.

Chairing: A.E. Dixon, MD, ATSF, Burlington, VT
D. Rastogi, MBBS, MS, Bronx, NY

9:15 **A Patient's Perspective**
L. Clark, Irving, TX

9:20 **Asthma and Obesity in 2019**
D. Rastogi, MBBS, MS, Bronx, NY

9:25 **Pathophysiology of Phenotype in the Asthma of Obesity**
J.H.T. Bates, PhD, DSc, ATSF, Burlington, VT

9:40 **The Interrelation Between Asthma and Sleep-Disordered Breathing**
M. Teodorescu, MD, MS, Madison, WI

9:55 **Obesity Oxidative Stress and Asthma**
F. Holguin, MD, MPH, Aurora, CO

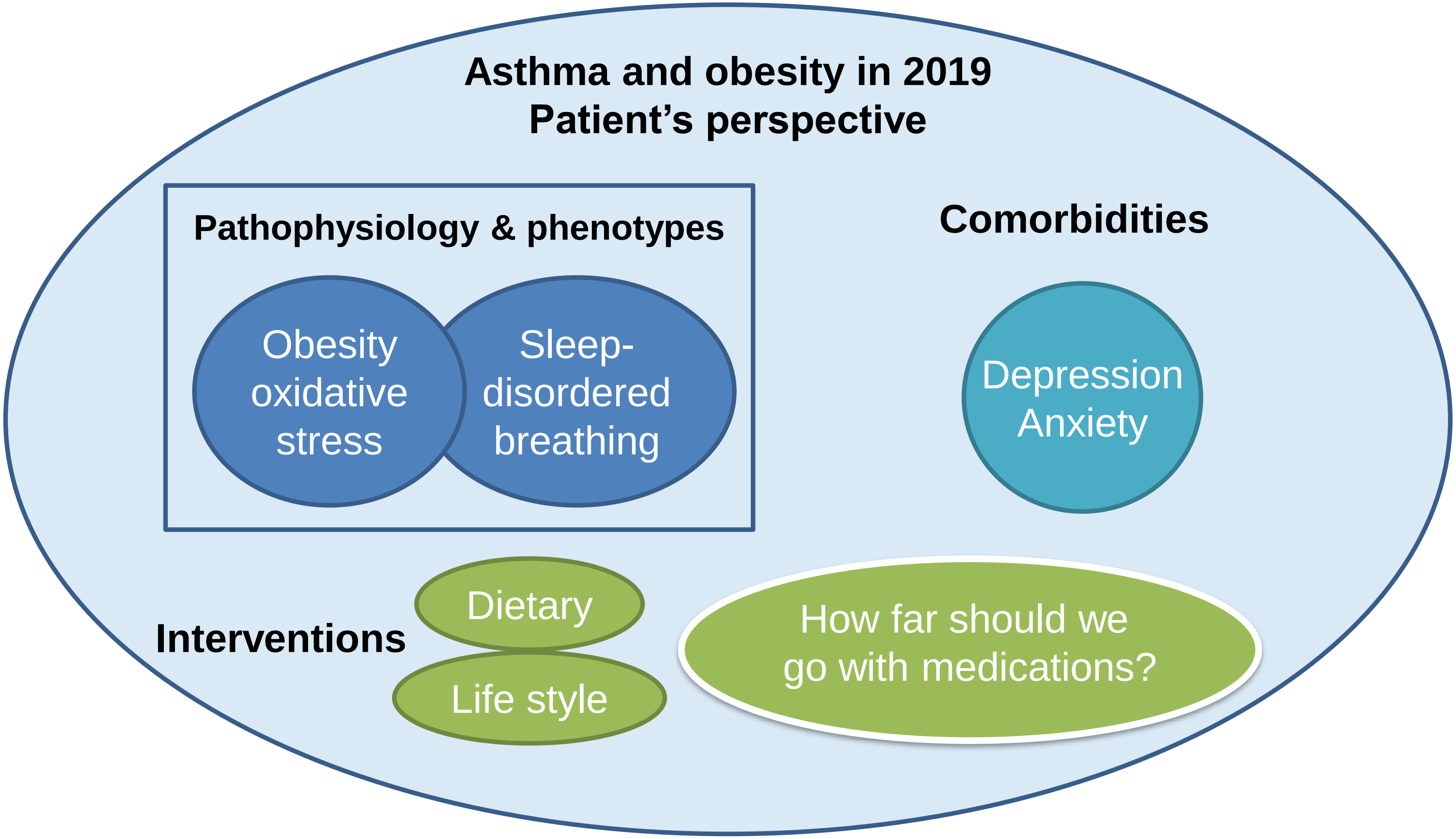
10:10 **Dietary Interventions for Obese Asthma**
L.G. Wood, PhD, New Lambton Hts, Australia

10:25 **Lifestyle Interventions for Asthma and Obesity**
S.M. Nyenhuis, MD, Chicago, IL

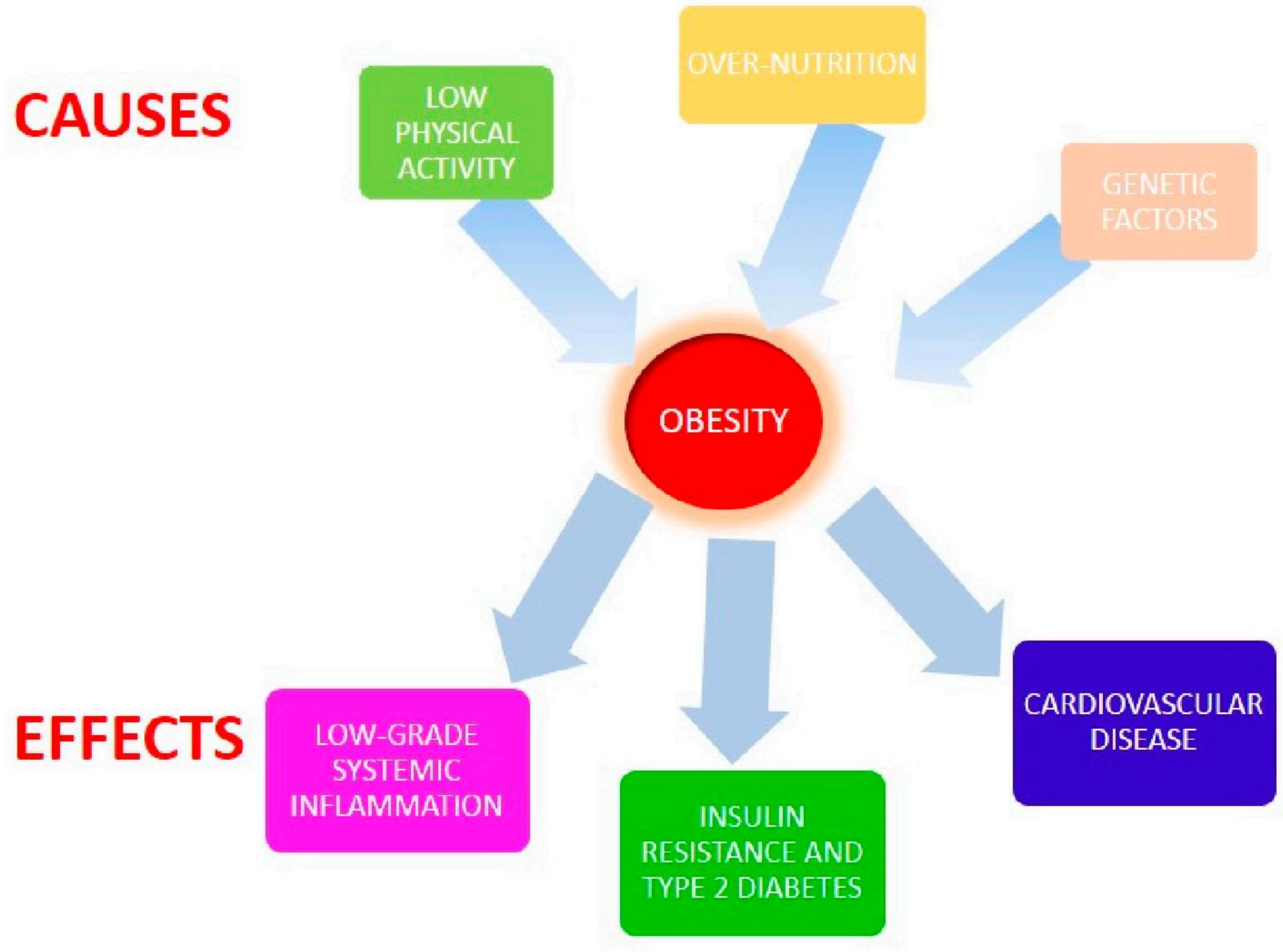
10:40 **Depression, Anxiety and Obese Asthma**
K. Lavoie, PhD, MA, BA(Hons), Montreal, Canada

10:55 **Controlling Obese Asthma: How Far Should We Go with Medications?**
A.E. Dixon, MD, ATSF, Burlington, VT

Treating asthma in patients with obesity : the need for a new approach



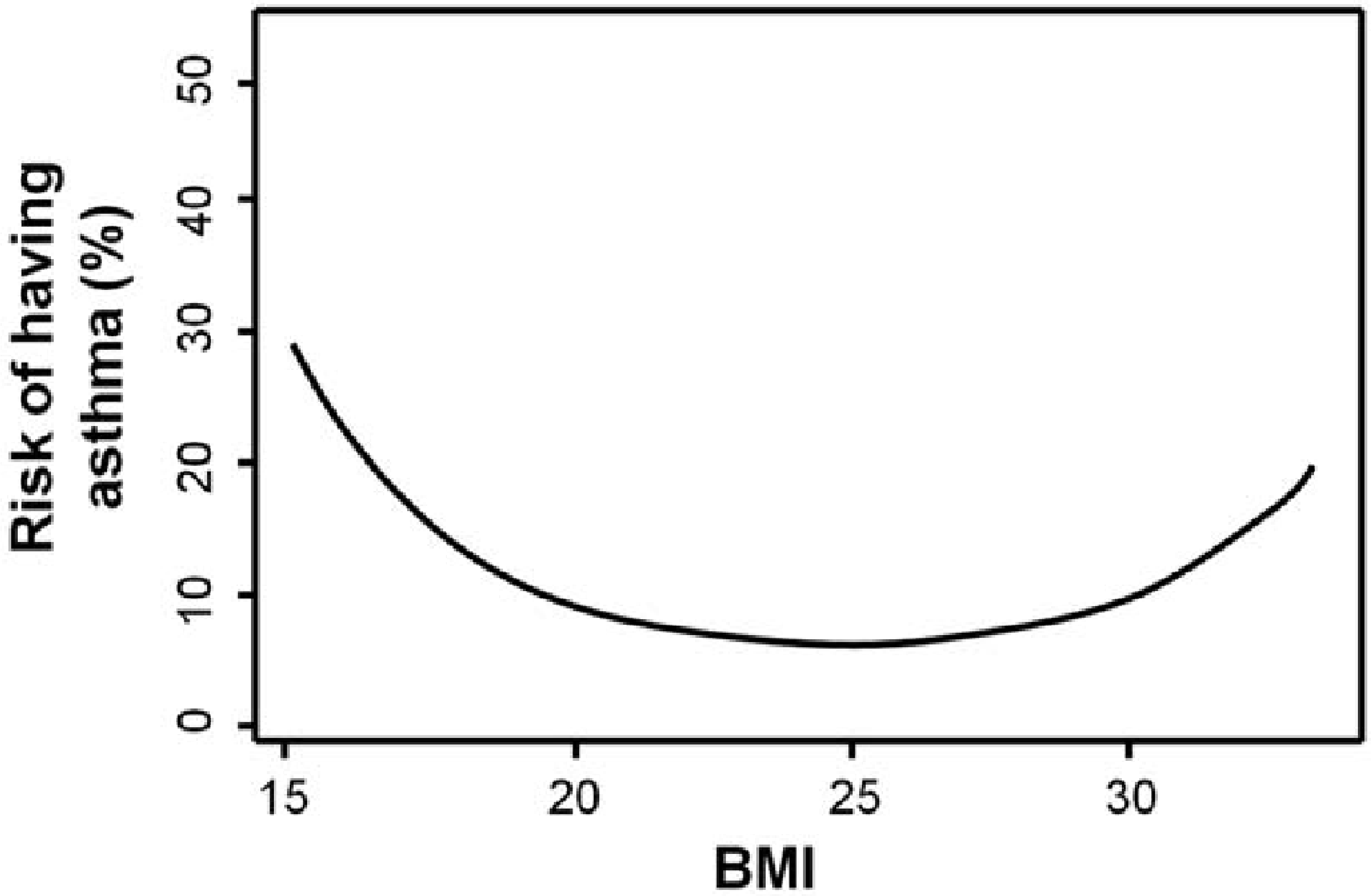
Causes and effects of obesity



Gomez-Llorente MA *et al. Int J Mol Sci*. 2017 Jul 11;18(7)

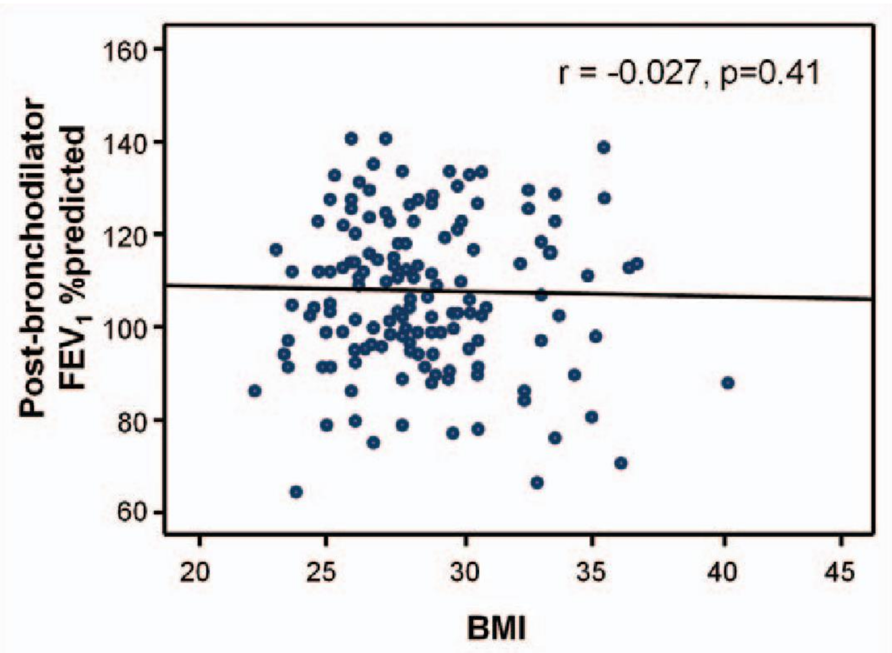
Relation between BMI and risk of asthma

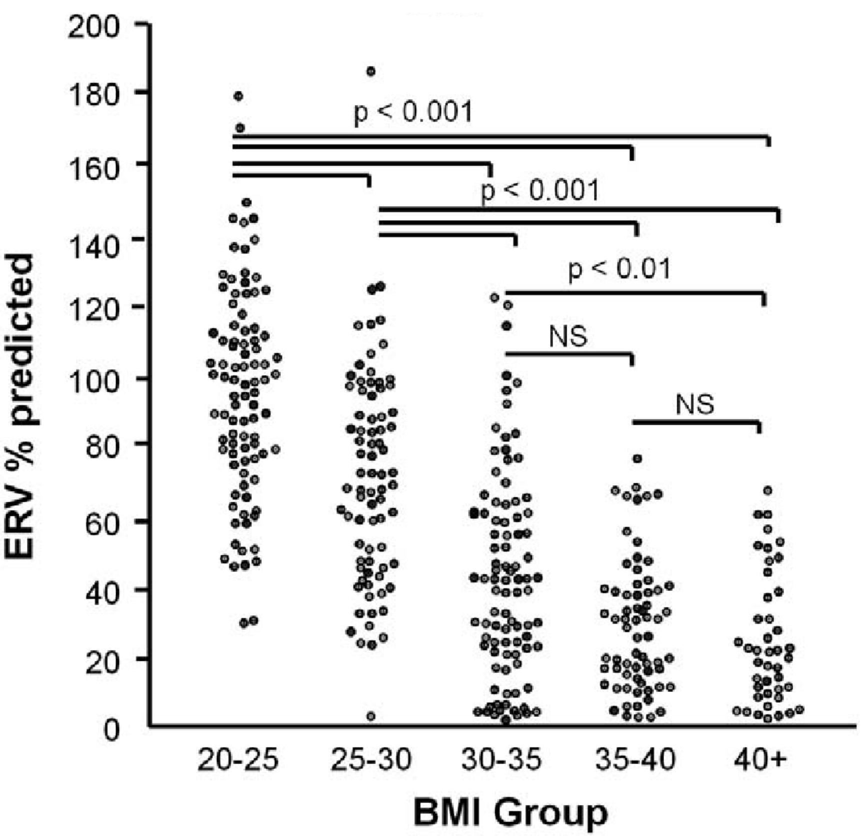
Adjusting for age, intensity of cigarette smoking, atopy, and familial correlations



Carpaij OA *et al. Curr Opin Pulm Med*. 2018 Jan;24(1):42-49

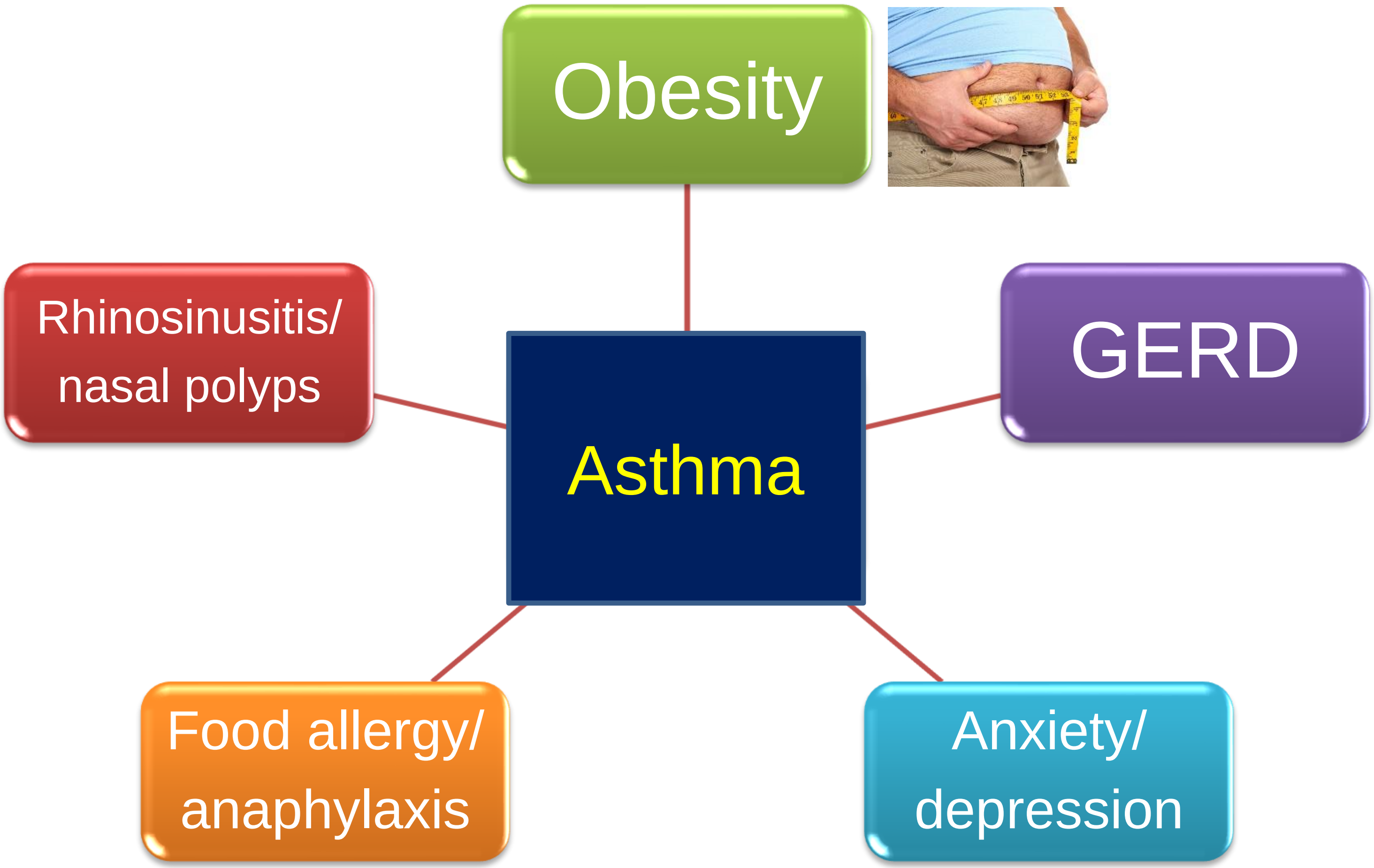
Association of BMI and lung function





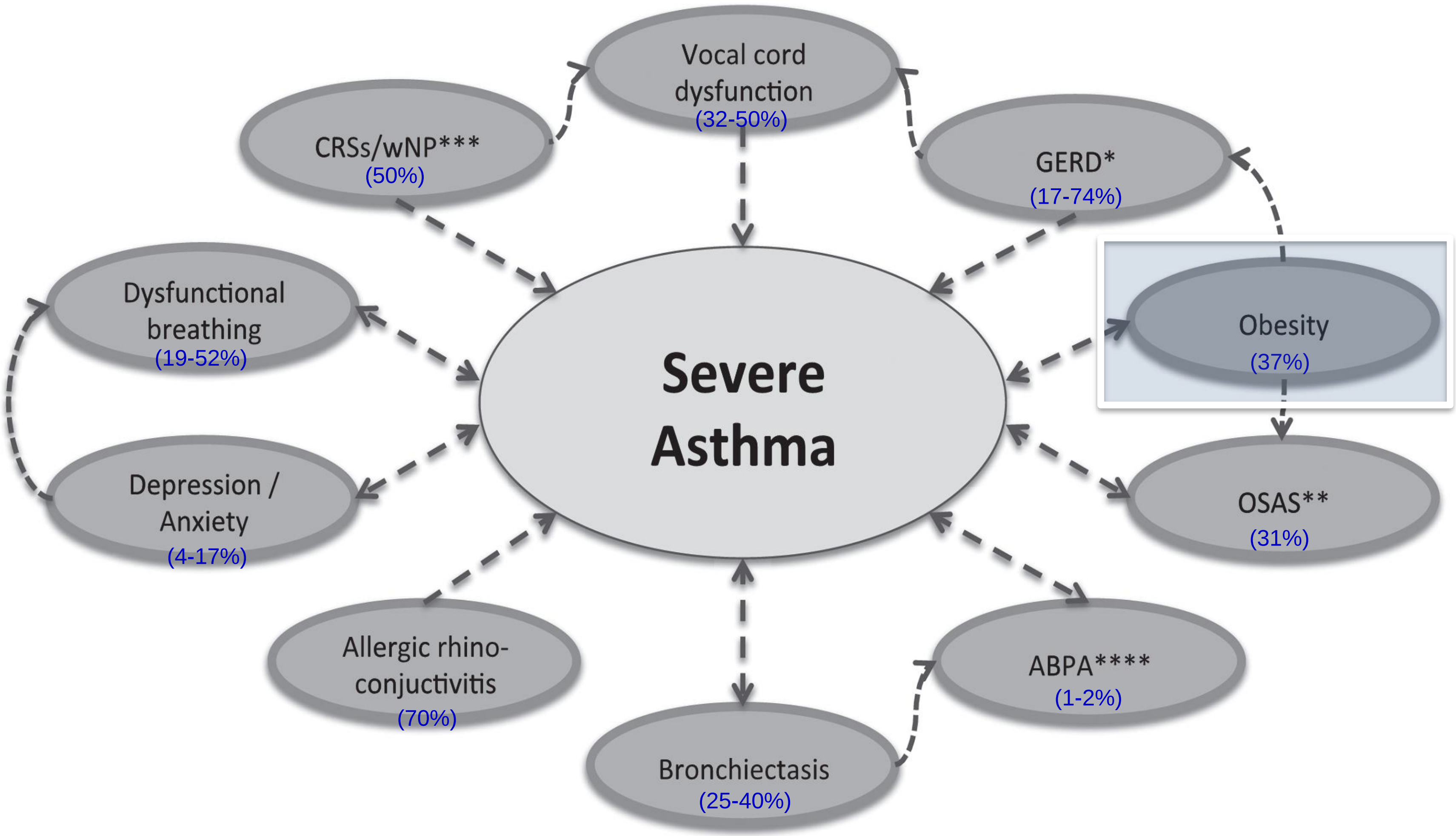
Carpaij OA *et al. Curr Opin Pulm Med*. 2018 Jan;24(1):42-49

Asthma and comorbidities



Global Initiative for Asthma (GINA) 2018

Prevalence of co-morbidities in severe asthma



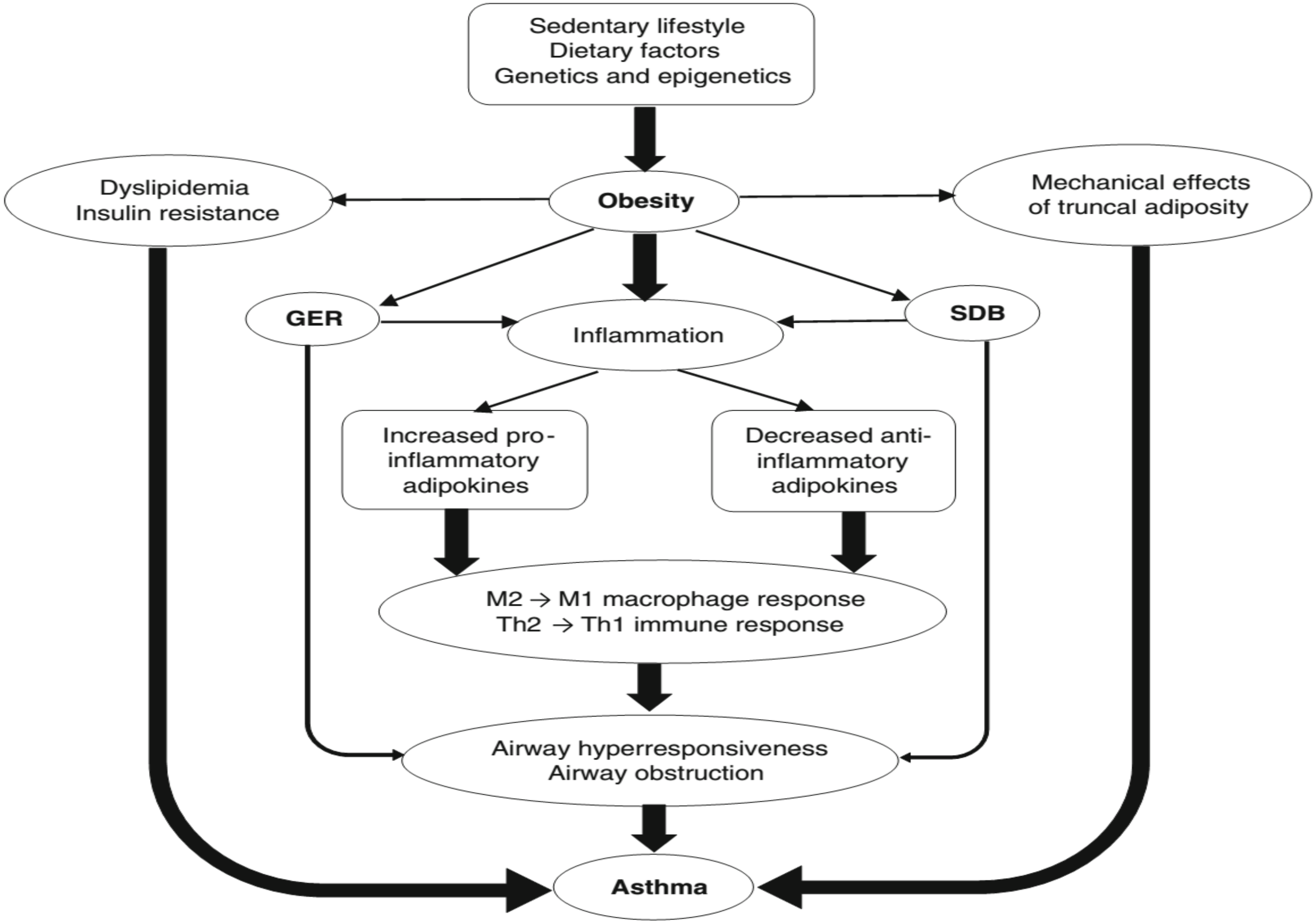
Porsbjerg C *et al. Respirology*. 2017 May;22(4):651-661

Relative prevalence of co-morbidities between phenotypes of severe asthma

	Early-onset allergic asthma	Late-onset eosinophilic asthma	Late-onset non-eosinophilic asthma
Rhinosinusitis (CRSsNP)	+	+++	+++
Nasal polyps (CRSwNP)	+	+++	+
Allergic rhinoconjuctivitis	+++	+	+
DB	+	+	+++
VCD	+	+	++
Anxiety	+	+	+++
Depression	+++	+	+
Obesity	+	++	+++
OSAS	+	+	++
Gastrointestinal reflux	+	+++	+++
Bronchiectasis	+	++	++
ABPA	+	++	++

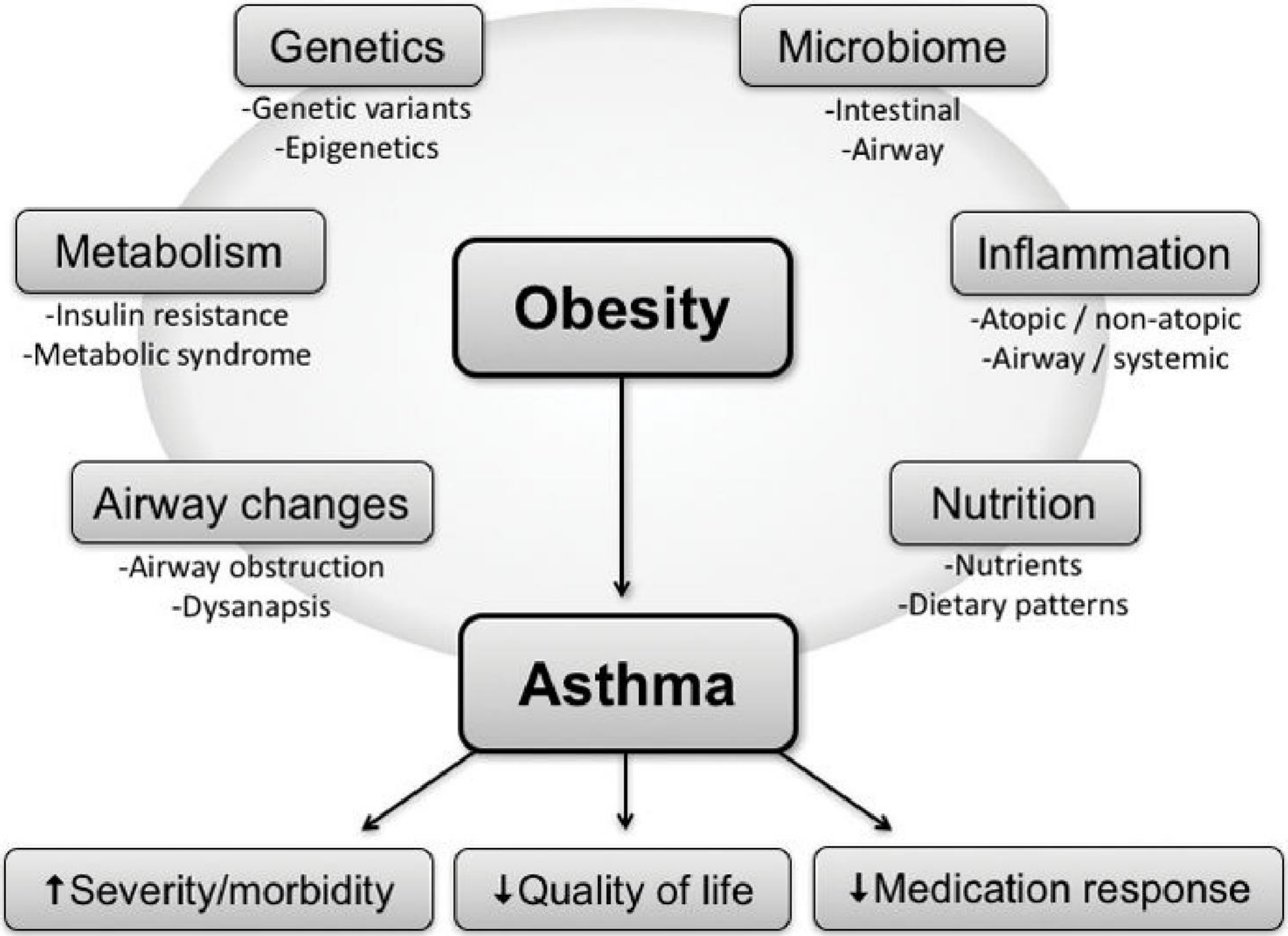
Porsbjerg C *et al. Respirology*. 2017 May;22(4):651-661

Interplay between obesity, gastroesophageal reflux, SDB and asthma



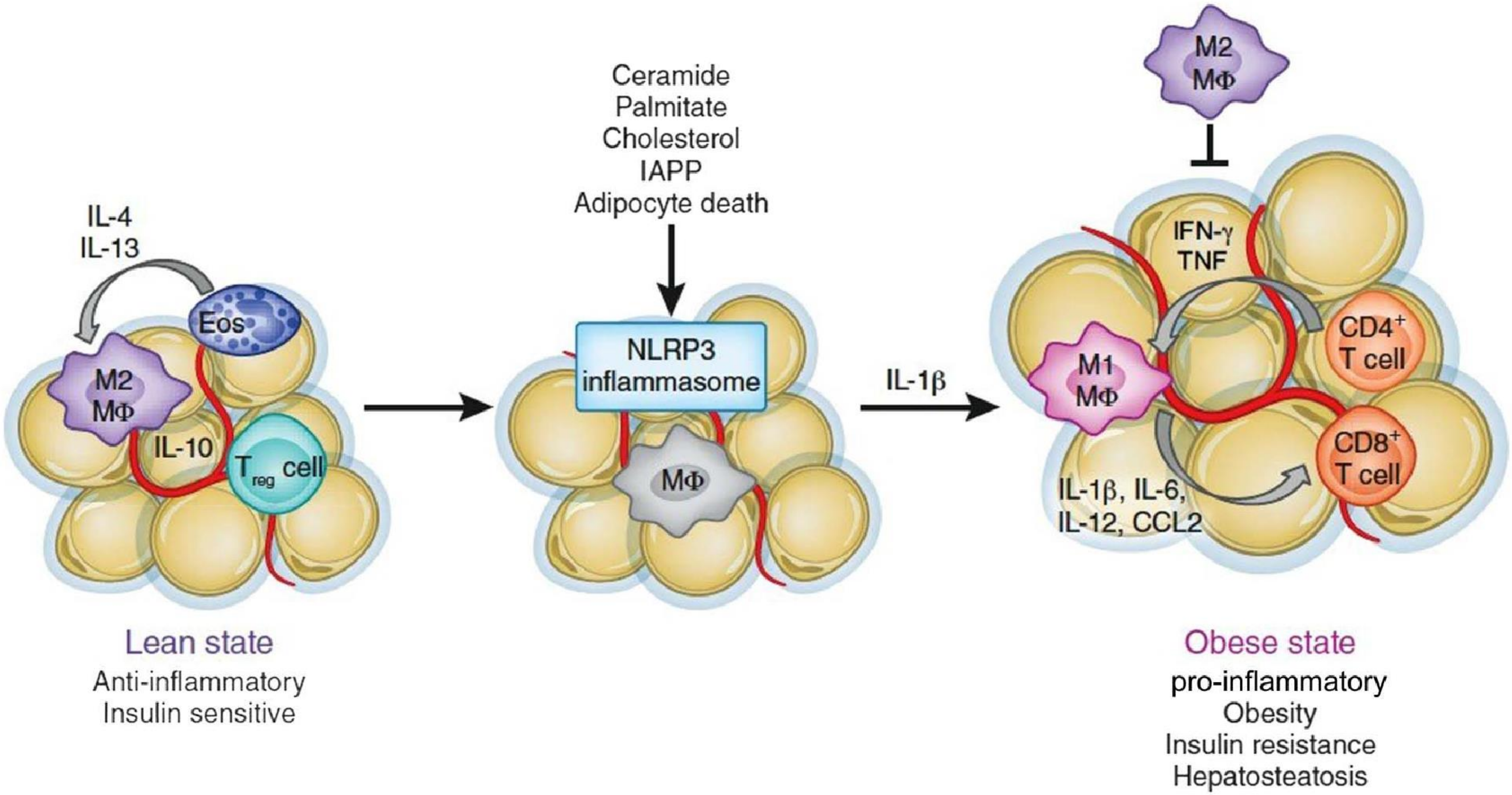
Gupta S *et al. Indian J Pediatr*. 2018 Oct;85(10):887-892

Multifactorial effects of obesity on asthma



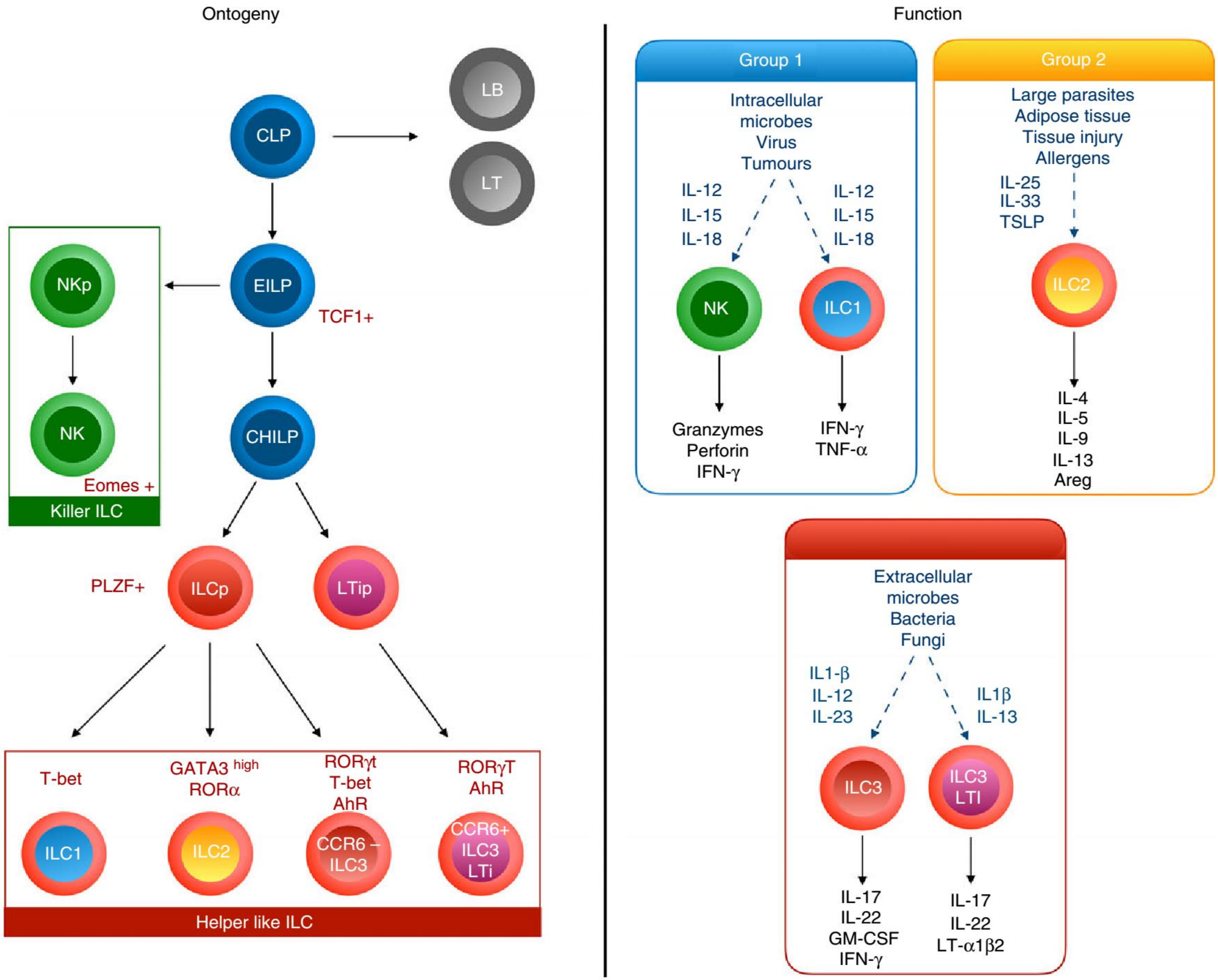
Forno E *et al. Curr Opin Allergy Clin Immunol*. 2017 Apr;17(2):123-130

Inflammasomes fuel obesity-induced inflammation



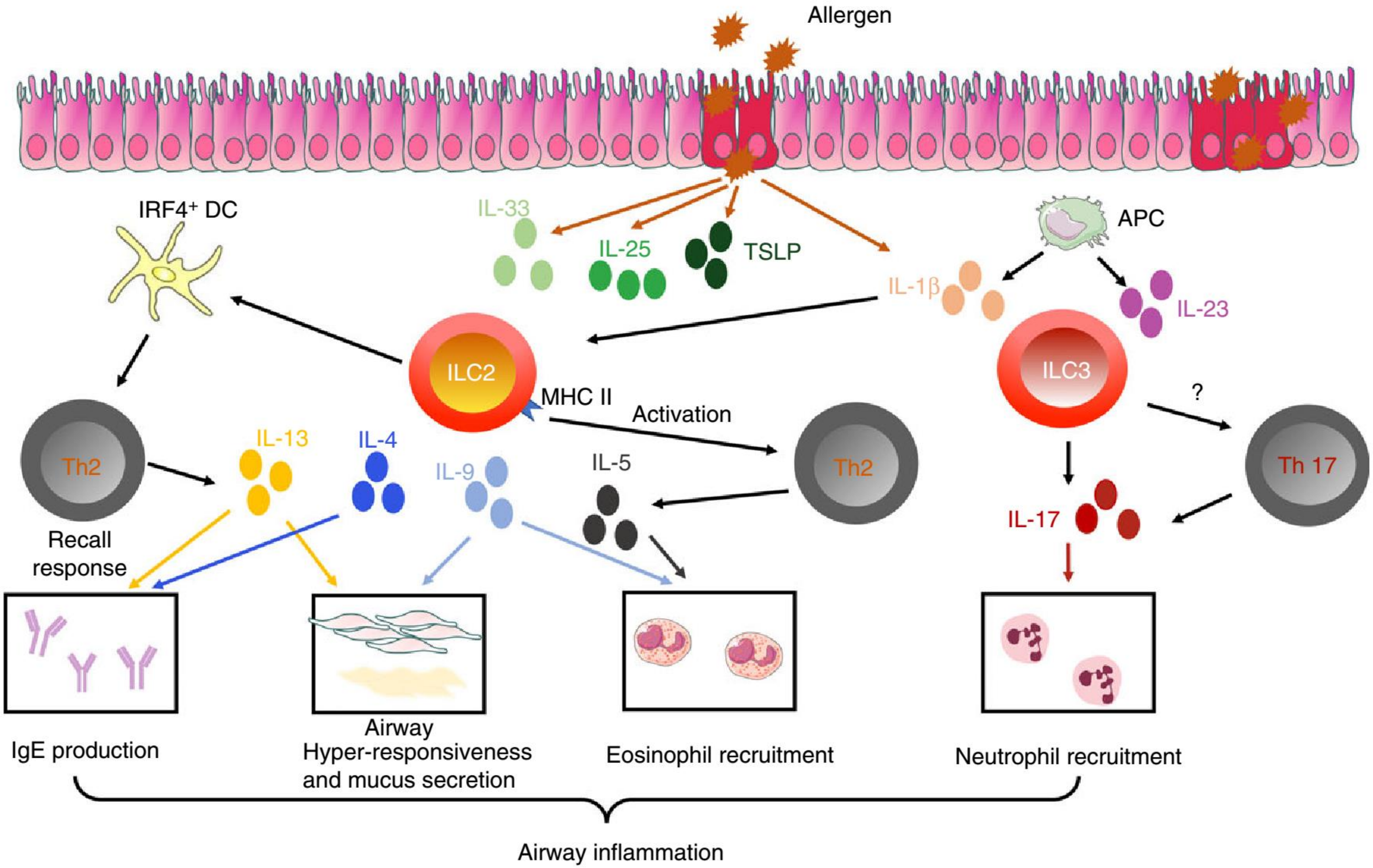
Umetsu DT. *Thorax*. 2017 Feb;72(2):174-177

Innate lymphoid cells at interface between obesity and asthma



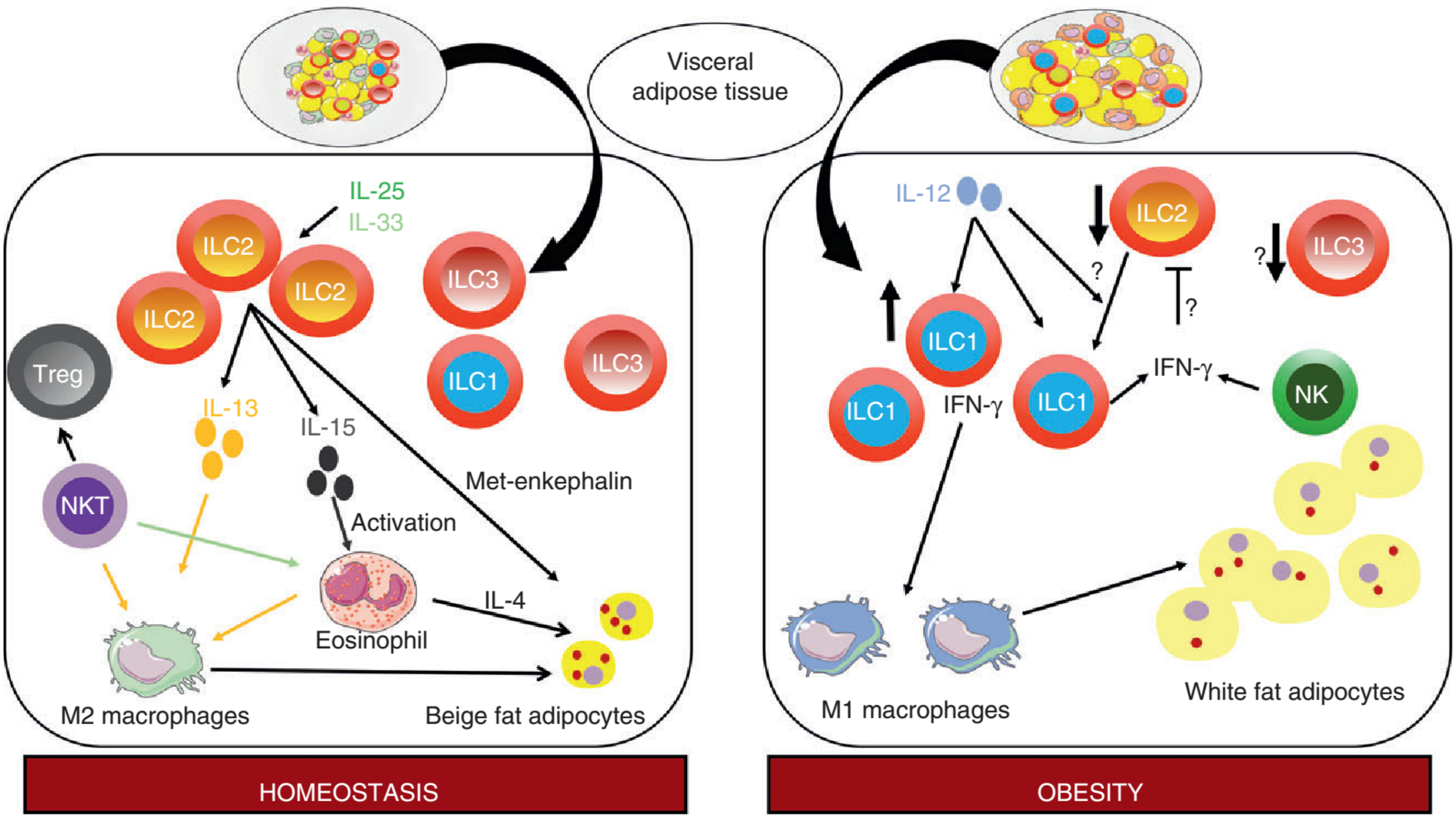
Everaere L *et al. Immunology*. 2018 Jan;153(1):21-30

Role of ILCs in asthma



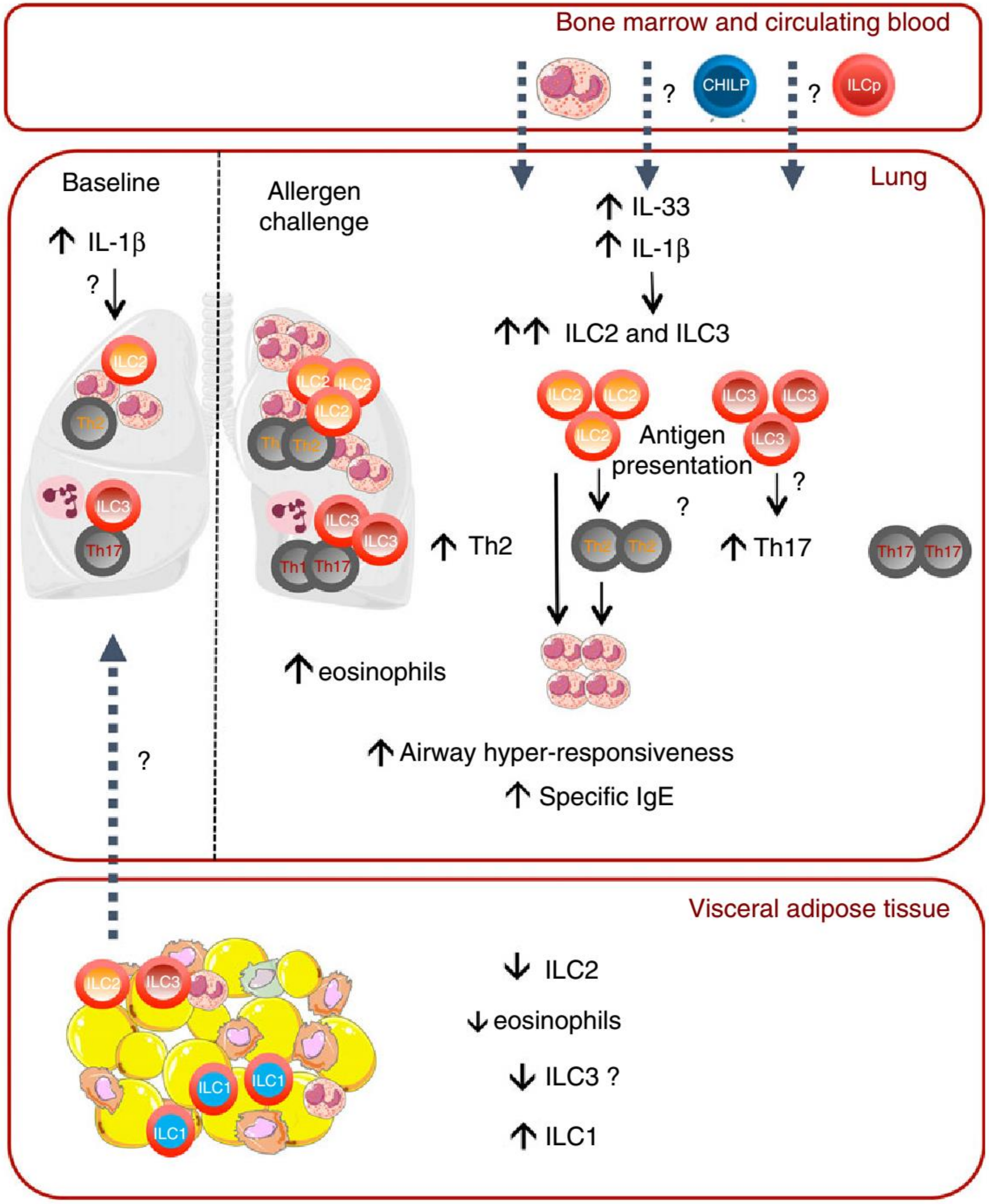
Everaere L *et al. Immunology*. 2018 Jan;153(1):21-30

ILCs in visceral adipose tissue



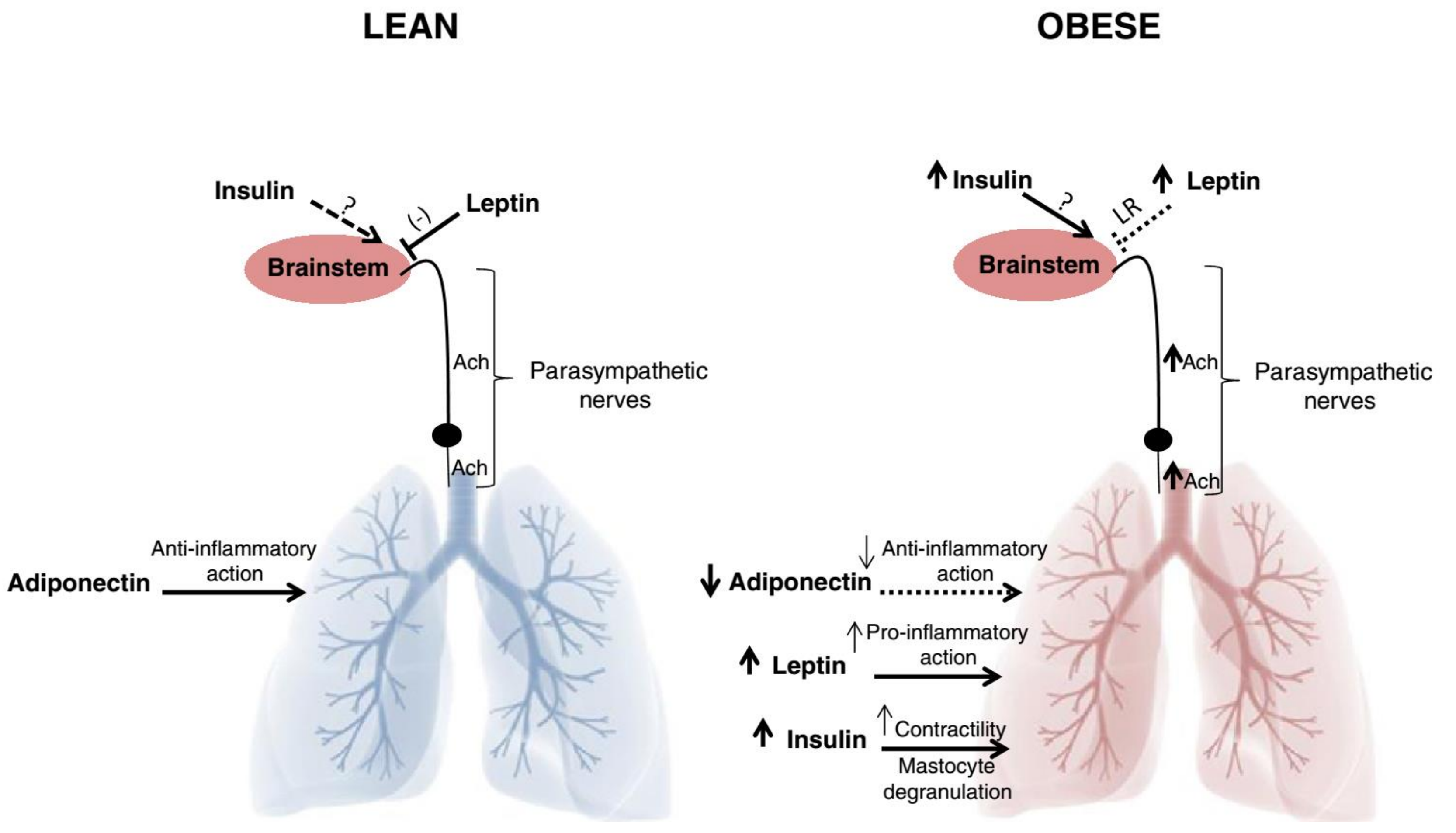
Everaere L *et al. Immunology*. 2018 Jan;153(1):21-30

Redistribution of ILCs in obesity: a link with asthma?



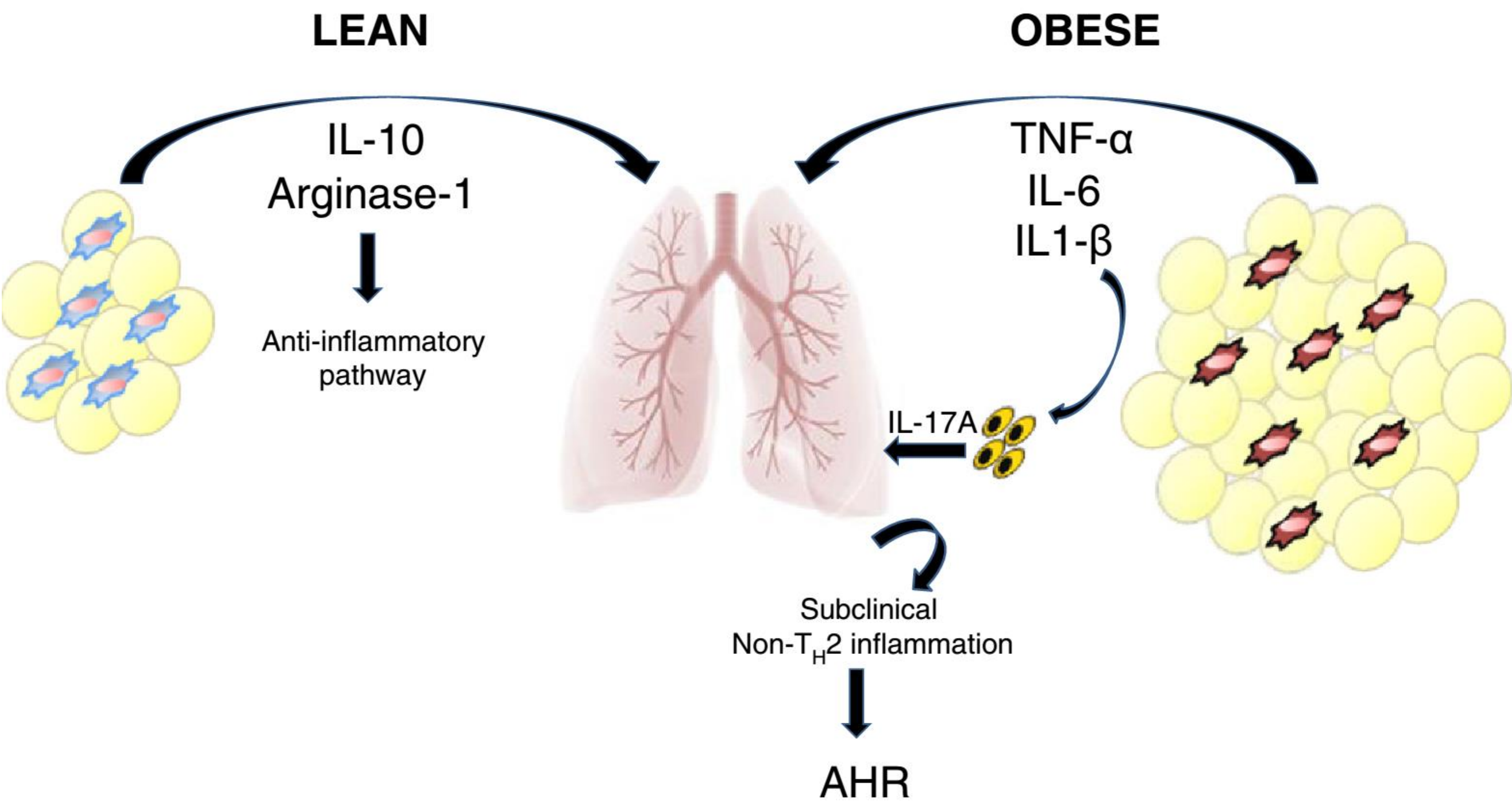
Everaere L *et al. Immunology*. 2018 Jan;153(1):21-30

Hormonal regulation of airway responsiveness under physiological and obesity conditions



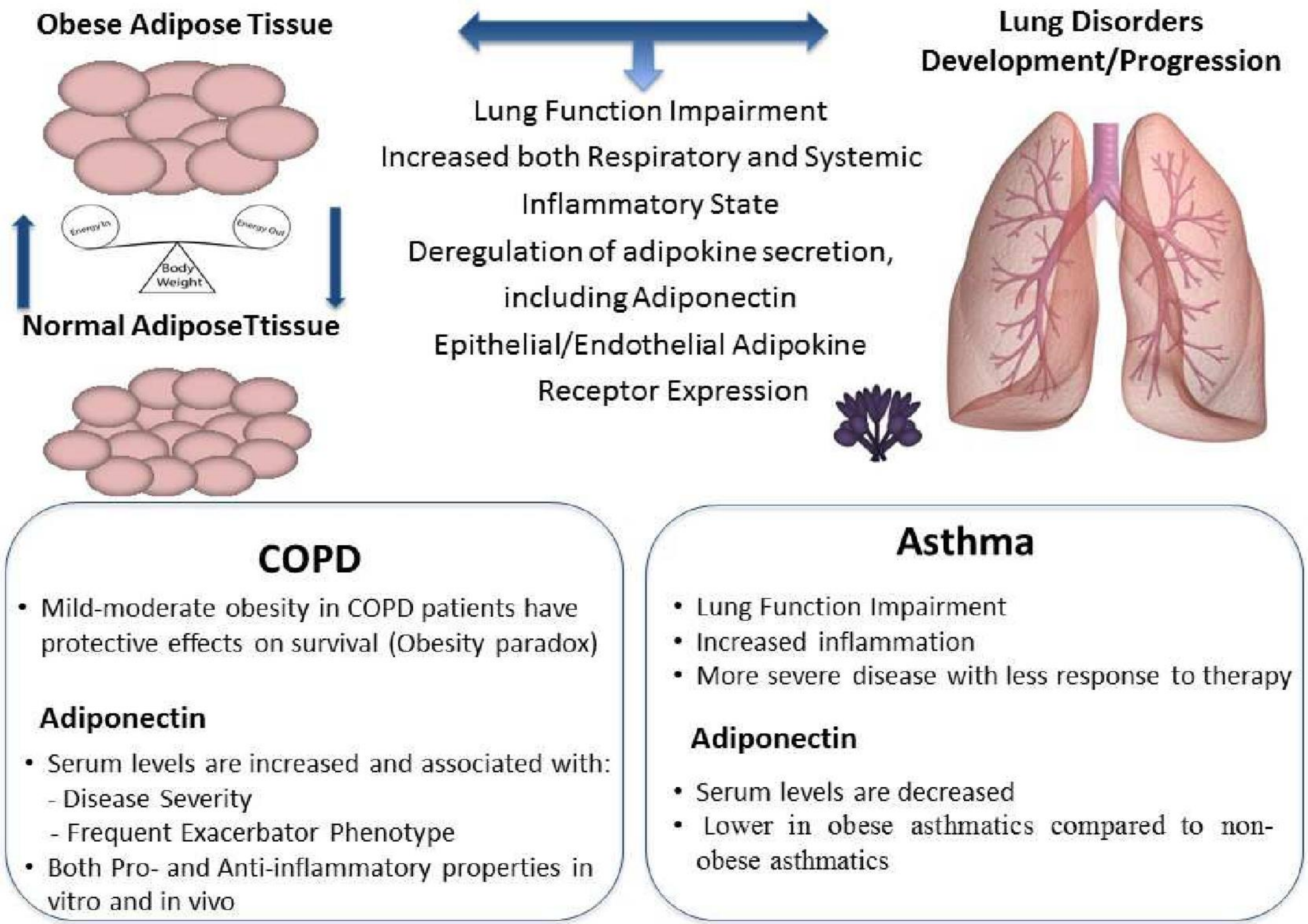
Leiria LO *et al. Metabolism*. 2015 Feb;64(2):172-81

Inflammation in lungs from obese and lean mice



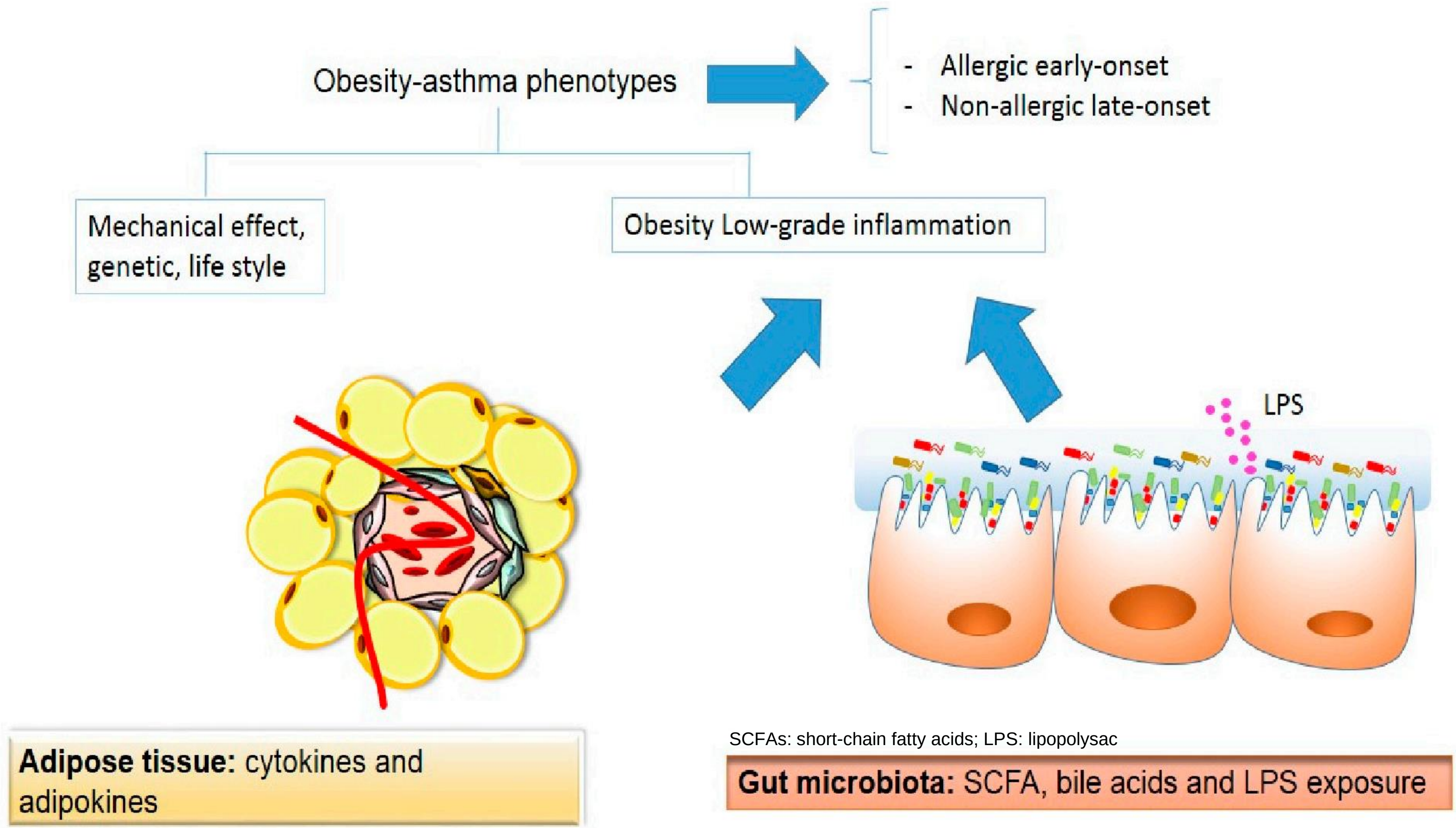
Leiria LO *et al. Metabolism*. 2015 Feb;64(2):172-81

Adipose tissue-respiratory system interaction: Role of Adiponectin



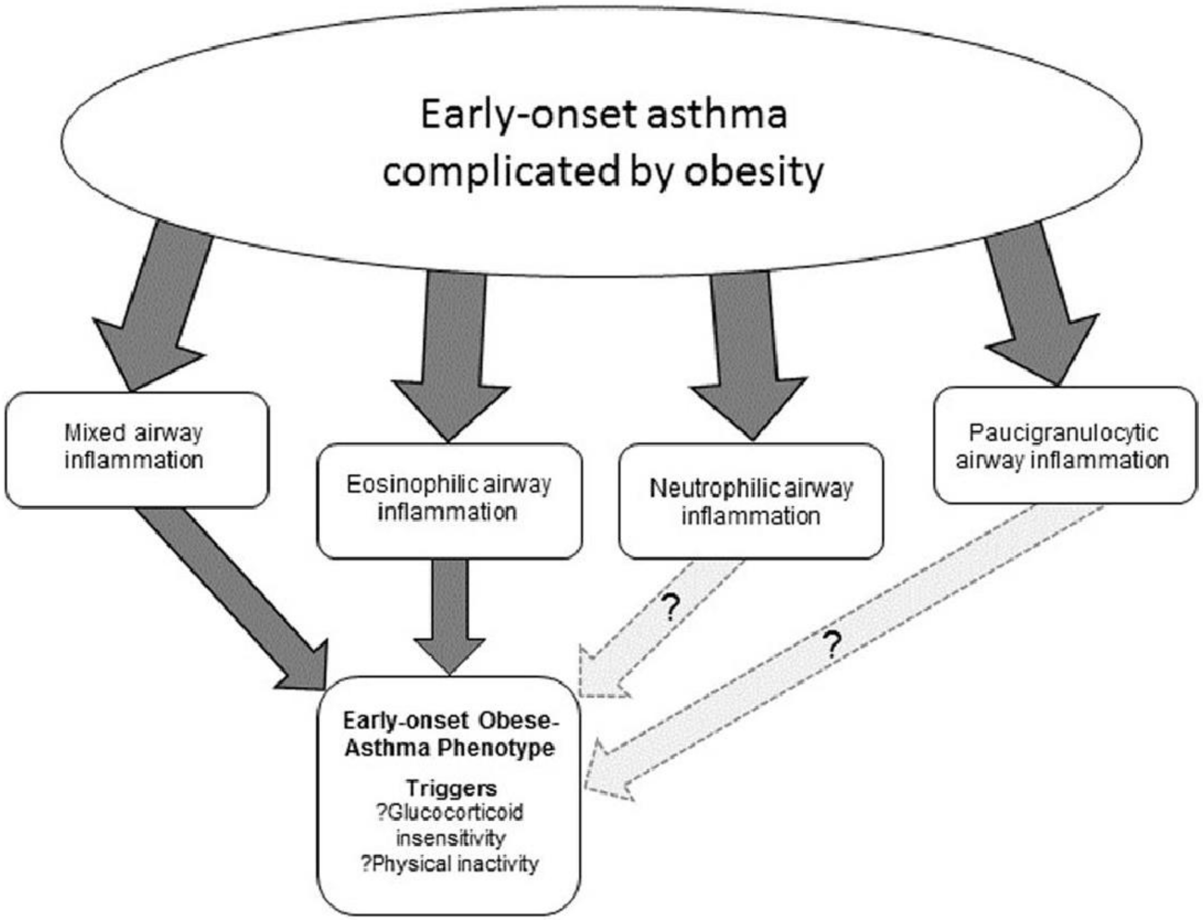
Bianco A *et al. Pulm Pharmacol Ther*. 2017 Apr;43:20-25

Linking mechanisms between obesity and asthma



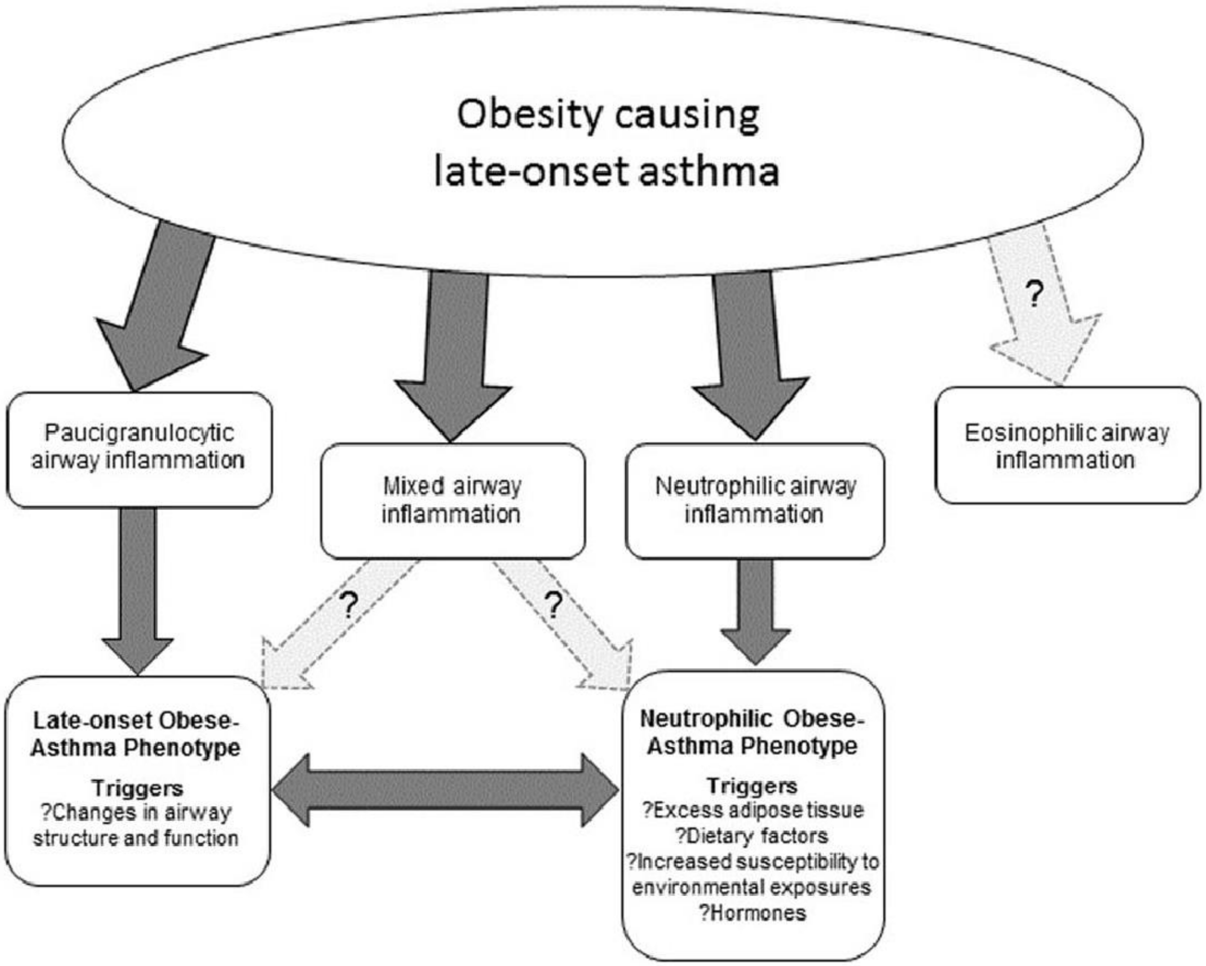
Gomez-Llorente MA *et al. Int J Mol Sci*. 2017 Jul 11;18(7)

Obese-asthma phenotypes



Scott HA *et al*. Curr Allergy Asthma Rep. 2017 Aug;17(8):53

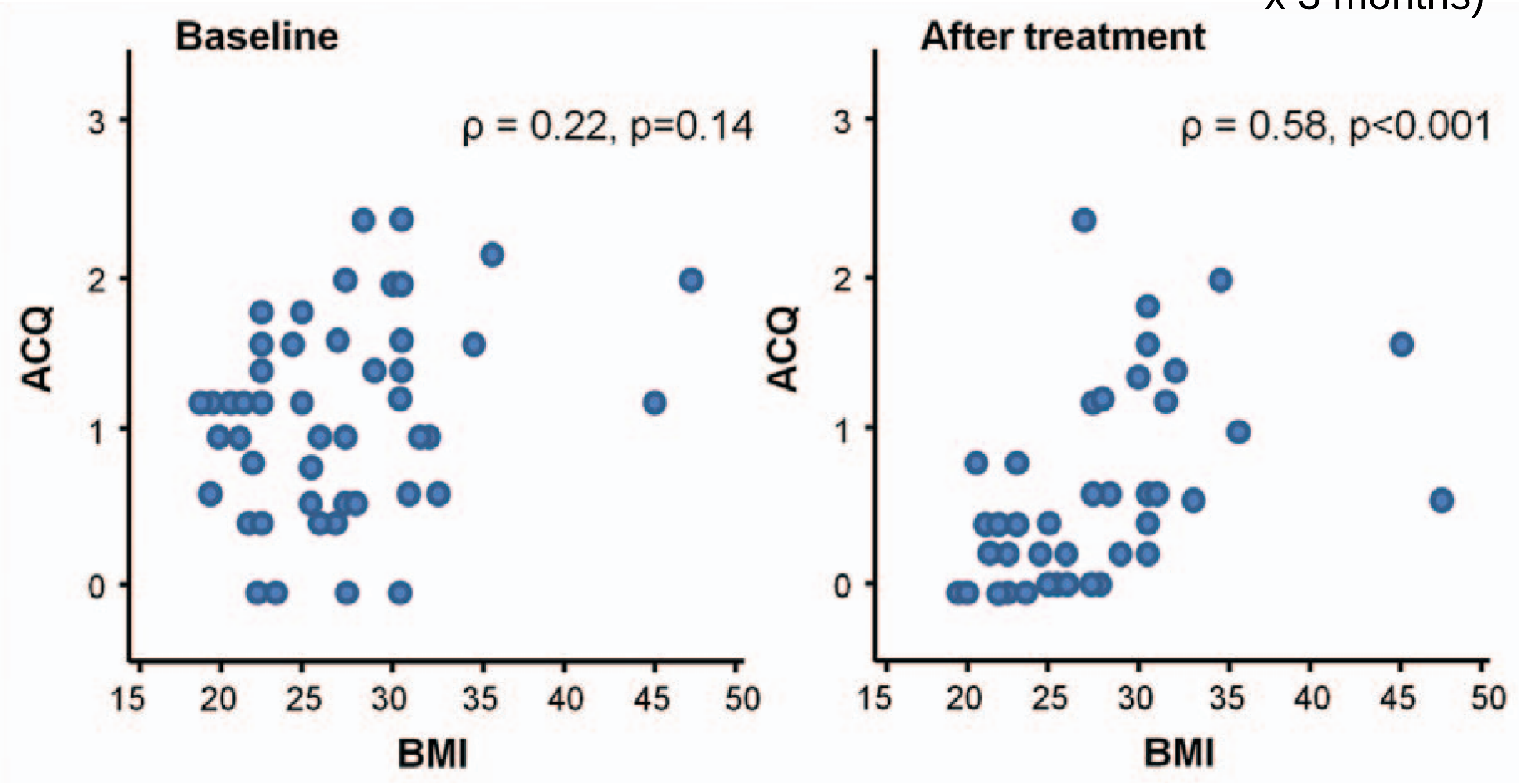
Obese-asthma phenotypes



Scott HA *et al*. Curr Allergy Asthma Rep. 2017 Aug;17(8):53

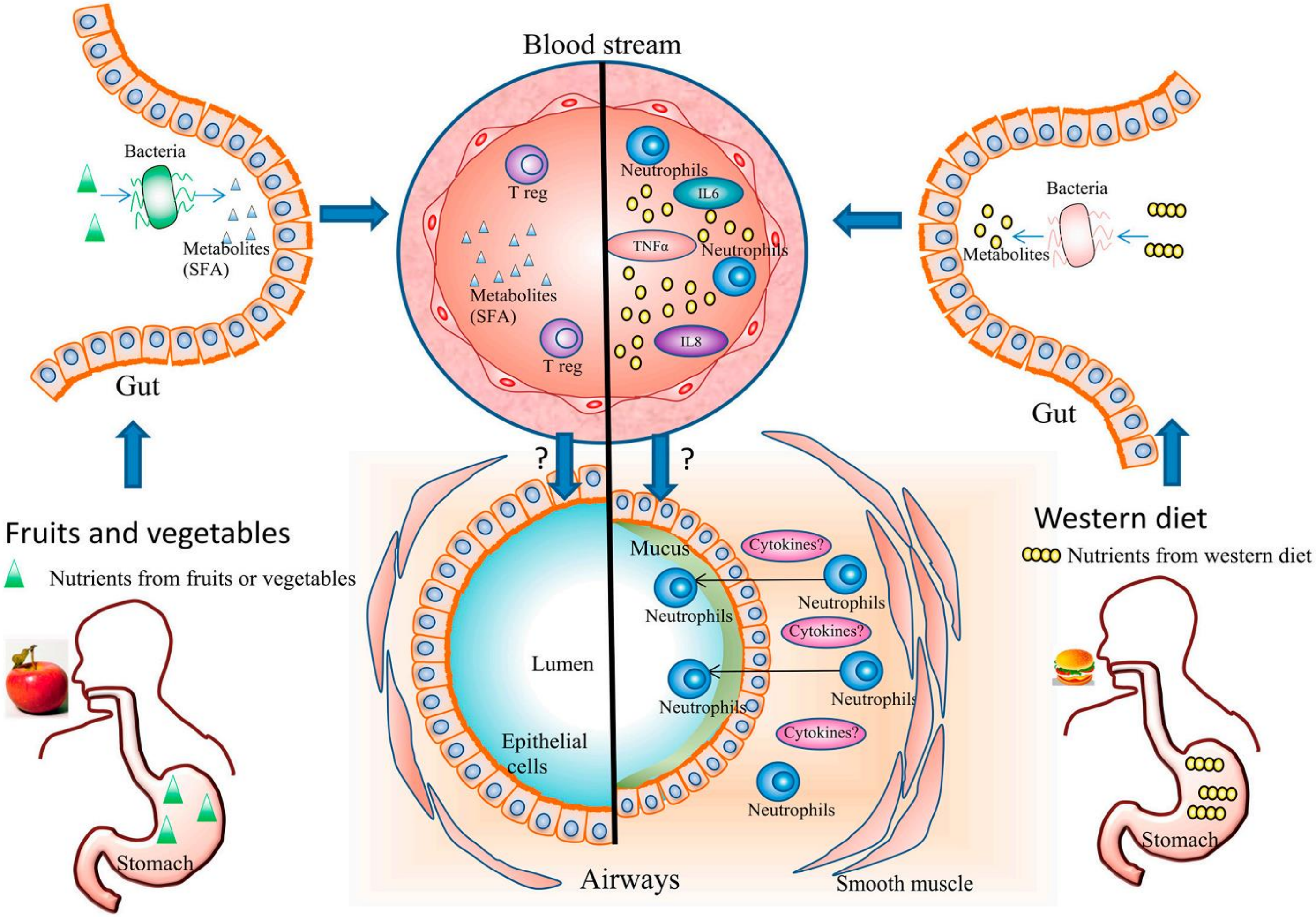
Extent of obesity correlates with poor asthma control despite high-dose ICS

(high dose ICS x 3 months)

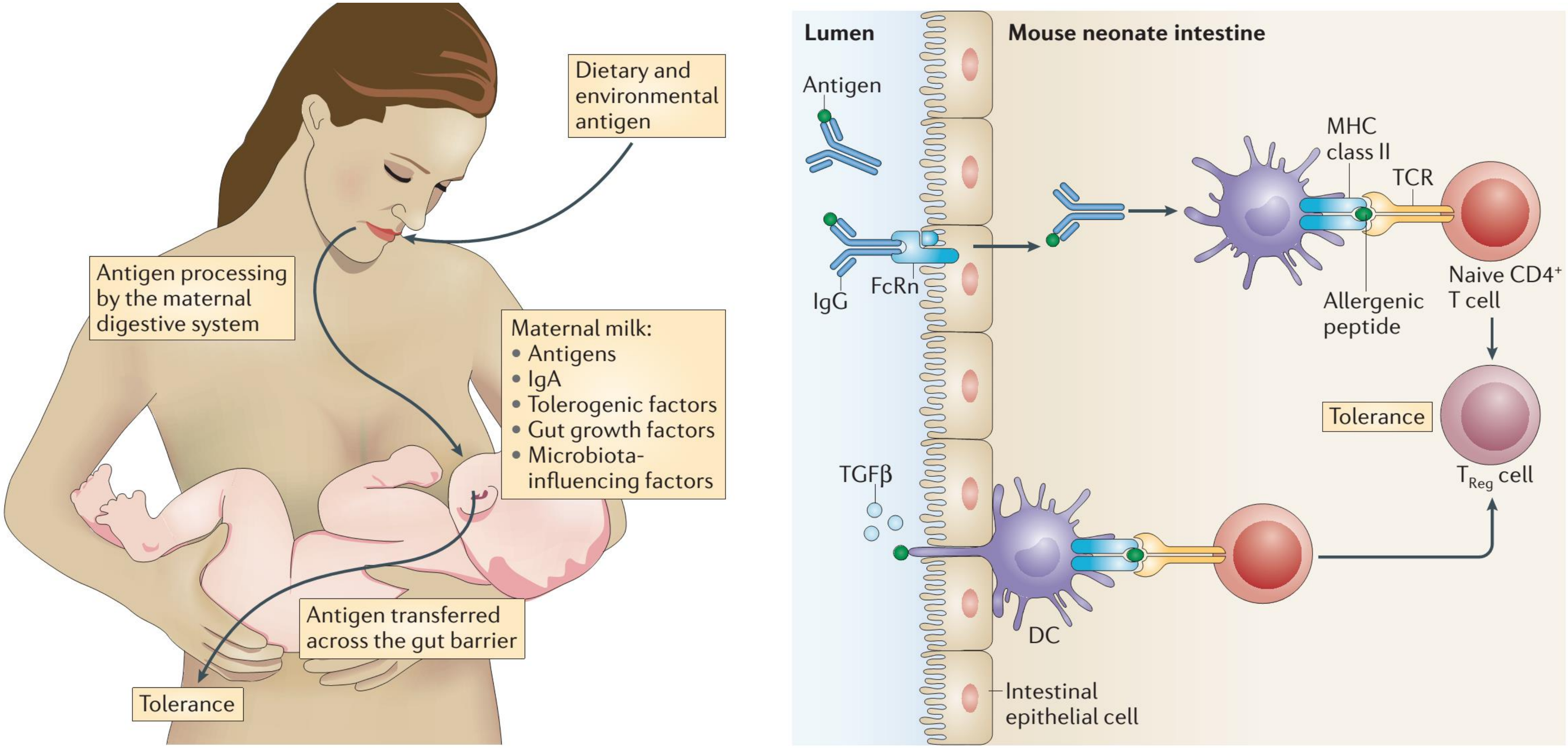


Carpaij OA *et al. Curr Opin Pulm Med*. 2018 Jan;24(1):42-49

Systemic and airway effects of dietary patterns on asthma

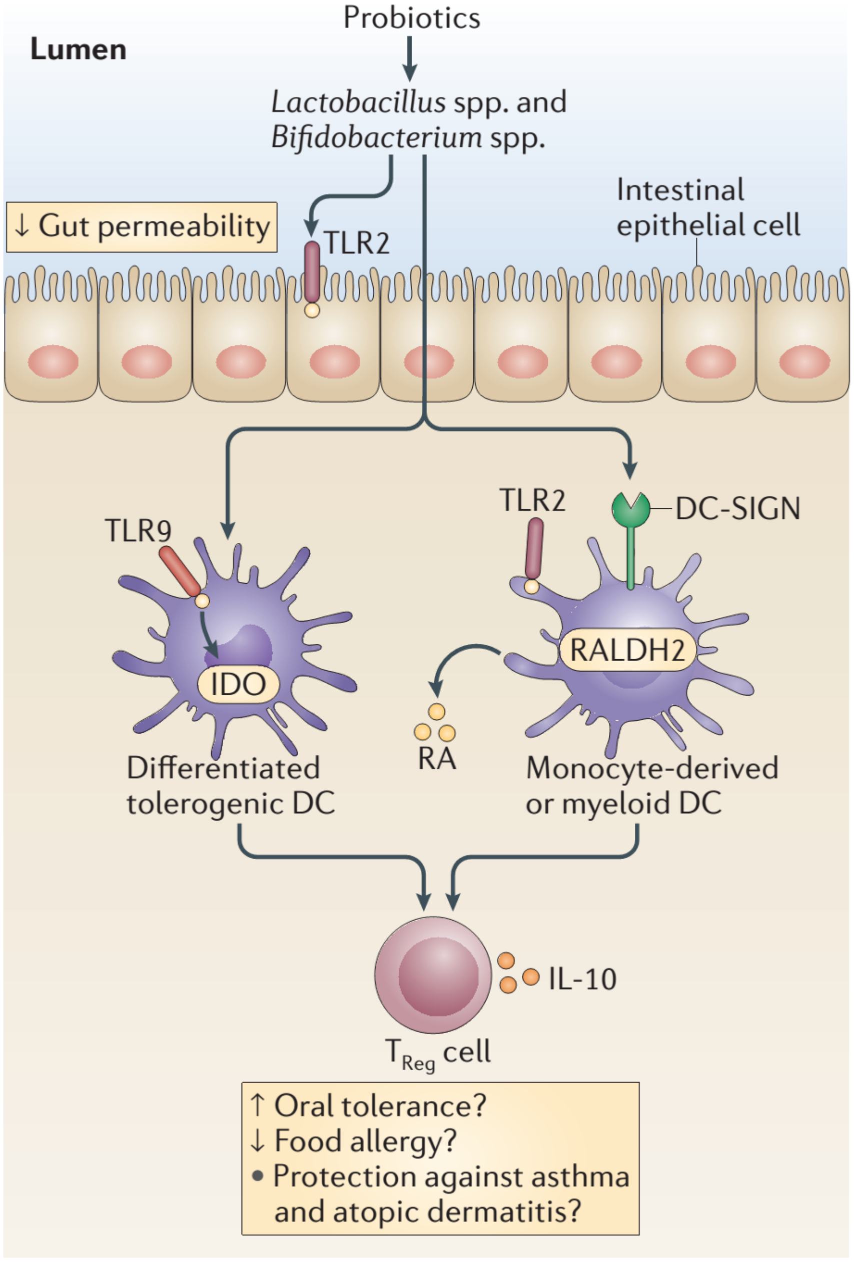


Mechanisms of mother-to-child transfer of protection against allergic airway inflammation



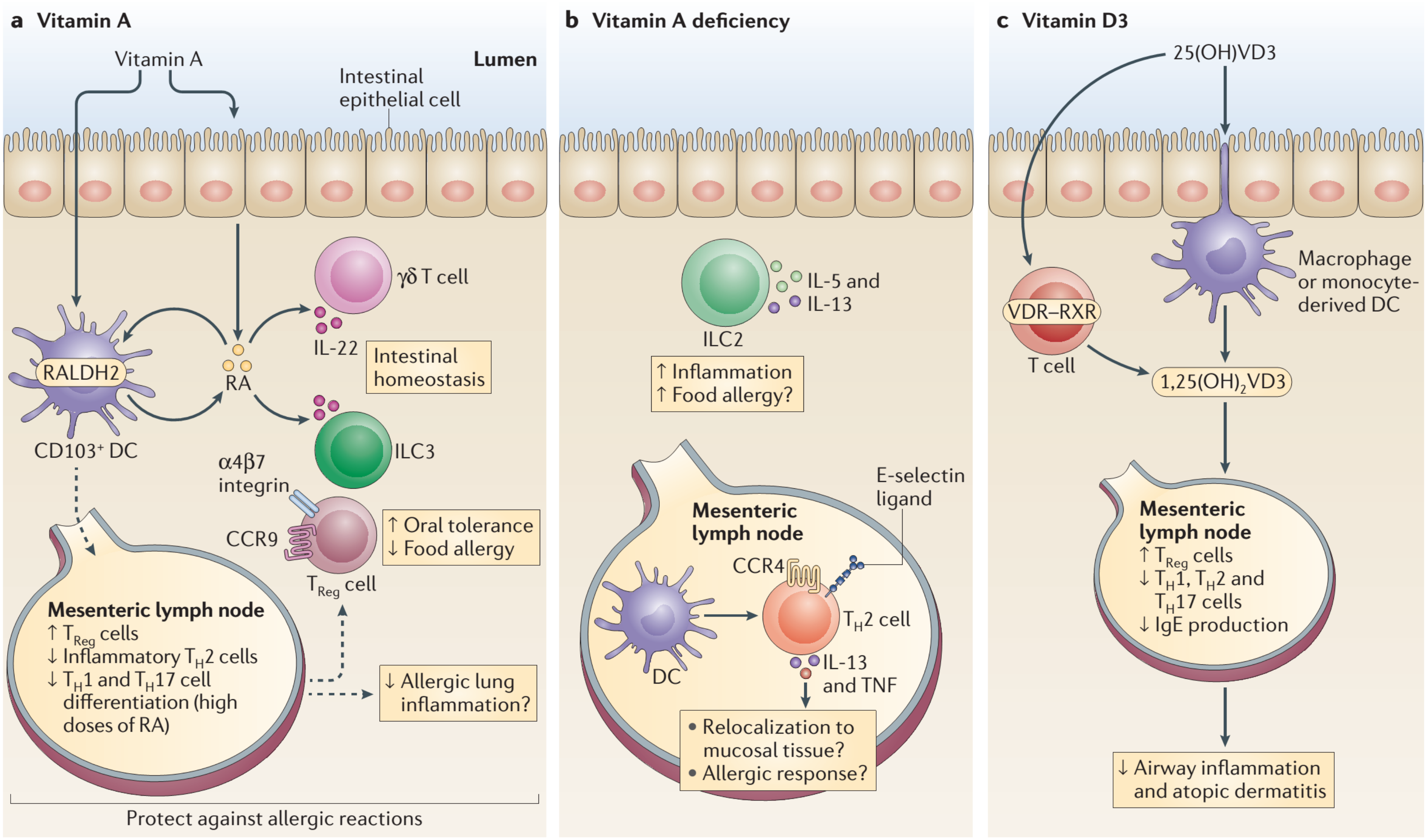
Julia V *et al. Nat Rev Immunol*. 2015 May;15(5):308-22

Possible mechanisms of the beneficial effects of probiotics in allergy



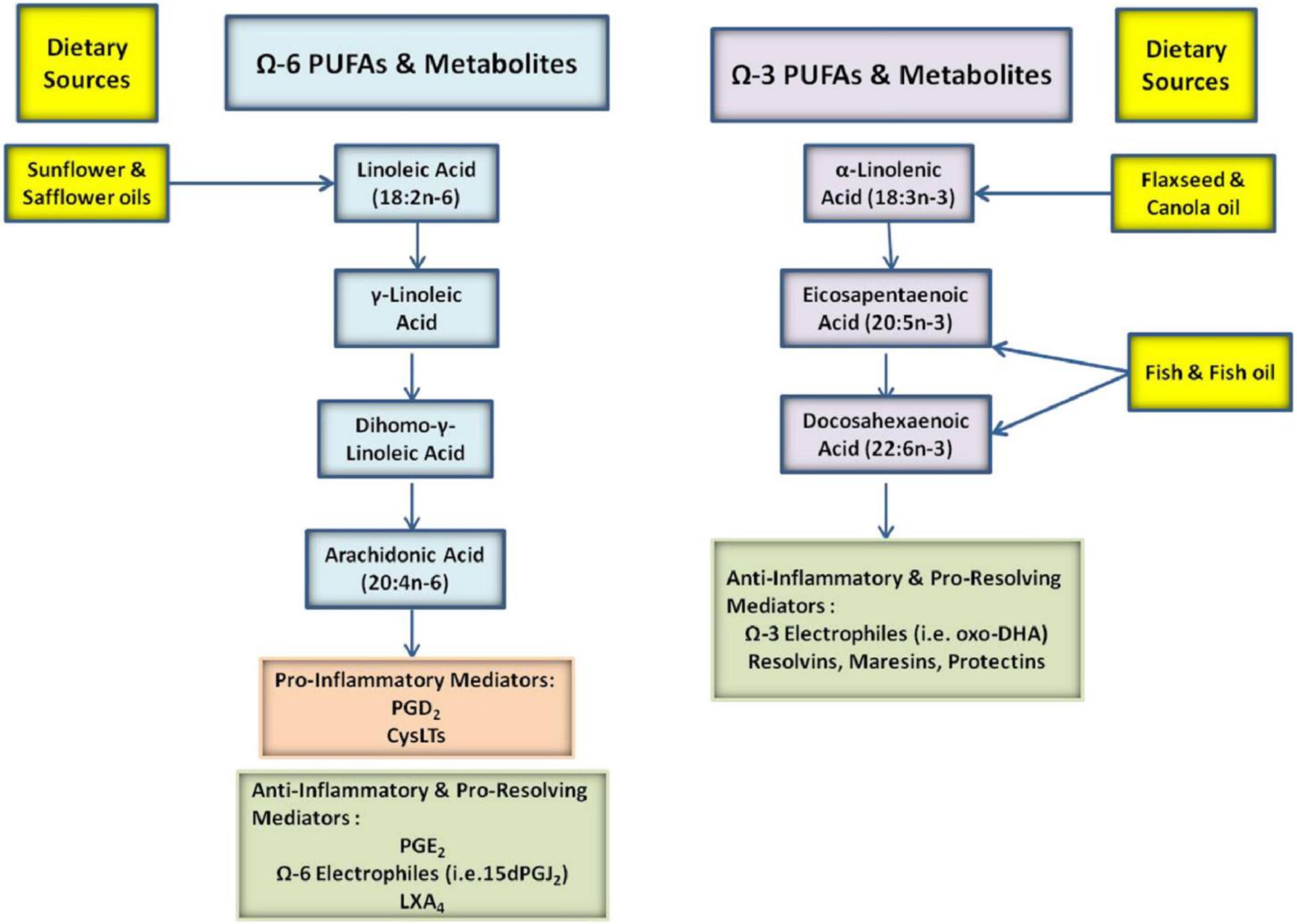
Julia V *et al. Nat Rev Immunol*. 2015 May;15(5):308-22

Impact of vitamin A and vitamin D3 on allergic reactions



Julia V *et al. Nat Rev Immunol*. 2015 May;15(5):308-22

Lipid mediators derived from Ω-6 and Ω-3 fatty acids



Wendell SG *et al. J Allergy Clin Immunol*. 2014 May;133(5):1255-64

CONCLUSIONS:
The evidence shows that, for **obese adults with asthma**, the best dietary intervention seems to be **caloric restriction**, *regardless of specific dietary components*.

- Weight ↓ ≥7.5% from baseline as a result of **caloric restriction** can be beneficial for improving disease control, quality of life, and pulmonary function in obese patients with asthma.

- A dietary pattern rich in **foods** with potential **antioxidant** effect had an impact in improving asthma control, but with *little clinical significance*.
- **Antioxidant supplementation** improves asthma control with **magnesium** supplementation and less decline in lung function with **vitamin C** supplementation.
- **Fatty acid** supplementation demonstrated effects on weight loss and improvement of asthma control and lung function.
- Supplementation with **propolis** and **caffeine** reported significant increases in FEV1.

- Conversely, studies of **high dietary salt** intake reported greater declines in lung function.

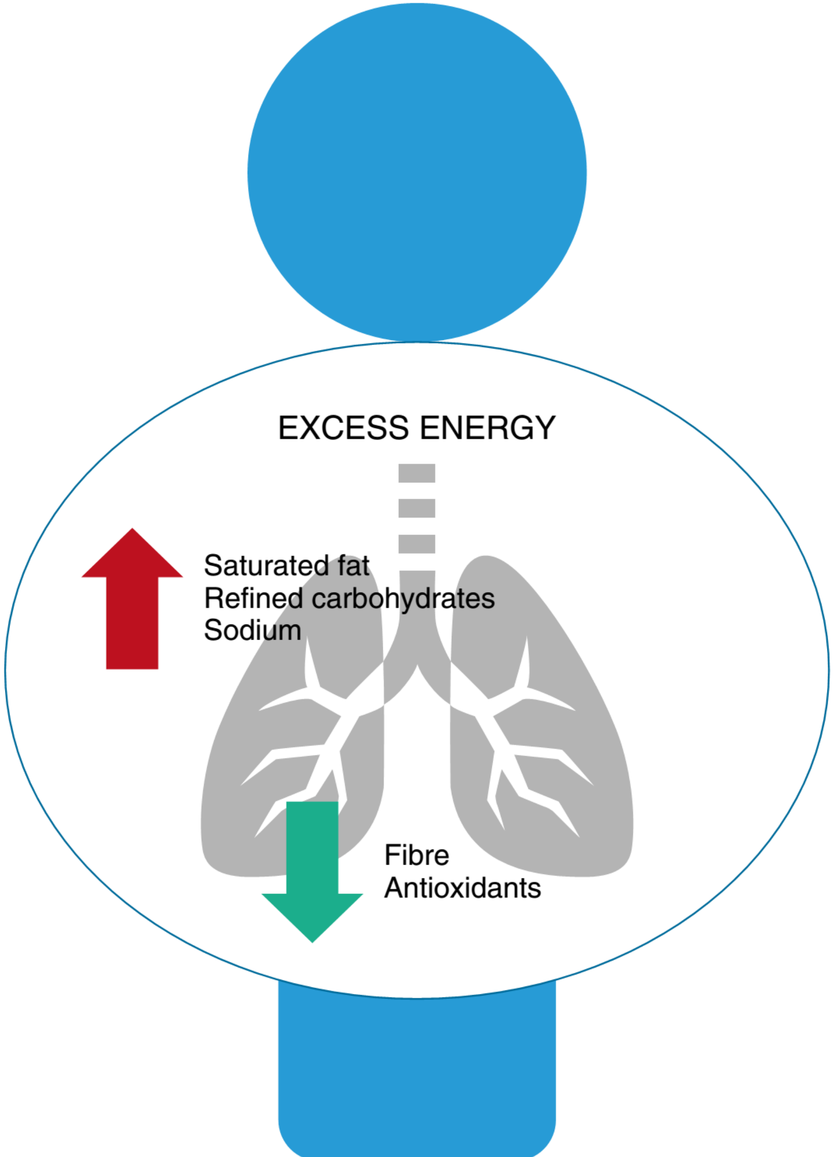
Forte GC *et al. Crit Rev Food Sci Nutr*. 2018 Jul 24;58(11):1878-1887

Diet, obesity, and asthma

- **Western dietary patterns**
  - excess energy intake
  - regular consumption of processed or "fast" foods
  - limited consumption of fruits, vegetables, and whole grains.

➔ high intake of saturated fat, refined carbohydrates, and sodium
➔ low intake of fiber, vitamins, and other phytochemicals.

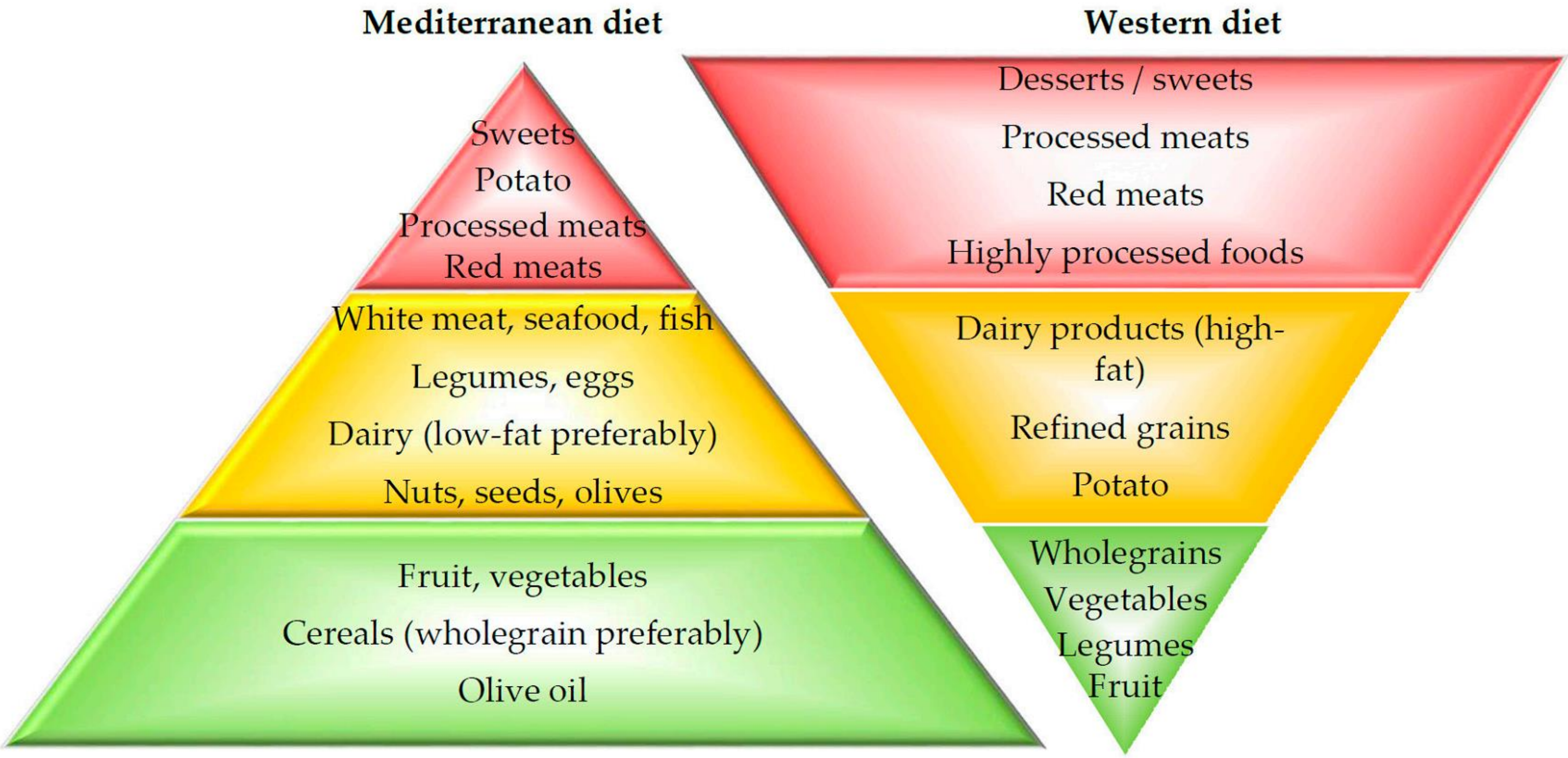
- Associated with increased risk of chronic inflammatory diseases, including asthma



OBESOGENIC DIET = INFLAMMATORY DIET

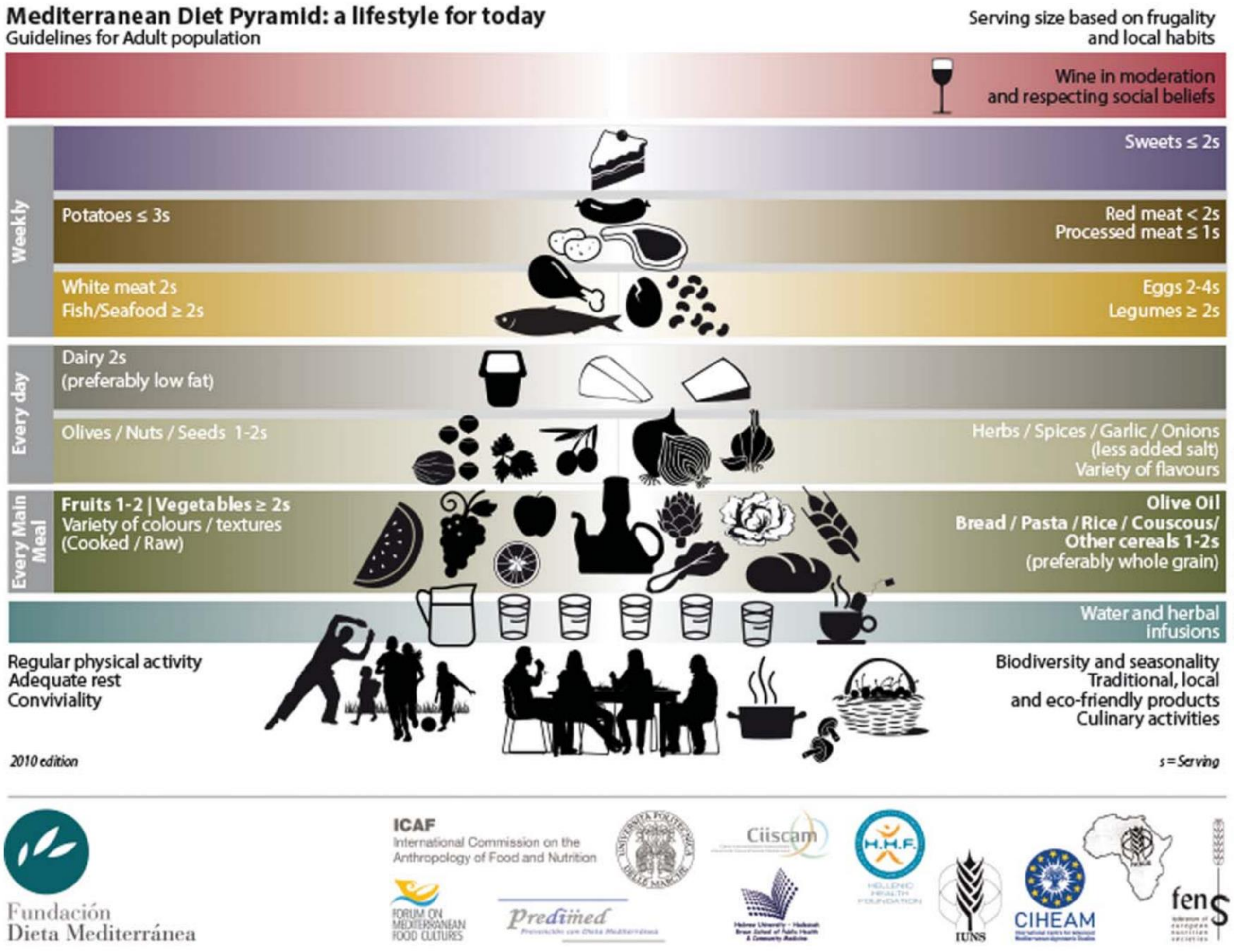
Wood LG *et al. Ann Am Thorac Soc*. 2017 Nov;14(Supplement_5):S332-S338

Mediterranean vs Western diets



Guilleminault L *et al. Nutrients*. 2017 Nov 8;9(11). pii: E1227

Mediterranean diet pyramid



Medina-Remón A *et al. Crit Rev Food Sci Nutr*. 2018 Jan 22;58(2):262-296

Association between Mediterranean patterns and asthma

Authors (year of study)	Country	Type of study	Sample size	Age range (years)	Gender	Follow up	Main outcome	Results	Adjustments
Arvaniti et al. (2011)	Greece	Cross sectional	700	10–12	Children (323 boys)	/	Asthma symptom	Higher adherence to Med-Diet was associated with a lower prevalence of any asthma symptom (OR = 0.86; 95%CI: 0.75 to 0.98).	Age, sex, BMI, physical activity status, energy intake.
Barros et al. (2008)	Portugal	Cross sectional	174	25–55	♂ 32 ♀142	/	Asthma	High adherence to a Med-Diet ↓the risk of uncontrolled asthma by 78% (OR = 0.22; 95%CI: 0.05 to 0.85). Higher intake of fresh fruit ↓ the probability of having noncontrolled asthma (OR = 0.29; 95%CI: 0.10 to 0.83), while a higher intake of ethanol had the opposite effect (OR = 3.16; 95%CI: 1.10 to 9.11)	Gender, age, education, energy intake and current use of inhaled corticosteroid.
Castro-Rodriguez et al. (2008)	Spain	Cross sectional	1,784	3.28–4.88	Children	/	Current wheeze	Med-Diet was a protective factor for current wheezing (OR = 0.54; 95%CI: 0.33 to 0.88).	Age, birth weight, livestock during pregnancy, delivery by cesarean, antibiotic consumption during the first year, acetaminophen consumption during the previous 12 months, rhinoconjunctivitis, dermatitis, paternal asthma, maternal asthma, maternal age, maternal education level, current paternal smoking, current maternal smoking, vigorous physical activity frequency, cats at home in the last 12 months.
de Batlle et al. (2008)	Mexico	Cross sectional	1,476	6–7	Children	/	Ever asthma, ever wheezing, current wheezing	Adherence to Med-Diet was negatively associated with ever asthma (OR = 0.60; 95% CI: 0.40 to 0.91) and ever wheezing (OR = 0.64; 95% CI: 0.47 to 0.87).	Sex, maternal education, exercise, current tobacco smoking at home, maternal asthma, maternal rhinitis.
Garcia-Marcos et al. (2007)	Spain	Cross sectional	20,106	6–7	Children	/	Current occasional asthma, current severe asthma	Med-Diet was a protective factor for current severe asthma in girls (OR = 0.90; 95% CI: 0.82 to 0.98).	Older and younger siblings, maternal smoking.
Grigoropoulou et al. (2011)	Greece	Cross sectional	1125	10–12	Children (529 boys)	/	Ever asthma	Higher Mediterranean score was associated with a lower prevalence of ever-asthma (OR = 0.84; CI: 0.77 to 0.91). Urban areas, OR = 0.81; CI: 0.73 to 0.91; rural areas OR = 0.87; CI: 0.75 to 1.00	Environmental factors (details unknown).
Nagel et al. (2010)	20 countries	Cross sectional	50,004	8–12	Children	/	Ever asthma, current wheeze, and atopic wheeze	Higher adherence to Med-Diet was associated with a lower prevalence of ever asthma (OR = 0.95; 95% CI: 0.92 to 0.99) and current wheezing (OR = 0.97; 95% CI: 0.94 to 0.99).	Age, sex, environmental tobacco smoke, parental atopy, exercise, number of siblings.
Chatzi et al. (2007)	Spain	Longitudinal	967	6.5	507 pregnant women and 460 children	6.5 years	Persistent wheeze, atopic wheeze	Higher adherence to Med-Diet was a protective factor of persistent wheeze (OR = 0.22; CI: 0.08 to 0.58) and atopic wheeze (OR = 0.30; CI: 0.10 to 0.90).	Sex, maternal and paternal asthma, maternal social class and education, BMI, total energy intake, children adherence to Med-Diet at age 6.5.
Chatzi et al. (2013)	Spain, Greece	Longitudinal	2,516	29–33	2,516 pregnant woman-infant pairs	1 year	Wheeze in the first year of life	Adherence to Med-Diet during pregnancy was not associated with wheeze in the first year of life	Maternal age; education; maternal history of asthma; smoking during pregnancy; parity; duration of breastfeeding; child's age at assessment; child's sex.
Castro-Rodriguez et al. (2010)	Spain	Longitudinal	1,409	14.1–19.1 months	1,409 pregnant woman-infant pairs	1 year	Ever wheezing during the first year	Med-diet score (excluding olive oil) was not associated with infants' ever wheezing during the first year. However, olive oil was protective against ever-wheezing (OR = 0.57; CI: 0.4 to 0.9)	Sex, exclusive breastfeeding, day care attendance, eczema, maternal asthma, smoking during pregnancy, siblings, mold on household wall, preterm birth, olive oil.

Medina-Remón A *et al. Crit Rev Food Sci Nutr*. 2018 Jan 22;58(2):262-296

Diet and risk of asthma or wheezing

Diet	Diet During Life Stages					
	Pregnancy		Childhood		Adulthood	
	Effect	Evidence	Effect	Evidence	Effect	Evidence
Post-natal breast feeding			✓ [56]	Very strong	⊖ [57]	Low
Mediterranean diet	⊖ [58–63]	Low	⊖ [59,63–68]	Low	⊖ [69–71]	Low
Fruit	⊖ [58,61,63,72–77]	Low	✓ [78–81]	Low	✓ [69,82,83]	Low
Vegetables	⊖ [58,61,63,72–77]	Low	✓ [78–81]	Low	✓ ** [70,83–85]	Very low
Fast food	⊖ [60,63,86,87]	Low	✗ [63,88,89]	Low	⊖ [90]	Low
“Western” diet	⊖ [91–93]	Low	✗ [88,94–97]	Very low	⊖ [90,98–100]	Low
Meat	⊖ [62,101]	Low	✗ [63]	Low	⊖ [90]	Low
Fish	⊖ [74,77,92,102–108]	Low	✓ * [95,105,108–113]	Low	⊖ [69–71]	Low
Vitamin A	⊖ [114–116]	Low	⊖ [117,118]	Low	?	?
Vitamin B	⊖ [114,119,120]	Low	?	?	?	?
Vitamin C	⊖ [75,114,115,121,122]	Low	?	?	?	?
Vitamin D	✓ [101,123–125]	Very Strong	⊖ [126]	Low	?	?
Vitamin E	✓ [75,101,115,121,122,127]	Low	?	?	✓ *** [128,129]	Low
LC n-3 PUFA (Fish oil)	✓ [130–132]	Strong	⊖ [133–135]	Very Strong	⊖ [113,136,137]	Low

✓ Beneficial effect; ✗ negative effect; ⊖ No effect; ? = no data.

Diet and asthma control

Diet	Childhood		Adulthood	
	Effect	**Evidence**	**Effect**	**Evidence**
Mediterranean diet	✔ [153,154]	Low	⊖ [170,171]	Strong
Fruit	✔ [155,156]	Very low	✔ [174]	Strong
Vegetables	✔ [156]	Very low	✔ [174]	Strong
Fast food	✖ [156,158,159]	Very low	✖ [183]	Very low
"Western" diet	?	?	✖ [181]	Very low
Meat	?	?	✖ [182]	Low
Fish	?	?	?	?
Vitamin A	?	?	?	?
Vitamin B	?	?	?	?
Vitamin C	✔ [166]	Low	⊖ [176]	Strong
Vitamin D	✔ [167]	Strong	⊖ [178]	Strong
Vitamin E	?	?	⊖ [177]	Strong
LC *n*-3 PUFA (Fish oil)	⊖ [160–163]	Strong	⊖ [161]	Very strong

✔ Beneficial effect; ✖ negative effect; ⊖ No effect; ? = no data.

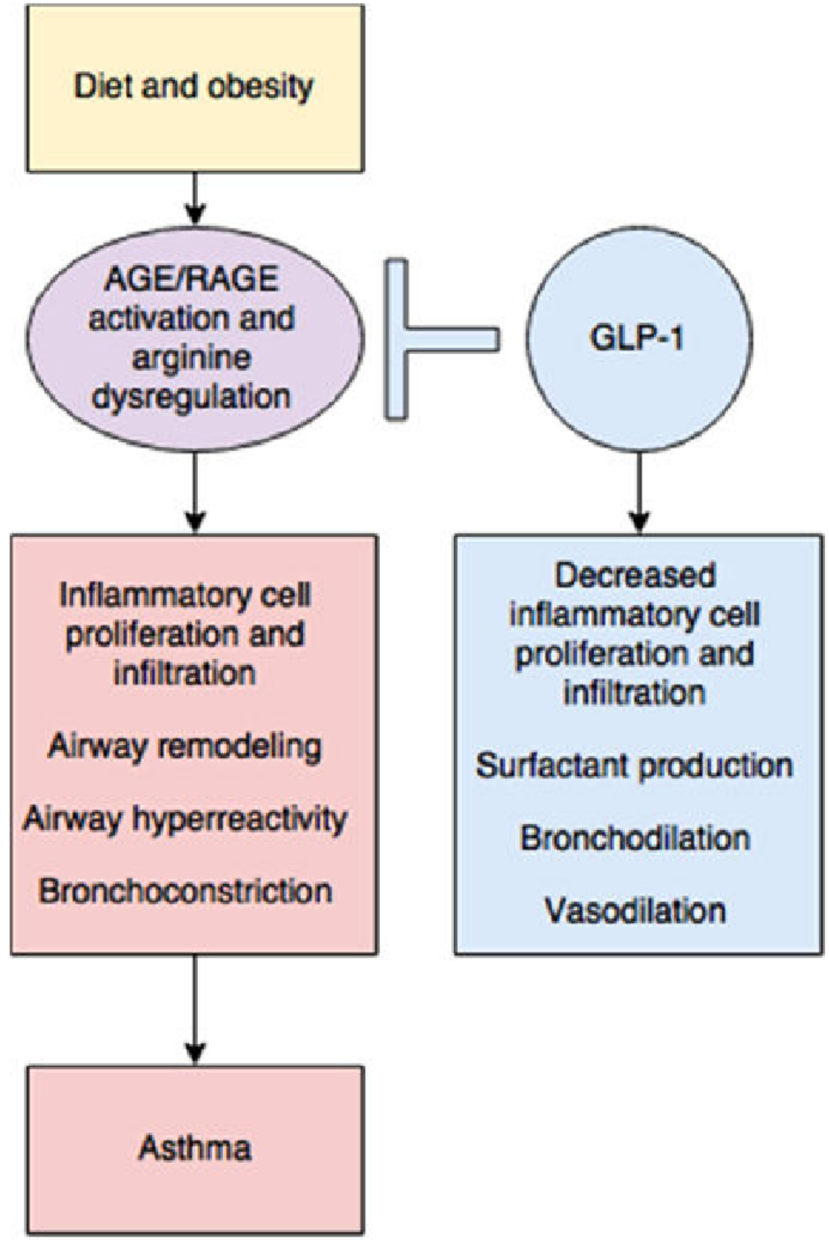
Guilleminault L *et la. Nutrients*. 2017 Nov 8;9(11). pii: E1227

Diet and lung function in asthma

	Childhood		Adulthood	
	Effect	**Evidence**	**Effect**	**Evidence**
New born Breast feeding	⊖ [185–187]	Low	?	?
Mediterranean diet	✔ [43,188]	Very low	⊖ [43,170,171,188]	Strong
Fruit	⊖ [43]	Very low	✔ [172–174]	Strong
Vegetables	⊖ [43]	Very low	✔ [174]	Strong
Fast food	?	?	?	?
“Western” diet	?	?	?	?
Meat	?	?	⊖ [71]	Low
Fish	?	?	?	?
Vitamin A	⊖ [118]	Low	?	?
Vitamin B	?		⊖ [175]	Very low
Vitamin C	✔ [166,189]	Strong	✔ [197]	Strong
Vitamin D	⊖ [190–192]	Very strong	⊖ [190,191,198]	Very strong
Vitamin E	✔ [193]	Strong	⊖ [197]	Strong
LC *n*-3 PUFA (Fish oil)	⊖ [194]	Strong	⊖ [194]	Strong

✔ Beneficial effect; ✖ negative effect; ⊖ No effect; ? = no data.

Glucagon-like peptide 1: A potential anti-inflammatory pathway in obesity-related asthma



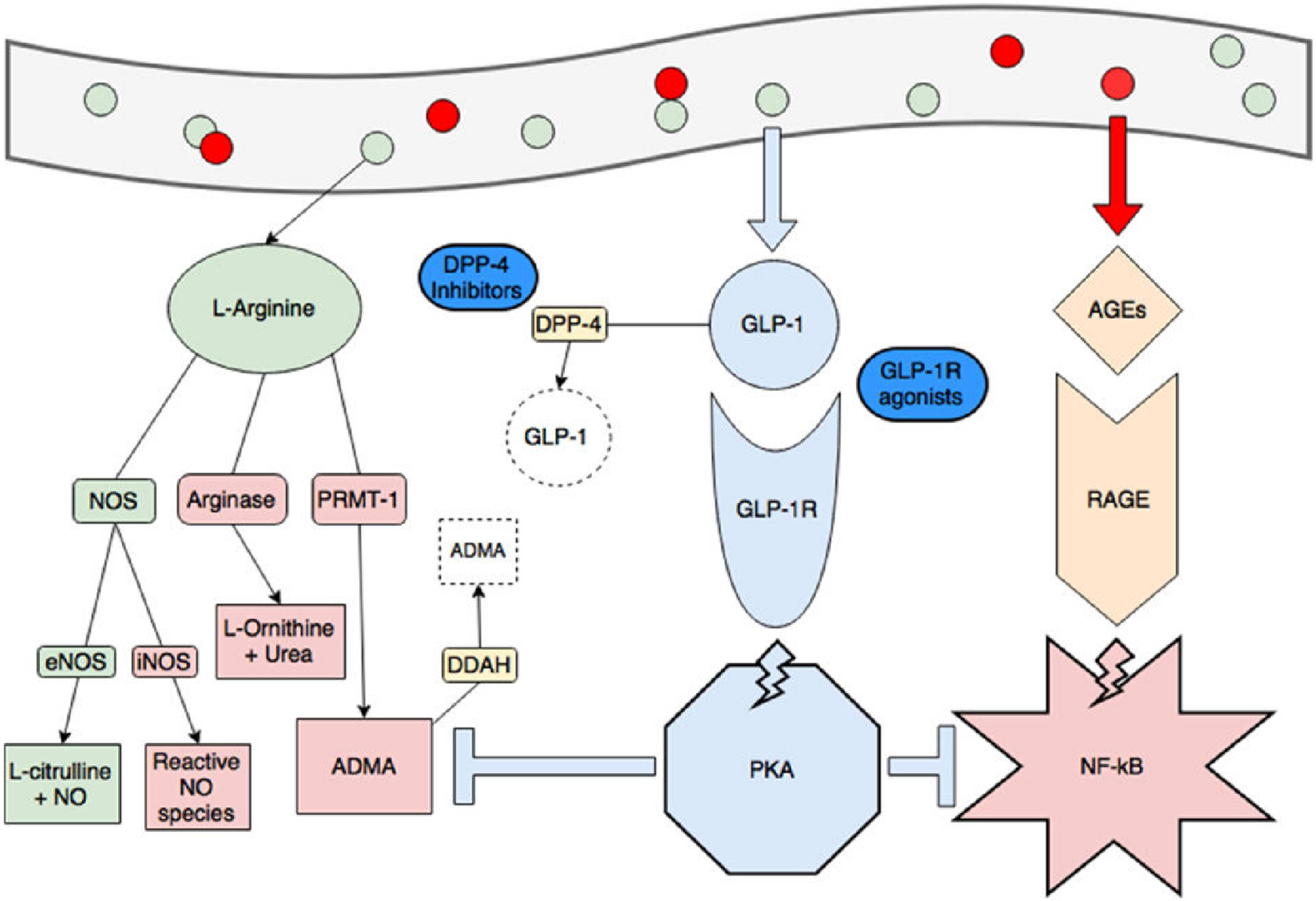
- Diet and obesity ➔
  - dysregulated arginine metabolism
  - ↑ production of advanced glycation end products (AGE) and subsequent activation of their receptor (RAGE)

➔ inflammation and asthma.

- The GLP-1 pathway may be critical to attenuating this inflammation

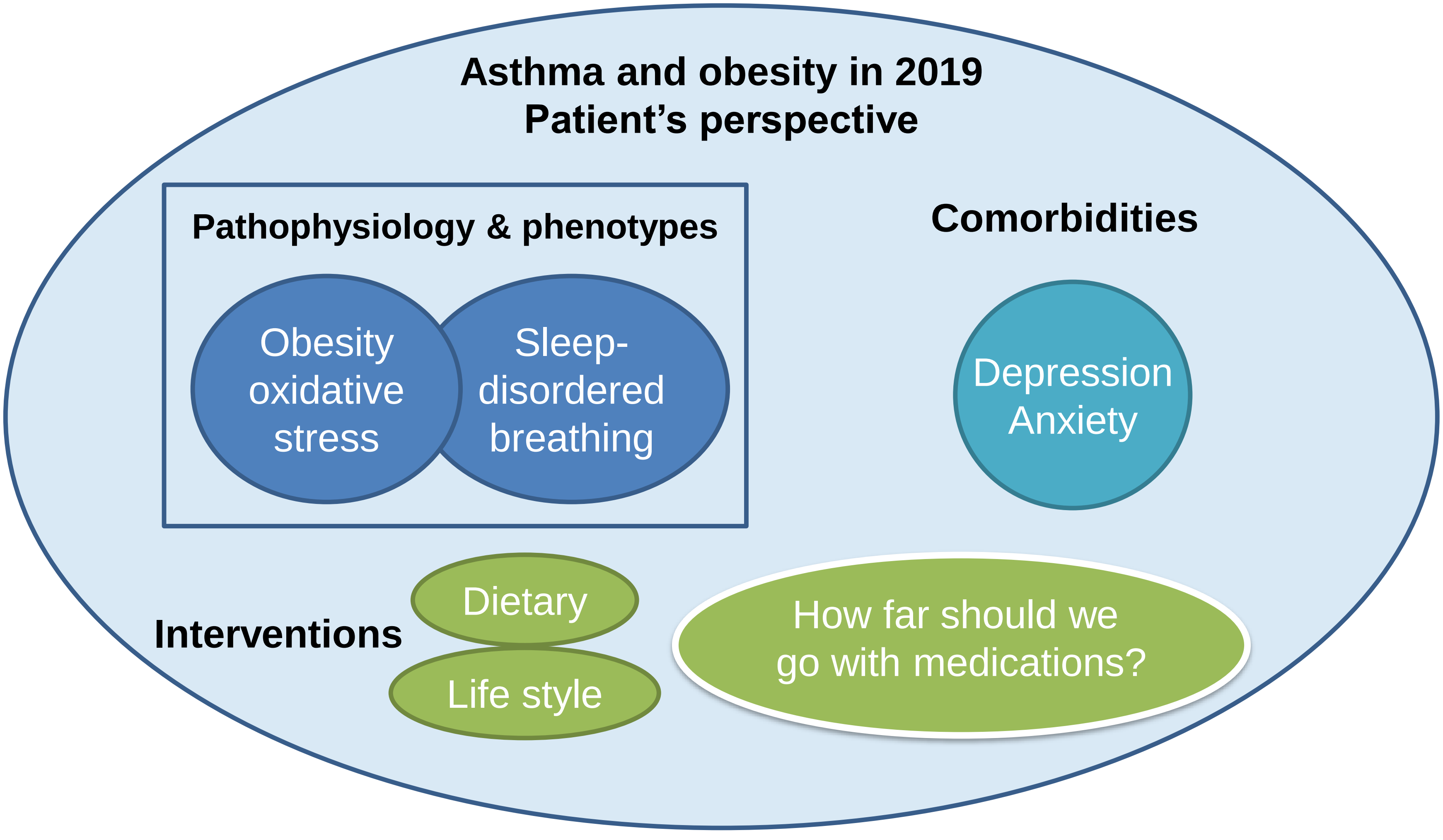
Glucagon-like peptide 1:

A potential anti-inflammatory pathway in obesity-related asthma



Nguyen *DV et al. Pharmacol Ther*. 2017 Dec;180:139-143

Treating asthma in patients with obesity : the need for a new approach




THANK YOU
FOR YOUR ATTENTION