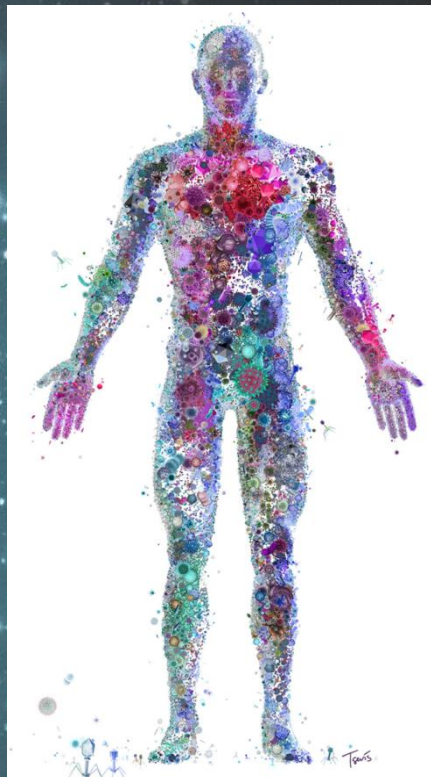
Convegno "Alimentazione e sicurezza alimentare nella malattia celiaca"
25 febbraio 2023 – Grand Hotel Adriatico - Montesilvano

CELIACHIA E MICROBIOTA INTESTINALE



Dott. Maria Teresa ILLICETO

Gastroenterologia ed Endoscopia Digestiva Pediatrica - OC Pescara
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CO-EVOLUZIONE
DEL MICROBIOMA INTESTINALE (oltre 3 milioni)
e GENOMA UMANO (23000)

esseri umani e microbiota intestinale sono in una relazione simbiotica

ipotesi di un "**SUPER ORGANISMO**" composto dall'organismo umano e dai microbi

Il microbiota intestinale svolge importanti compiti metabolici e immunologici, e la compromissione della sua composizione potrebbe alterare l'omeostasi e portare allo sviluppo di malattia

Ianiro G, Gasbarrini A, et al.
Therapeutic modulation of gut microbiota: current clinical applications and future perspectives.
Curr Drug Targets. 2014;15:762-770.

MICROBIOTA e CELIACHIA

PATOGENESI - ESORDIO

EVOLUZIONE e PROGRESSIONE

TERAPIA

MALATTIA IMMUNO-MEDIATA SISTEMICA INDOTTA DALLE PROLAMINE DEL GRANO E DI ALTRI CEREALI TOSSICI IN SOGGETTI GENETICAMENTE SUSCETTIBILI

SPECIFICO PROFILO SIEROLOGICO E ISTOLOGICO

HLA DQ2 (DQA1* 0501- DQB1*0201) 90%
HLA DQ8 (DQA1*0301 – DQB1*0302) 5%
OMOZIGOSI DQB1*0201 RISCHIO AUMENTATO
GENI NON-HLA

30% POPOLAZIONE GENERALE HLA DQ2 o DQ8
PREVALENZA 0.5-1% NEL MONDO

SOLO MINIMA PERCENTUALE SVILUPPERA' CELIACHIA
GEMELLI OMOZIGOTI CONCORDANZA NON 100%

FATTORI AMBIENTALI ADDIZIONALI TRIGGER SU RISPOSTA INNATA ED ADATTIVA

PATOGENESI E MANIFESTAZIONE MALATTIA

Akoberg A.K. Et al «Role of the gut microbiota in the pathogenesis of coeliac disease and potential therapeutic implications» European J Nutr 2020 59:3369-3390

PATOGENESI

CARDINI DELLA RISPOSTA AUTOIMMUNE

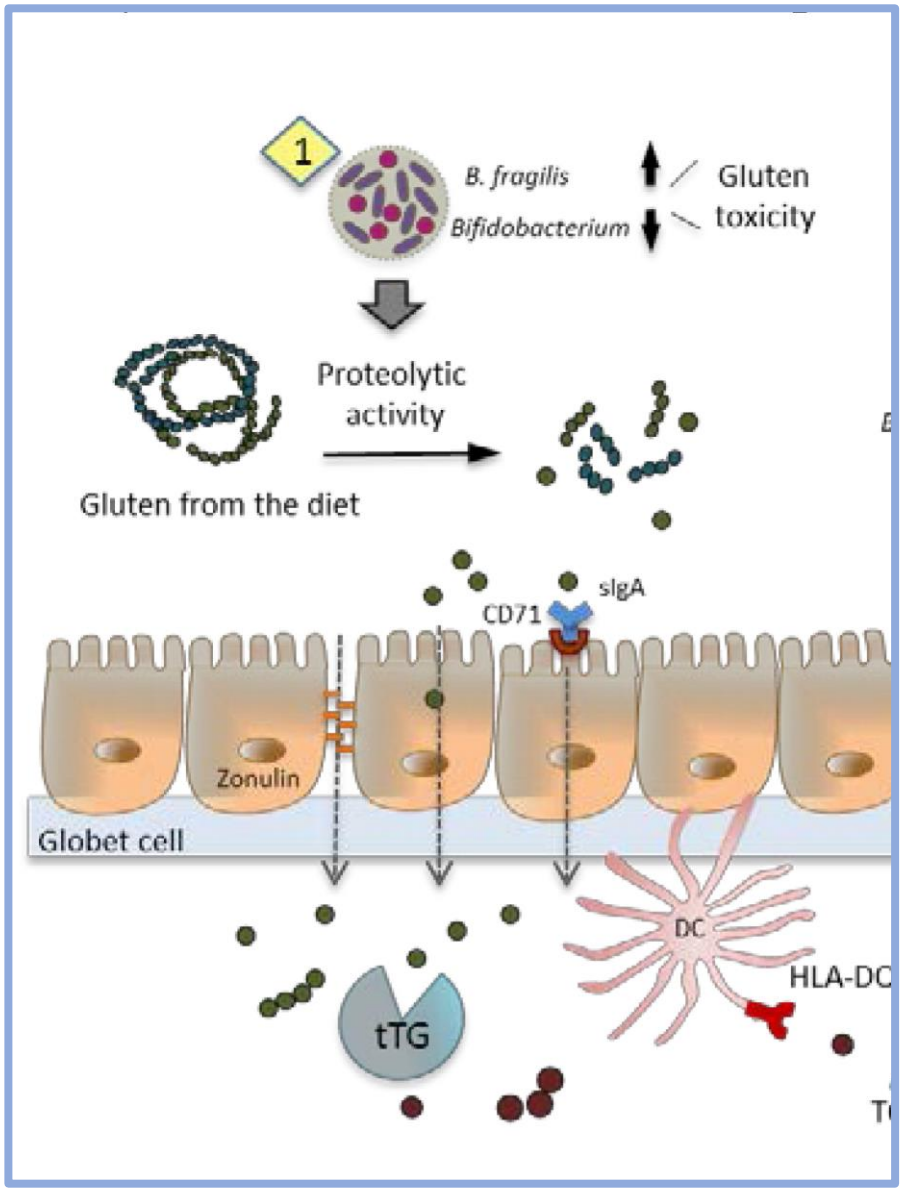
GENETICA

GLUTINE: gliadina

Le sequenze **ROSSE** esercitano effetto CITOTOSSICO.

La sequenza **VERDE** media, attraverso il recettore CXCR3, il rilascio della chemochina CXC **INTERLEUCHINA 8**, ad azione pro-infiammatoria

Le sequenze **BLU** favoriscono l'aumento del rilascio della proteina **ZONULINA** con conseguente aumento della permeabilità intestinale: ciò comporta una permeazione di sostanze tossiche e patogene (*leaky-gut*)



Caio G et al «Celiac disease: a comprehensive current review» BMC Medicine 2019

PATOGENESI

CARDINI DELLA RISPOSTA AUTOIMMUNE

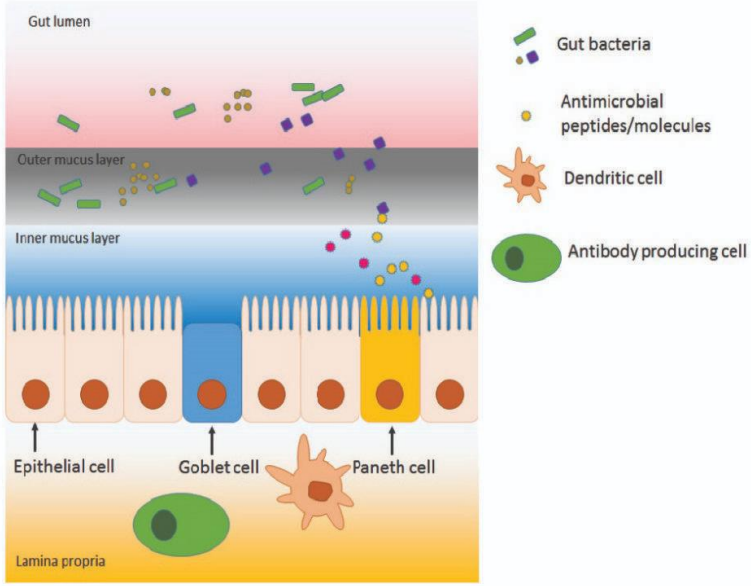
GENETICA
GLUTINE: gliadina
PERDITA FUNZIONE BARRIERA INTESTINALE

MUCUS COMPOSITION

Review

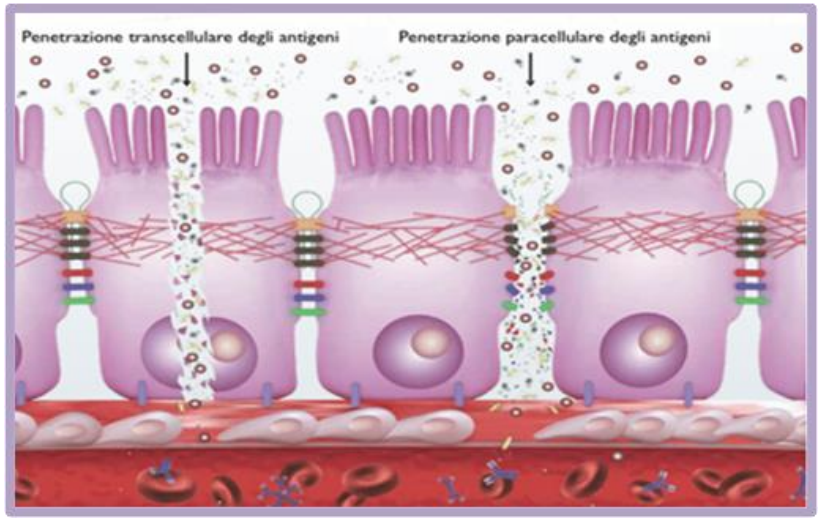
Intestinal Barrier Function in Gluten-Related Disorders

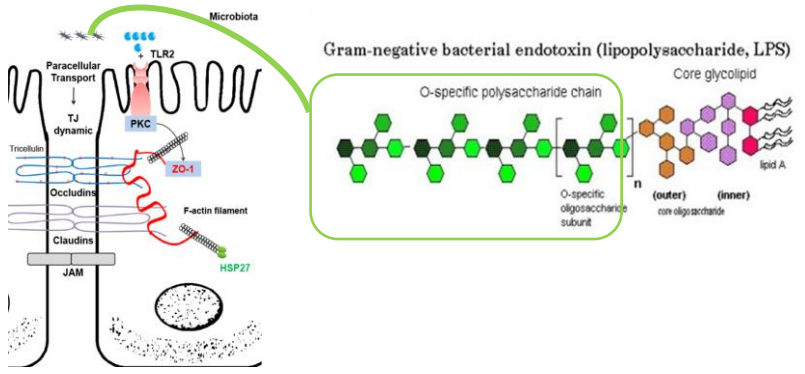
Danielle Cardoso-Silva [1,†], Deborah Delbue [1,†], Alice Itzlinger [1], Renée Moerker Sebo Withoff [2], Federica Branchi [1] and Michael Schumann [1,*]



Nutrients 2019; 11, 2325

EPITHELIAL BARRIER



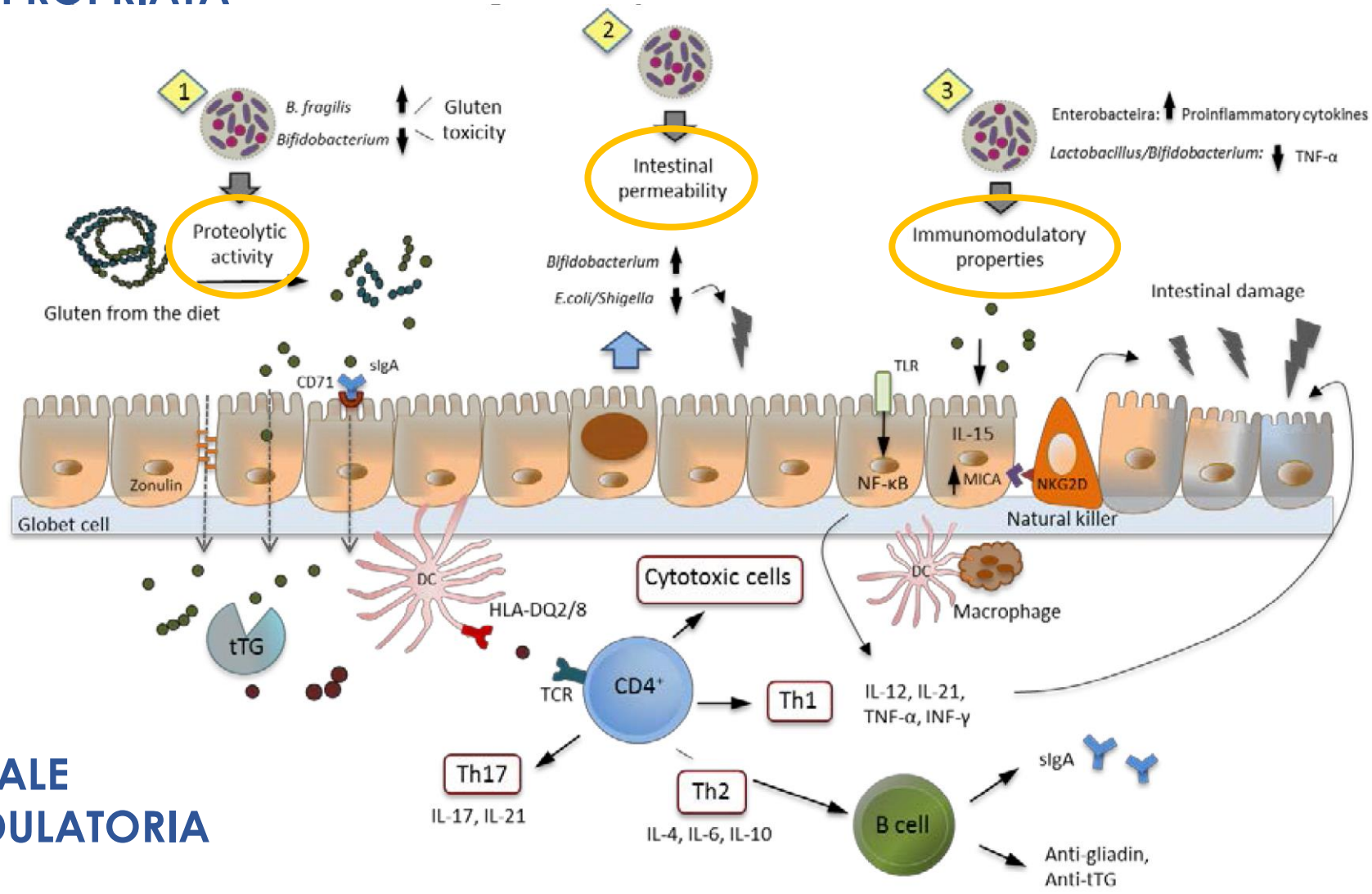


Caio G et al «Celiac disease: a comprehensive current review» BMC Medicine 2019

CARDINI DELLA RISPOSTA AUTOIMMUNE

RISPOSTA IMMUNITA' PRO-INFIAMMATORIA

RISPOSTA IMMUNITA' INAPPROPRIATA



MICROBIOTA INTESTINALE

- PROTEOLISI
- PERMEABILITA' INTESTINALE
- ATTIVITA' IMMUNOMODULATORIA

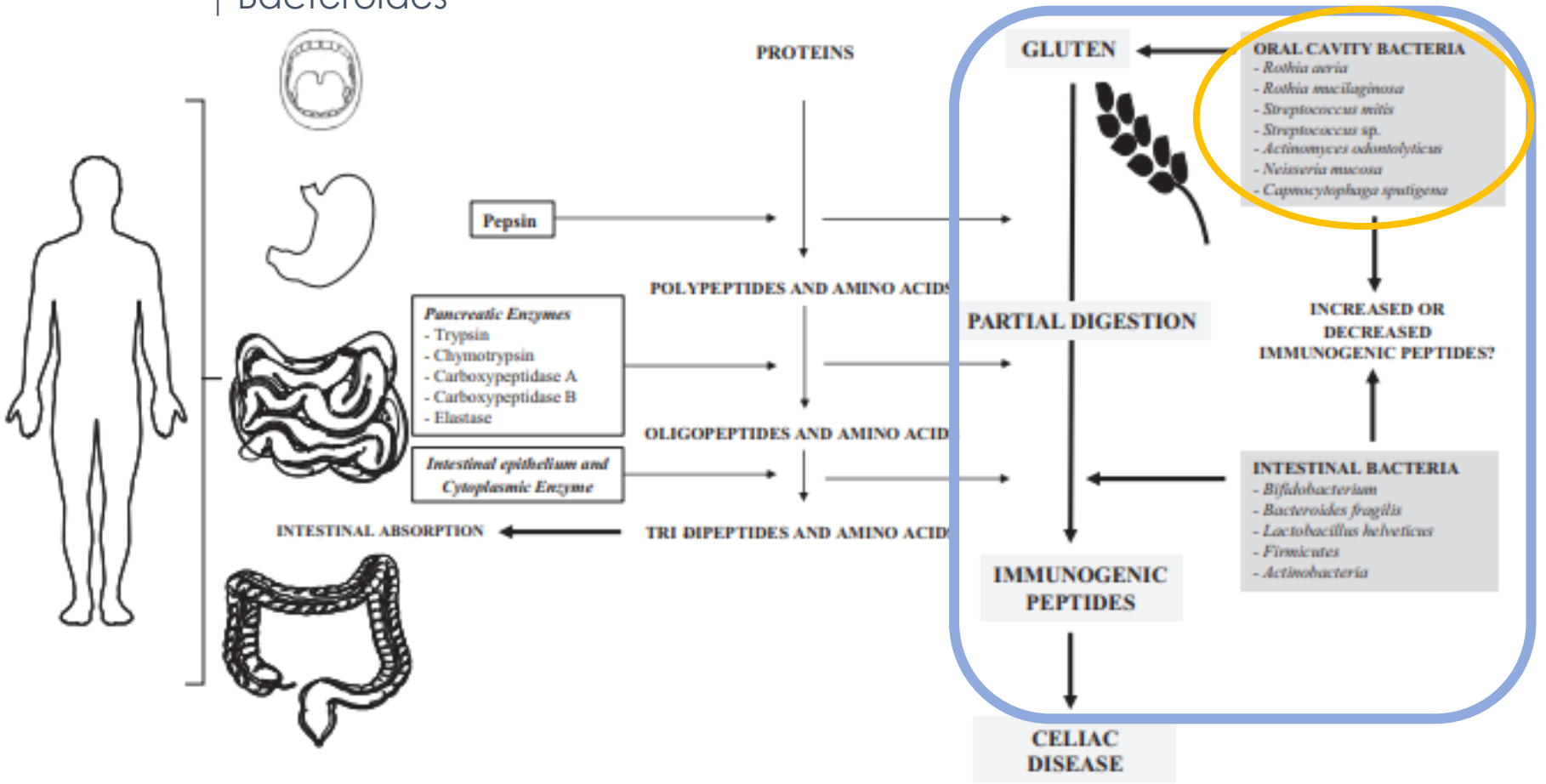
Akoberg A.K. Et al «Role of the gut microbiota in the pathogenesis of coeliac disease and potential therapeutic implications» European J Nutr 2020 59:3369-3390

MICROBIOTA ORALE

Vari batteri presenti in natura nella placca dentale umana HANNO MOSTRATO ATTIVITA' DI PEPTIDASI anche vs i domini immunogenici 33-mer e 26-mer

CELIACHIA ATTIVA – REFRATTARIA VS HC

↑ Lactobacillus spp
↑ Proteobacteria
↑ Bacteroides



AK Bascuñán "Dietary Gluten as a Conditioning Factor of the Gut Microbiota in Celiac Disease" Adv Nutr 2020;11:160–174.

CARATTERIZZARE MICROBIOTA CELIACHIA

18 STUDI

11	7	3
💩	💩	💩💩

ETEROGENEITA'
PROCEDURE e DISEGNO STUDIO

NON IDENTIFICABILE MICROBIOTA TIPICO DUODENALE o FECALE

↓ gram+/gram–
↑ BATTERI gram- e PATOGENI

↑ Bacteroides/Prevotella/E. Coli
Clostridium, Staphylococcus, Eubacterium rectal, C. coccoides, Atopobium
↓ Bifidobacterium, Lactobacillus

frontiers in Pediatrics

SYSTEMATIC REVIEW
published: 22 April 2021
doi: 10.3389/fped.2021.652208

Fecal and Duodenal Microbiota in Pediatric Celiac Disease

*Diyora Abdukhakimova[1], Kuanysh Dossybayeva[1] and Dimitri Poddighe[1,2]**

[1] Department of Medicine, Nazarbayev University School of Medicine (NUSOM), Nur-Sultan, Kazakhstan, [2] Department of Pediatrics, National Research Center for Maternal and Child Health, University Medical Center, Nur-Sultan, Kazakhstan

Background and Objective: The gut microbiota plays a role in regulating the host immunity. Therefore, alterations in gut microbiota (or dysbiosis) have been investigated in several gastrointestinal diseases, including Celiac Disease (CD). The aim of this study is to summarize the main characteristics of the gut microbiota in pediatric CD.

Methods: We performed a systematic review to retrieve the available studies investigating the gut microbiota in pediatric CD patients and controls. In detail, after the screening of >2,200 titles from the medical literature, 397 articles were assessed for eligibility based on the abstracts: of those, 114 full-text original articles were considered as eligible according to the aim of this systematic review.

Results: The final search output consisted of 18 articles describing the gut microbiota of CD children and including one or more control groups. Eleven pediatric studies provided information on the duodenal microbiota and as many investigated the fecal microbiota; three articles analyzed the microbiota on both fecal and duodenal samples from the same cohorts of patients.

Conclusion: Due to the heterogeneity of the experimental procedures and study design, it is not possible to evidence any specific celiac signature in the fecal and/or duodenal microbiota of CD children. However, some specific components of the fecal microbiota and, in detail, *Bifidobacterium* spp. (e.g., *Bifidobacterium longum*) may deserve additional research efforts, in order to understand their potential value as both probiotic therapy and diagnostic/prognostic biomarker.

CARATTERIZZARE MICROBIOTA CELIACHIA

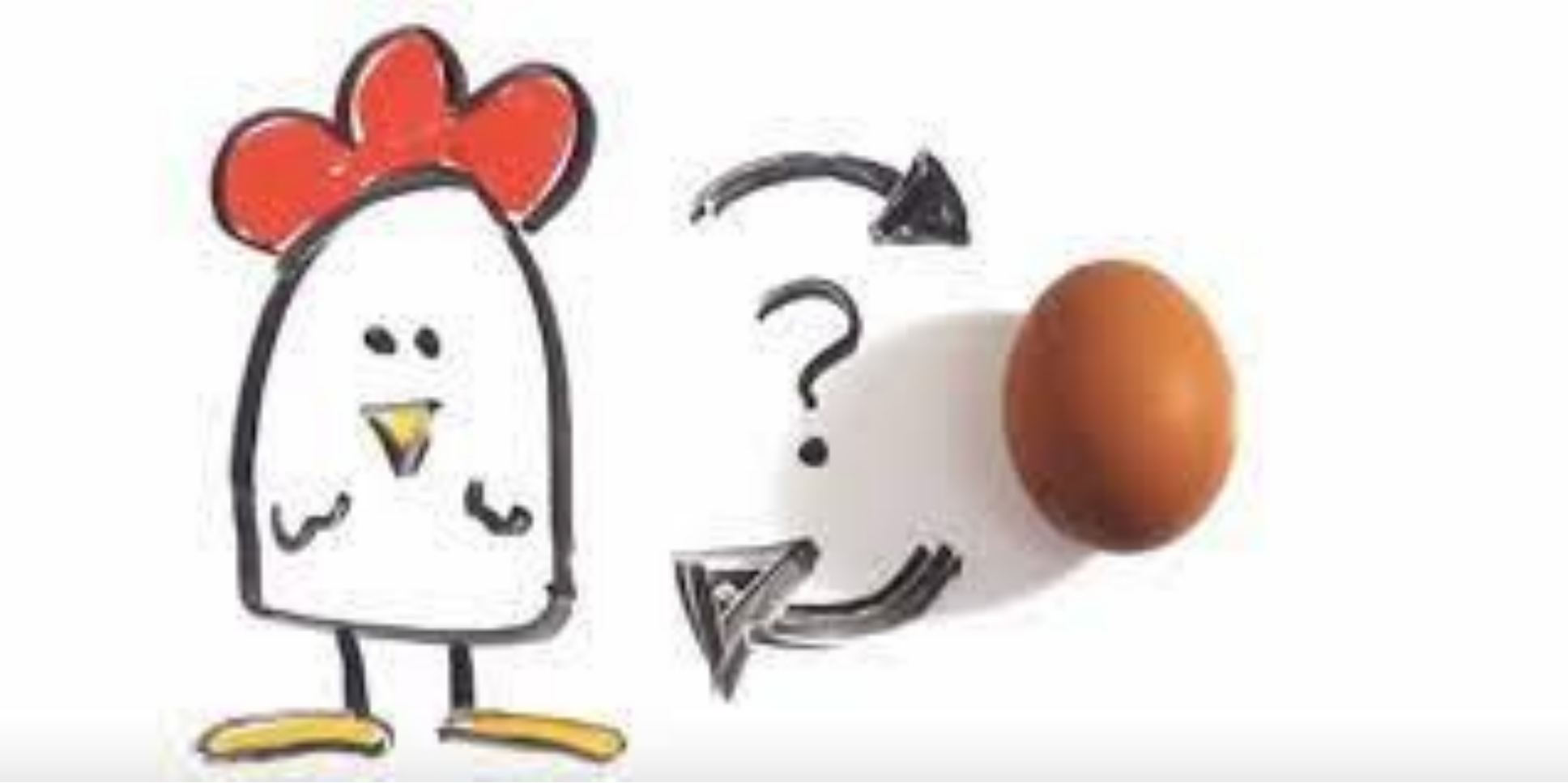
CORRISPONDENZA SIGNIFICATIVA DISBIOSI BIFIDOCENTRICA (MARKER)

Bifidobacterium longum correlava sempre nei 2 tipi di campioni e nei 3 gruppi

BIOMARKER DIAGNOSTICO?

POTENZIALE RISORSA TERAPEUTICA?

Abdukhakimova D et al «Fecal and duodenal microbiota in pediatric celiac disease»
Frontiers in Pediatr Apr 2021 Vol 9



INFLUENZA DEL GENOTIPO HLA-DQ SUL MICROBIOTA DEI LATTANTI A RISCHIO DI CELIACHIA

Studio prospettico su bambini HLA DQ2/DQ8 vs bambini non predisposti

SVILUPPO PRECOCE CELIACHIA

16% ENTRO I 3 AA

38% OMOZIGOSI DQ2 ENTRO I 5 AA

FATTORI AMBIENTALI PRECOCI!

APLOTIPO HLA A RISCHIO

ANALISI MICROBIOTA FECALE A 7 gg, 1 e 4 mesi

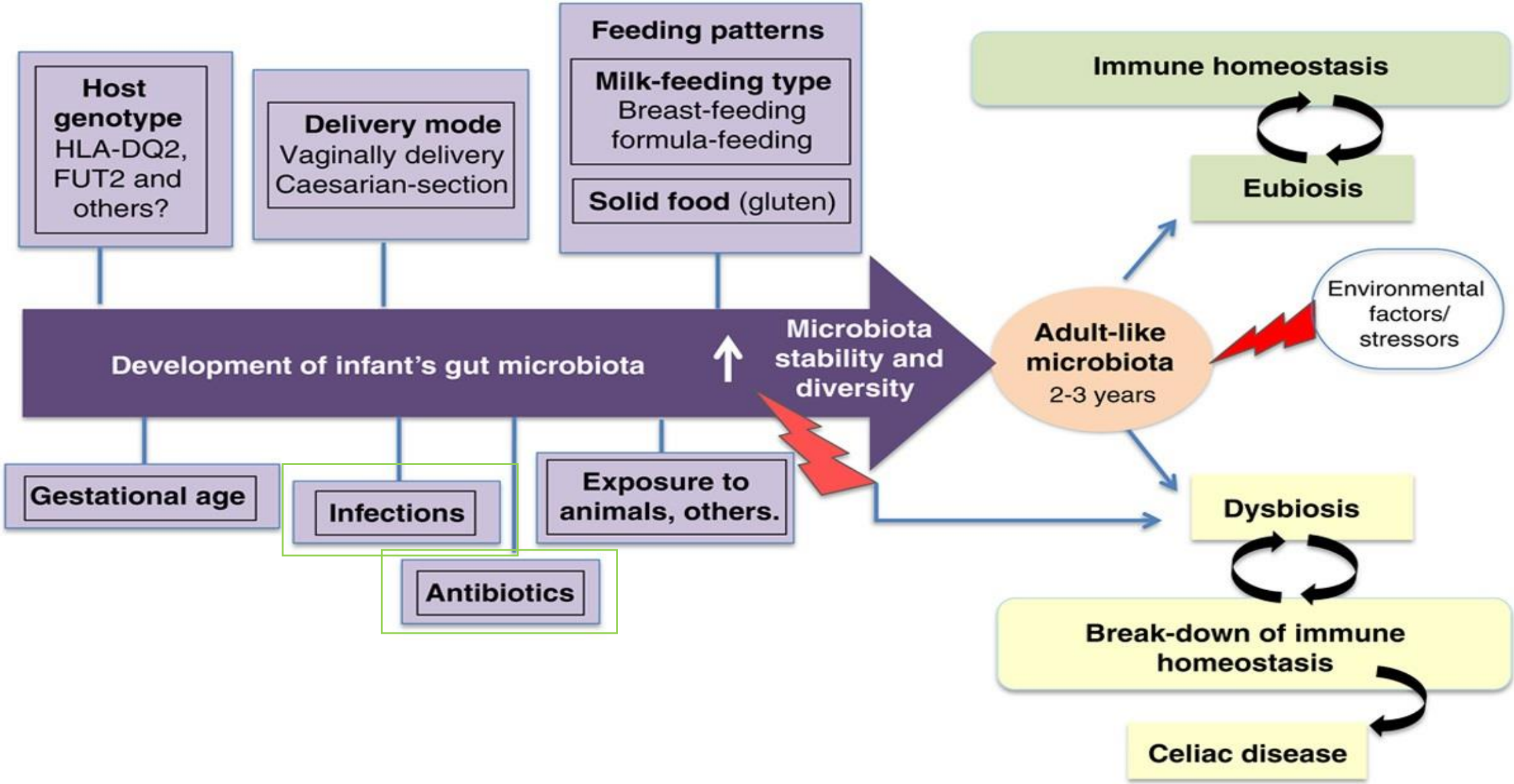
< Bifidobacterium e B. longum

> Staphylococcus spp, Bacteroides fragilis

Correlazione tra

> >Bifidobacteria 1-4 mesi e BASSO RISCHIO

>Staphylococcus spp, Bacteroides fragilis 1-4 mesi e ALTO RISCHIO


Host genotype HLA-DQ2, FUT2 and others?
Delivery mode Vaginally delivery Caesarian-section
Feeding patterns
Milk-feeding type Breast-feeding formula-feeding
Solid food (gluten)
Development of infant's gut microbiota
Microbiota stability and diversity
Gestational age
Infections
Antibiotics
Exposure to animals, others.
Adult-like microbiota 2-3 years
Immune homeostasis
Eubiosis
Environmental factors/ stressors
Dysbiosis
Break-down of immune homeostasis
Celiac disease

INFEZIONI

INFECTIONS, as well as the overgrowth of opportunistic pathogens, may initiate or contribute to the pathological process by increasing the production of inflammatory mediators (TNFa e IFN-γ)

Rotavirus nel bambino e Campylobacter nell'adulto (alterata permeabilità intestinale che favorirebbe il passaggio dei peptidi immunogenici del glutine attraverso la barriera intestinale)

Metagenomics of the faecal virome indicate a cumulative effect of enterovirus and gluten amount on the risk of coeliac disease autoimmunity in genetically at risk children: the TEDDY study

Katri Lindfors ,[1] Jake Lin,[1,2] Hye-Seung Lee,[3] Heikki Hyöty,[1] Matti Nykter,[1] Kalle Kurppa ,[1,4,5] Edwin Liu,[6,7] Sibylle Koletzk William Hagopian,[11] Jorma Toppari,[12,13] Annette- Beena Akolkar,[17] Jeffrey P Krischer,[3] Joseph F Petr Daniel Agardh ,[19] the TEDDY Study Group

Frequent exposure to enterovirus between 1 and 2 years of age was associated with increased risk of CDA.

The increased risk conferred by the **interaction** between enteroviruses and higher gluten intake indicate a **cumulative effect of these factors** in the development of CDA.

Gut 2019

ANTIBIOTICI

MODULARE COMPOSIZIONE e FUNZIONALITA' MICROBIOTA INTESTINALE
INFLUENZARE LO SVILUPPO DI PATOLOGIE CRONICHE

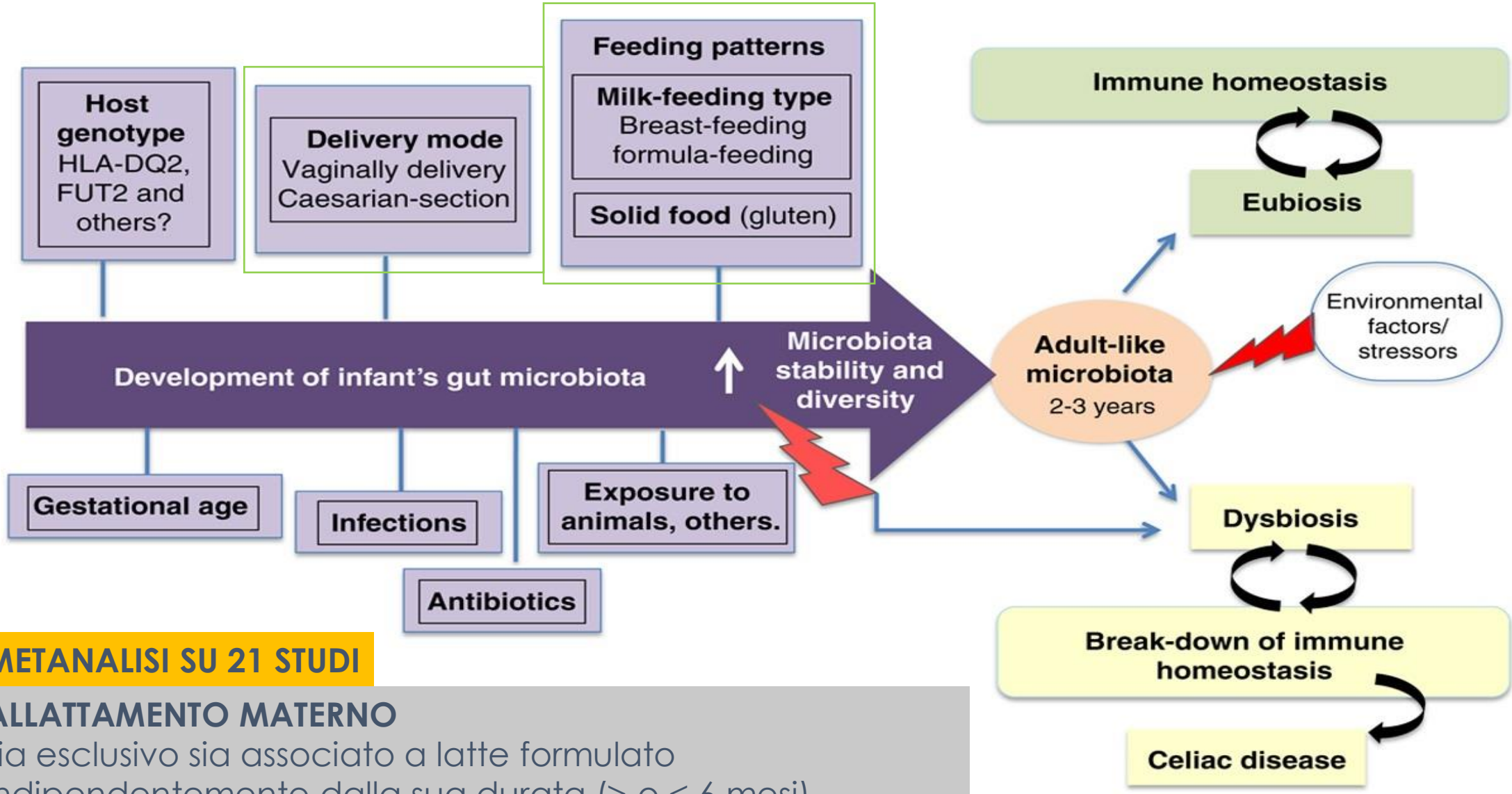
Studio di coorte su registro Naz. Danimarca e Norvegia **1,7 milioni bambini** **3346 CELIACHIA**	**SOMMINISTRAZIONE ANTIBIOTICI NEL PRIMO ANNO ASSOCIATA A DIAGNOSI SUCCESSIVA DI CELIACHIA** **ASSOCIAZIONE DOSE-DIPENDENTE** **ASSOCIAZIONE NUMERO DI CICLI-DIPENDENTE**

DATI CONFERMATI IN STUDI SU POPOLAZIONI SVEDESE, ITALIANA E NORD AMERICA

DISBIOSI INDOTTA DA ANTIBIOTICI

<< Bifidobacterium longum
>> Bacteroides fragilis

Dydensborg Sander S, et al «Association Between Antibiotics in the First Year of Life and Celiac Disease»
Gastroenterology 2019;156(8):2217–2229



METANALISI SU 21 STUDI

ALLATTAMENTO MATERNO

sia esclusivo sia associato a latte formulato
indipendentemente dalla sua durata (> o < 6 mesi)
non riduce il rischio di celiachia

Szajewska H et al «Gluten Introduction and the Risk of Coeliac Didease A position paper by ESPGHAN J Ped Gastroenterol Nutr 2016; 62 (3): 507-513

MADRI CELIACHE

MADRI non celiache

CAMPIONI LATTE
CITOCHINE
IGA SECRETORIE
HMO
MICROBIOTA

RIDOTTO NUMERO DI COPIE GENI
Bifidobacterium spp (P<0,026)

RIDOTTA COMPONENTE IMMUNOPROTETTIVA
TGF-β1, IgA, IFN-ϒ

MINORE EFFETTO PROTETTIVO??

Olivares M et al «Human milk composition differs in healthy mothers and mothers with celiac disease» Eur J Nutr 2015; Vol 54: 119-128

Complementary Feeding: A Position Paper by the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) Committee on Nutrition

*Mary Fewtrell, †Jiri Bronsky, ‡Cristina Campoy, §Magnus Domellöf, ||Nicholas Embleton, ¶Nataša Fidler Mis, #Iva Hojsak, **Jessie M. Hulst, ††Flavia Indrio, ‡‡§§Alexandre Lapillonne, and ||||¶¶Christian Molgaard

Celiac Disease

Celiac disease (CD) is a disorder in which consumption of gluten in a genetically susceptible individual results in an autoimmune reaction affecting the gut and other organs. It affects approximately 1% to 3% of the general population in most parts of the world, except for populations such as in Southeast Asia in which the human leukocyte antigen risk alleles (human leukocyte antigen-DQ2 and/or DQ8) are rare. There has been considerable discussion on whether infant feeding practices—notably the age at introduction of gluten and breast-feeding—can prevent the occurrence, exclude, late (, whil, only, aller, age (munity or CD during childhood in children at genetic risk for CD. Evidence from these RCTs showed that the age of gluten introduction into the infant's diet affected the incidence of each during the first 2 years, but not the cumulative incidence and prevalence of CD during childhood, thus indicating that primary prevention of CD through varying the timing of introduction of gluten is not possible at the present time (53,54). A systematic review that evaluated evidence from prospective observational studies published up to February 2015 also concluded that breast-feeding, any or at the time of gluten introduction, had no preventive effect on the development of C, and t, publi, feedi, show, the ir, on o amount of gluten intake and risk of CD, consumption of large quantities of gluten should be avoided during the first weeks after gluten introduction and during infancy. The optimal amounts of gluten to be introduced at weaning have, however, not been established. Although the risk of inducing CD through a gluten-containing diet exclusively applies to persons carrying at least one of the CD risk alleles, since genetic risk alleles are generally not known in an infant at the time of solid food introduction, the recommendations apply to all infants.

Nei soggetti a rischio **RITARDARE** l'introduzione del glutine nella alimentazione non previene ma ritarda l'esordio

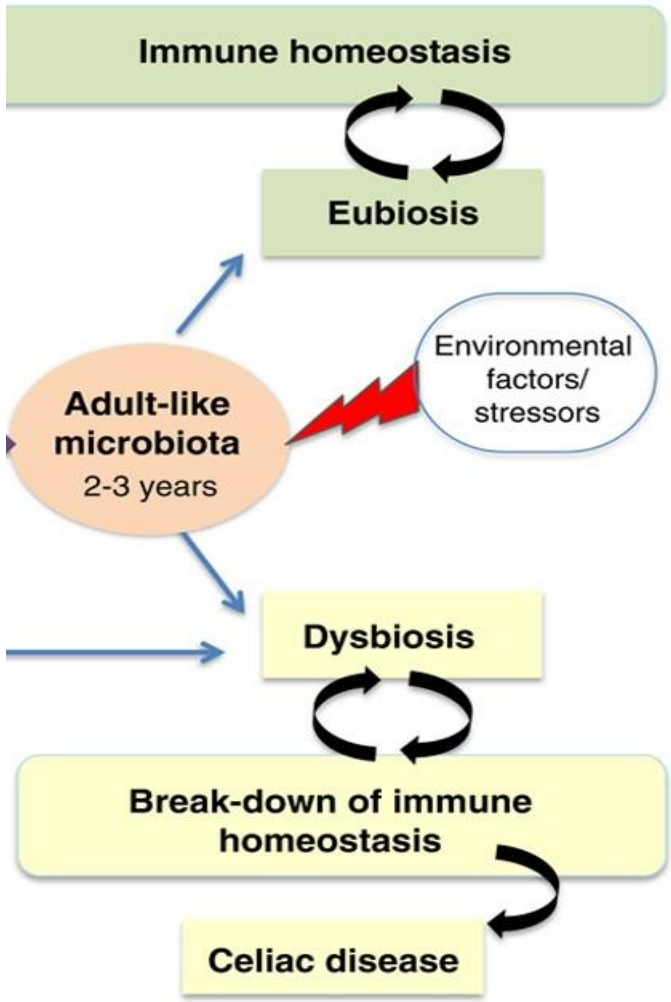
Trial CELIPREV (N Engl J Med 2014)
Randomizzato – multicentrico – prospettico 0-10 aa
Glutine 6 vs 12 mesi

Una introduzione **PRECOCE** non induce tolleranza, può però anticipare l'insorgenza dei sintomi e aumentarne la gravità

Trial PREVENT-CD (N Engl J Med 2014)
Randomizzato – multicentrico – prospettico 0-10 aa
Glutine microdosi 4-6 mesi per indurre tolleranza

INTRODUZIONE 4-7 MESI

Si scoraggia l'assunzione di grosse quantità di glutine nei primi mesi dopo la sua introduzione (quantità non precisata)

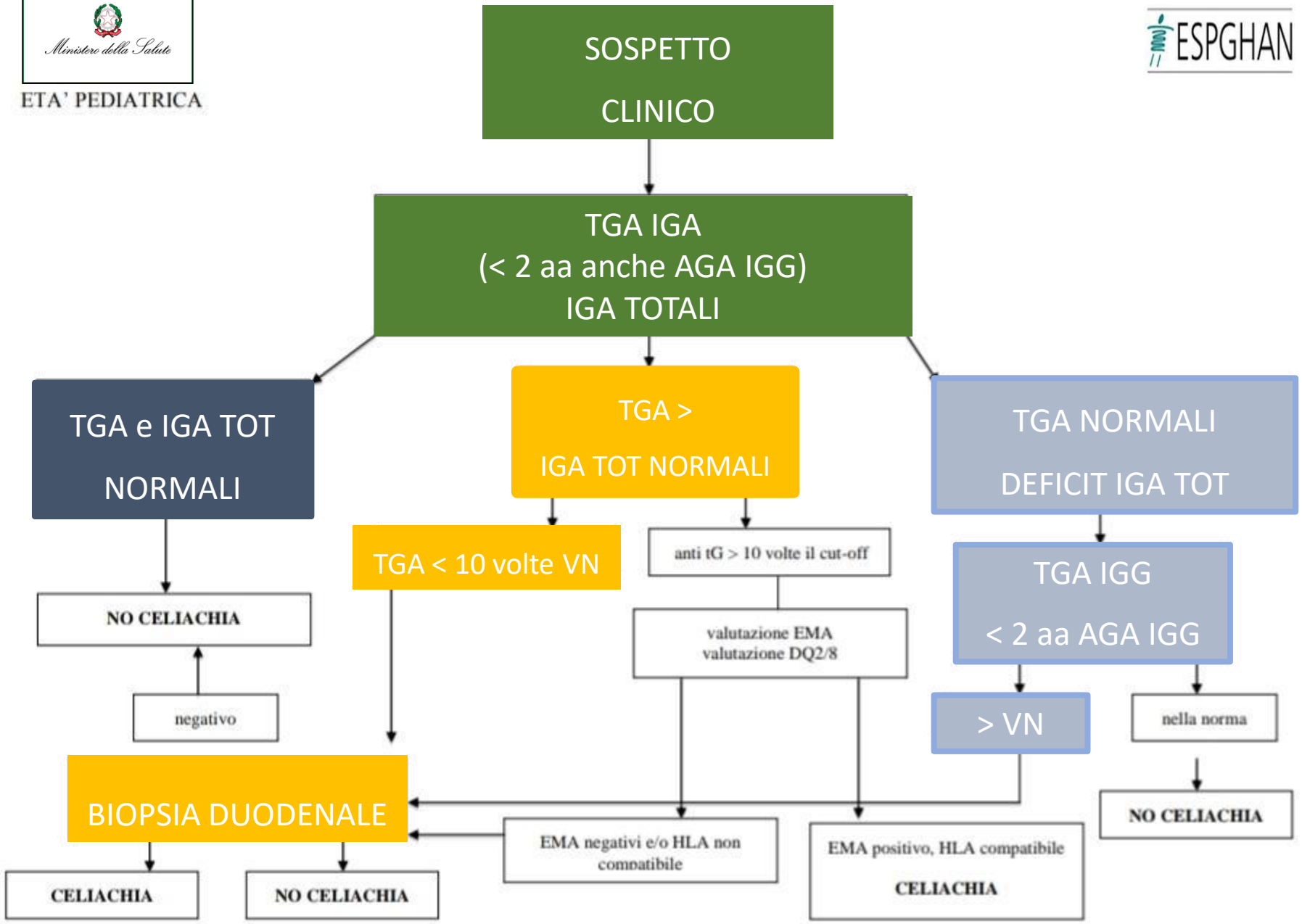


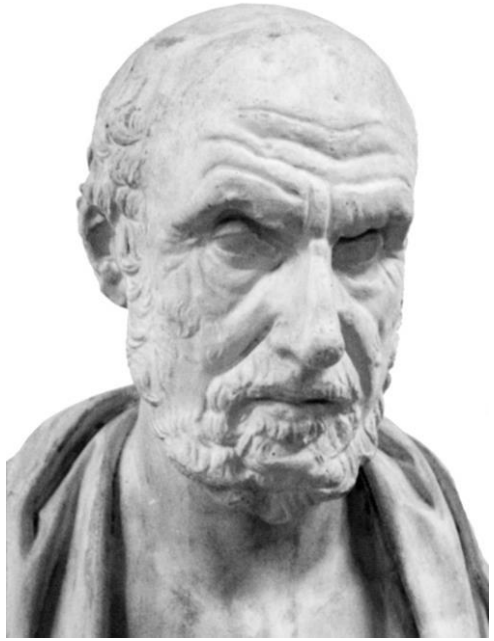
THE ENVIRONMENTAL-DEPENDENT DYSBIOSIS HYPOTHESIS

Ministero della Salute

ETA' PEDIATRICA

ESPGHAN





DIETA GLUTEN-FREE = UNICA TERAPIA EFFICACE

INTERVENTI DIETETICI →

VITAMINE, ORMONI,
ALTRI MACRONUTRIENTI

MODULAZIONE MICROBIOTA INTESTINALE
EFFETTI SPECIFICI

Bifidobacterium
Lactobacillus
Bacteroides
Clostridium
Eubacterium
Enterococcus
E.coli
Streptococcus

LIMITI DELLA DIETA SENZA GLUTINE

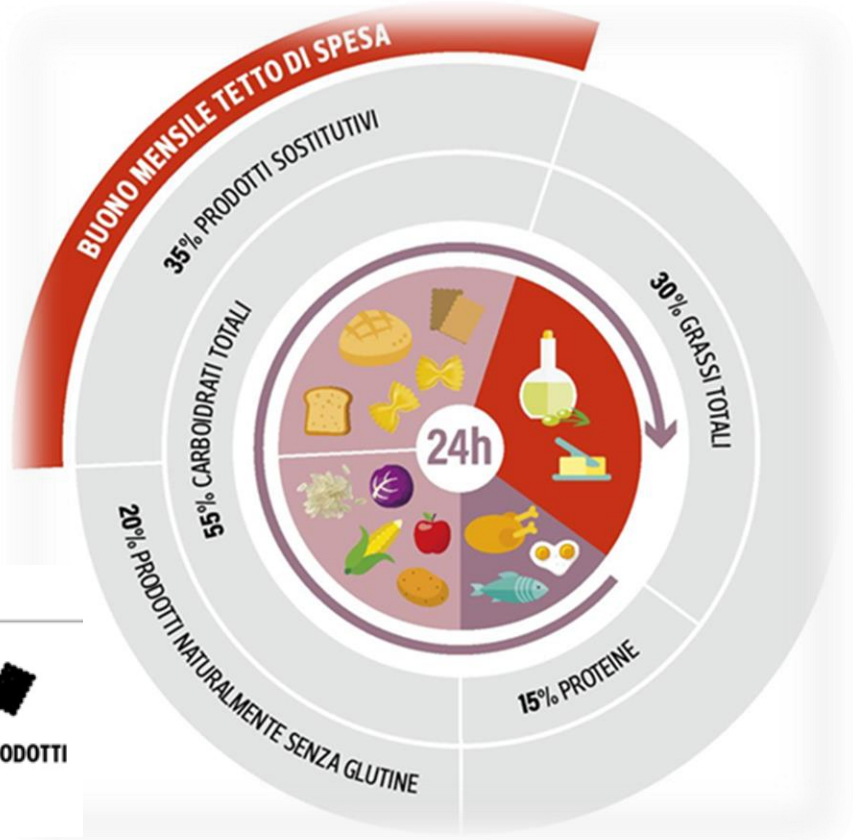
PROBLEMATICHE SOCIALI

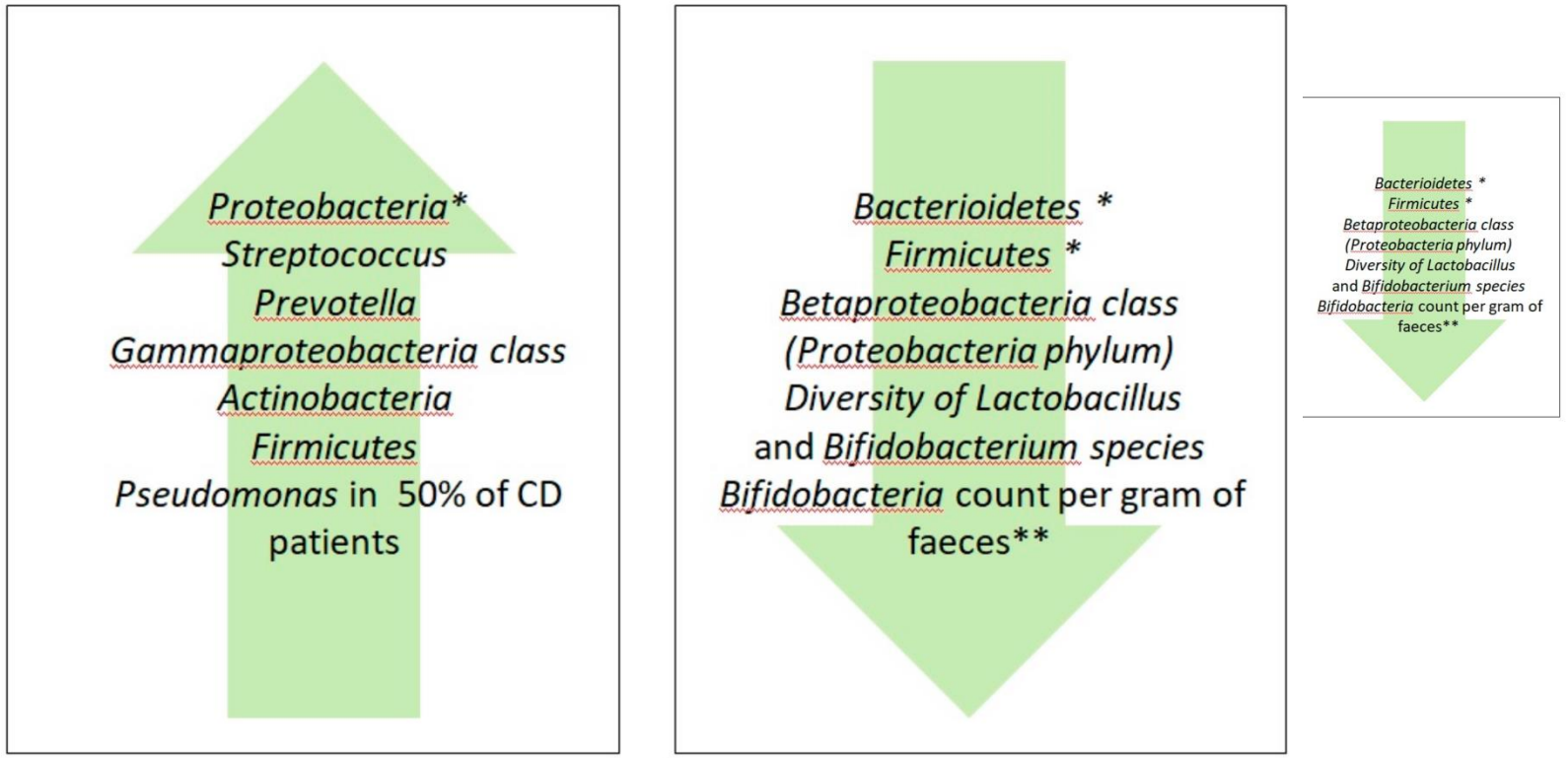
….l'aderenza alla dieta varia dal 40% al 90%... con recente trend in miglioramento
Hall et al, APT 2009 – Bulsa M et al, Nutrients 2018

PROBLEMATICHE FAMILIARI

PALATABILITA'

COSTI ELEVATI





Effects of gluten-free diet (GFD) on the abundance of bacterial populations in Celiac disease (CD) patients.

* CD patients with persisting gastrointestinal symptoms;
** CD patients with no active disease.

Caio G et al "Effect of Gluten-Free Diet on Gut Microbiota Composition in Patients with Celiac Disease and Non-Celiac Gluten/Wheat Sensitivity" *Nutrients* 2020, 12(6), 1832

Marciniak M et al «Multidimensional disadvantages of a gluten-free diet in celiac disease: a narrative review»

SINTOMI GI celiaci non trattati > celiaci trattati > controlli sani

(Questionario PedsQL-GS VALUTAZIONE SINTOMI GI)

Celiaci trattatati: SINTOMI MIGLIORANO DOPO 12 MESI !

NONOSTANTE LA DGF RIGOROSA

UNA PARTE DI PAZIENTI PRESENTA SINTOMI PERSISTENTI

Zafeiropoulou K et al «Alterations in intestinal microbiota of children with celiac disease at the time of diagnosis and on a gluten-free diet» Gastroenterolk 2020;159:2039-2051

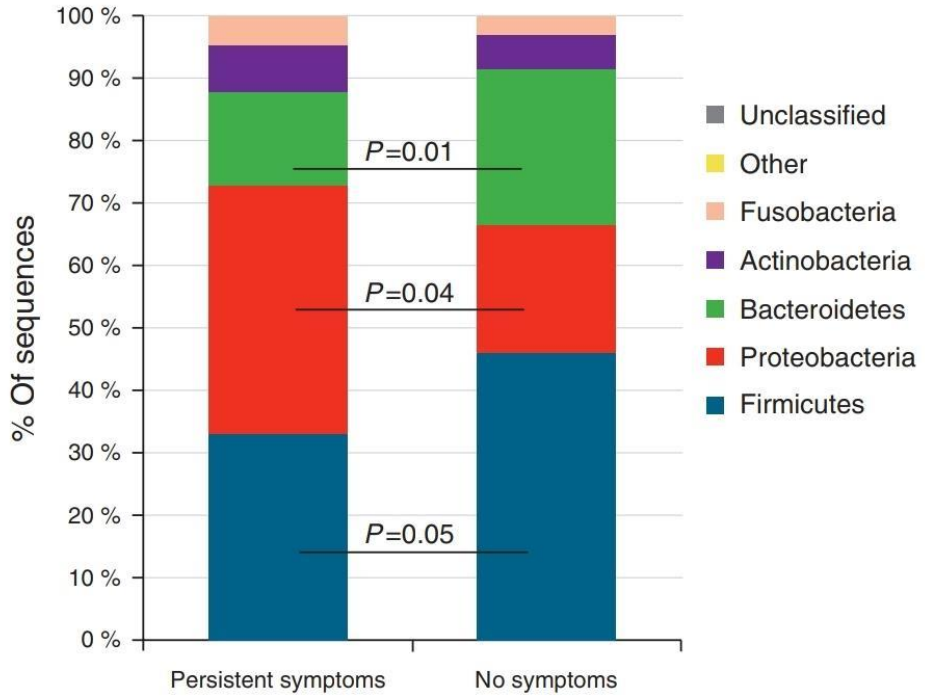
Akoberg A.K. Et al «Role of the gut microbiota in the pathogenesis of coeliac disease and potential therapeutic implications» European J Nutr 2020 59:3369-3390

Altered Duodenal Microbiota Composition in Celiac Disease Patients Suffering From Persistent Symptoms on a Long-Term Gluten-Free Diet

Pirjo Wacklin, PhD[1], Pilvi Laurikka[2], Katri Lindfors, PhD[3], Pekka Collin, MD[2,4], Teea Salmi, MD[2,5], Marja-Leena Lähdeaho, MD[3], Päivi Saavalainen, PhD[6], Markku Mäki, MD[3], Jaana Mättö, PhD[1], Kalle Kurppa, MD[3] and Katri Kaukinen, MD[2,7]

DISBIOSI INTESTINALE anche quando aderiscono correttamente alla **GFD**

Microbiota in Treated Celiacs With Persisting Symptoms



CELIACI REFRATTARI

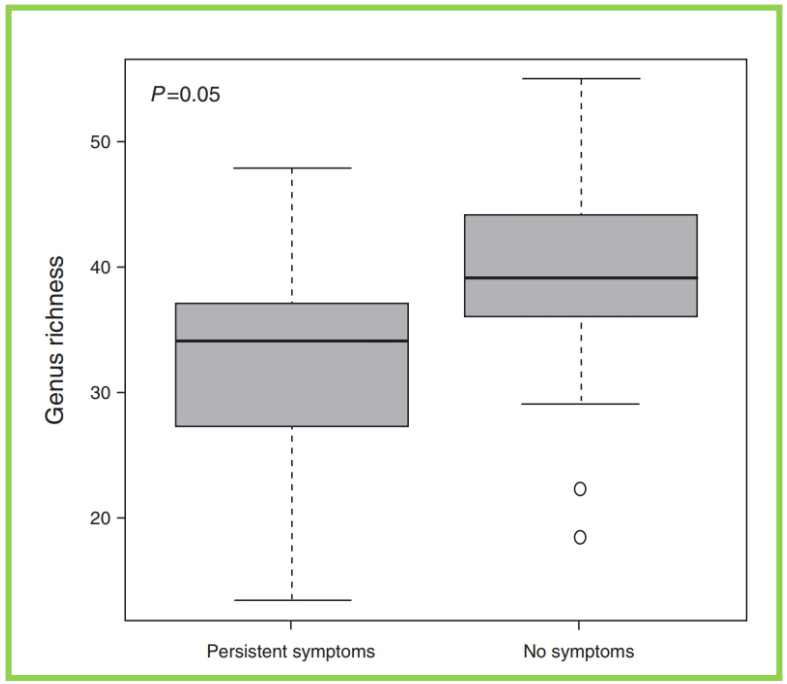
>>*Protebacteria* (p=0,04)

<<***Bacteroidetes*** (p=0,01)

<<***Firmicutes*** (p=0,05)

<<a-biodiversità

MICROBIOTA INFLUENZA RISPOSTA CLINICA ALLA DIETA



Wacklin P et al. - Am J Gastroenterol. 2014;109:1933–1941

Effects of a gluten-free diet on gut microbiota and immune function in healthy adult human subjects

Article in The British journal of nutrition · June 2009

Table 3. Composition of the faecal microbiota of healthy adults before and after following a gluten-free diet (GFD) analysed by qPCR.

Microbial group	Adults under standard diet (n=10)			Adults under GFD diet (n=10)			Mann-Whitney U-test *P-value
	Pr	†Median	IQR	Pr	†Median	IQR	
Bifidobacterium	10	8.85	7.84-9.24	10	7.79	7.43-8.45	0.020*
Bacteroides	10	8.61	8.03-9.20	10	8.21	7.25-9.21	0.450
C.coccoides	10	9.44	8.51-10.11	10	9.52	8.73-9.92	0.983
C. leptum	10	9.54	9.18-10.31	10	10.11	9.81-10.52	0.141
C. histolyticum	10	5.70	5.17-6.34	10	6.48	5.13-6.59	0.223
Lactobacillus	10	7.73	7.10-7.98	10	7.00	6.25-7.64	0.001*
E. coli	10	6.29	5.67-6.77	10	7.40	6.83-7.96	0.003*
Enterobacteriaceae	10	6.64	5.86-7.99	10	8.16	7.41-8.42	0.005*
***Bifidobacterium* species**							
B. longum	10	7.73	7.61-8.62	10	7.32	6.54-7.79	0.017*
B. breve	8	4.72	4.47-5.94	8	5.00	4.60-5.56	0.757
B. bifidum	10	6.75	6.73-6.76	10	6.75	6.75-6.85	0.208
B. adolescentis	7	5.71	4.83-8.65	8	6.73	5.39-7.80	0.975
B. catenulatum	10	6.81	6.05-8.44	10	6.66	5.88-8.13	0.538
B. angulatum	5	5.00	4.95-5.24	5	5.35	5.06-5.42	0.038*
B. lactis	6	5.82	5.21-6.58	5	4.89	4.62-5.63	0.201

†Data are shown as medians and interquartile range (IQR) of log of cell number per gram of faeces.

< *Faecalibacterium prausnitzii*
< *Bifidobacterium* spp

> *Escherichia coli*

GFD porta a riduzione delle popolazioni di batteri intestinali benefici e della capacità dei campioni fecali di stimolare il sistema immunitario dell'ospite.

….E INOLTRE…

NON ANNULLA INFILTRATO LINFOCITARIO

Persistent Intraepithelial Lymphocytosis in Celiac Patients Adhering to Gluten-Free Diet Is Not Abolished Despite a Gluten Contamination Elimination Diet.

Zanini B et al.

The gluten-free diet (GFD) is the only validated treatment for celiac disease (CD), but despite strict adherence, complete mucosal recovery is rarely obtained. The aim of our study was to assess whether complete restitutio ad integrum could be achieved by adopting a restrictive diet (Gluten Contamination Elimination Diet, GCED) or may depend on time of exposure to GFD. Two cohorts of CD patients, with persisting Marsh II/Grade A lesion at duodenal biopsy after 12-18 months of GFD (early control) were identified. Patients in Cohort A were re-biopsied after a three-month GCED (GCED control) and patients in Cohort B were re-biopsied after a minimum of two years on a standard GFD subsequent to early control (late control). Ten patients in Cohort A and 19 in Cohort B completed the study protocol. There was no change in the classification of duodenal biopsies in both cohorts. The number of intraepithelial lymphocytes, TCRγδ+ (T-Cell Receptor gamma delta) T cell and eosinophils significantly decreased at GCED control (Cohort A) and at late control (Cohort B), compared to early control. **Duodenal intraepithelial lymphocytosis persisting in CD patients during GFD is not eliminated by a GCED and is independent of the length of GFD.**

Nutrients. 2016 Aug 26;8(9). pii: E525.

Houston abbiamo **1** problema!!

Apollo 13

The use of microorganism to treat or prevant targeted diseases was conceived at the end of the last millenniumium.

New branch of applied microbiology:

«THERAPEUTIC MICROBIOLOGY»

Bozzi Cionci N et al
"Review: Therapeutic microbiology: the role of B. breve as food supplement for the prevention/treatment of paediatric diseases" Nutrients 2018, 10, 1723

Chi siete?

Quanti siete?

Cosa portate?

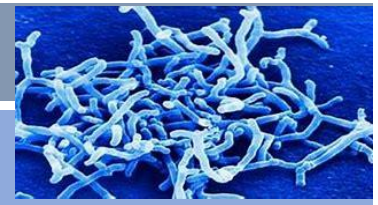
I probiotici sono microrganismi vivi che forniscono un impatto benefico per la salute sull'ospite se somministrati in quantità adeguate

SPECIFICITÀ CEPPO-CORRELATA

PER TERAPIA DI PRECISIONE

STUDI PRECLINICI
e SU CAVIE

BIFIDOBACTERIUM



SOPPRIMONO LE CITOCHINE PRO-INFIAMMATORIE INDOTTE IN VITRO DA FECI DI PZ CELIACI

RUOLO IMMUNOREGOLATORE BASSA PRODUZIONE CITOCHINE Th1 correlate
FENOTIPO T REGOLATORE (basato su induzione di > livelli di IL-10)

COMPORTAMENTO CEPPO-DIPENDENTE

B. longum CEC 7347

↓ citochine proinfiammatorie come TNFa
conseguente ridotto danno mucosa epiteliale

↓ produzione IFN da cell dendritiche derivate da monociti con stimolazione di gliadina
↑ rilascio IL-10

degrada peptidi di glutine riducendone la immunogenicità

B. infantis

↓ cell Paneth

LACTOBACILLUS

L. Casei

↓ citochine proinfiammatorie come TNFa
conseguente ridotto danno mucosa epiteliale

Lactobacillus

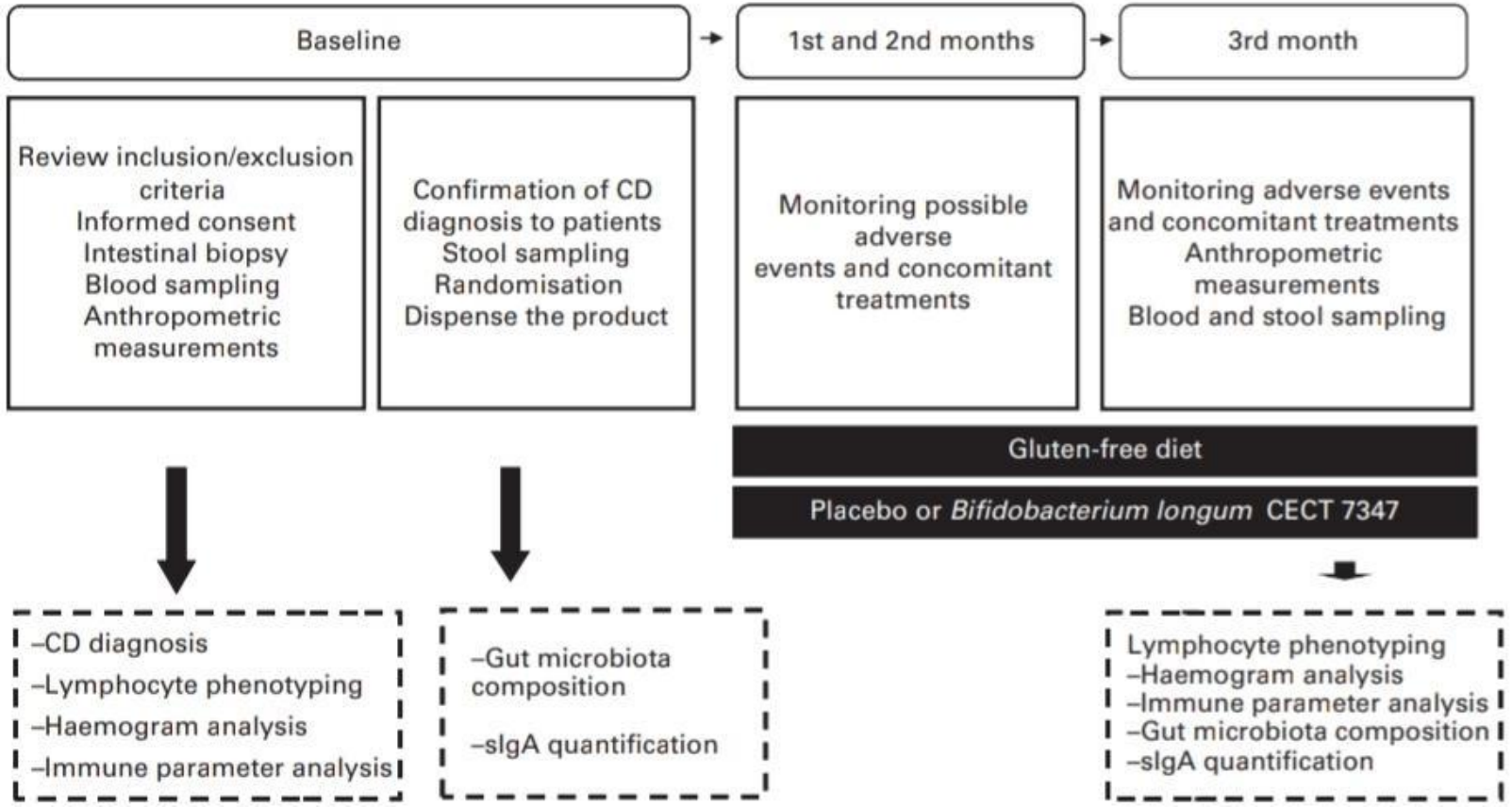
degrada peptidi di glutine riducendone la immunogenicità

Olshan KL et al «microbiota in celiac disease: microbes, metabolites, pathways and therapeutics»
Expert Rev Clin Immunol 2020

Double-blind, randomised, placebo-controlled intervention trial to evaluate the effects of *Bifidobacterium longum* CECT 7347 in children with newly diagnosed coeliac disease

British Journal of Nutrition (2014), **112**, 30–40
© The Authors 2014
Marta Olivares[1], Gemma Castillejo[2], Vicente Varea[3] and Yolanda Sanz[1]*

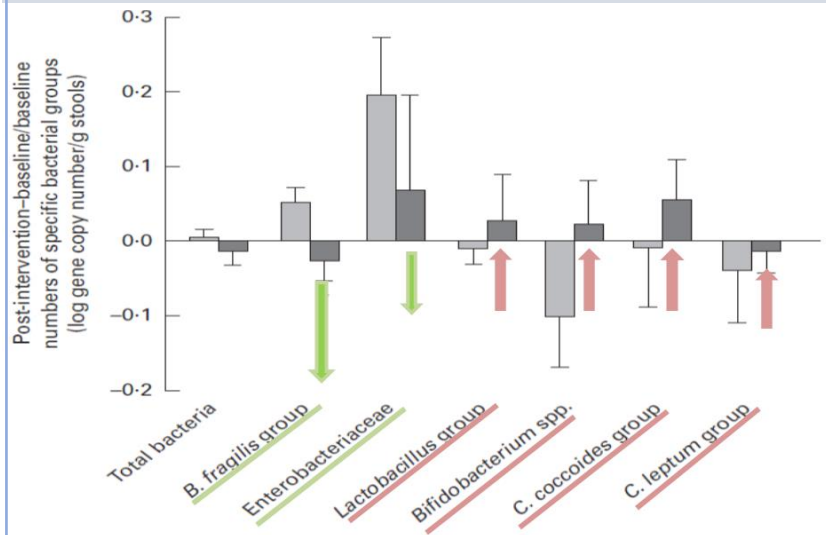
Studio clinico in doppio cieco, randomizzato, contro placebo per valutare gli effetti del *Bifidobacterium longum* CECT7347 (ES1) in bambini con malattia celiaca di recente diagnosi



↓ IgA SECRETORIE NELLE FECI

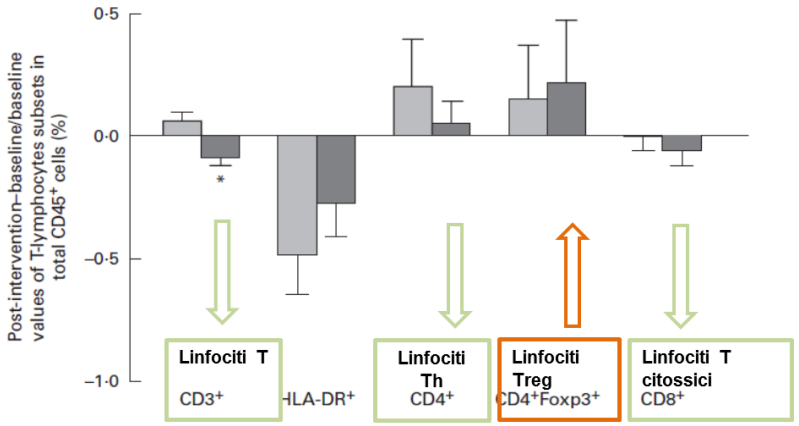
AZIONE NORMALIZZANTE DISBIOSI INTESTINALE

↓ PATOGENI OPPORTUNISTI MICROBIOTA



AZIONE NORMALIZZANTE ESPRESSIONE LINFOCITARIA

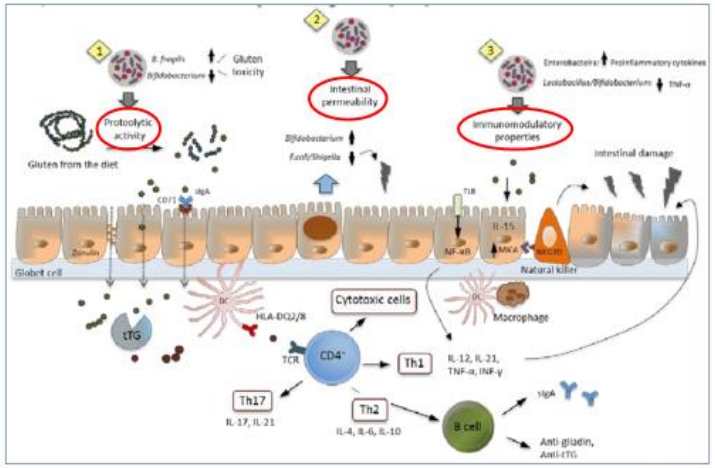
CAMBIAMENTI dei SUBSETS DI CD 45+



NONDIETARY THERAPIES FOR CELIAC DISEASE

2018

Potenziali meccanismi d'azione dei componenti del microbiota intestinale nella CELIACHIA.



Cenit MC, Sanz Y et al
« Intestinal microbiota and celiac disease: cause, consequence or co-evolution?» Nutrients 2015; 7:6900-6923
«Gut Microbiota and Risk of Developing Celiac Disease» J Clin Gastroenterol Dec 2016; 50:S148-S1252

Bifidobacterium longum ES1

TARGET

PEPTIDI GLIADINA

PERMEABILITÀ MEMBRANA

MODULAZIONE RISPOSTA IMMUNITARIA

EZIOLOGIA MULTIFATTORIALE CELIACHIA

MICROBIOTA RUOLO FONDAMENTALE

AUMENTO PATOGENI – RIDUZIONE SIMBIONTICI E/O COMMENSALI

RUOLO INFEZIONI – ANTIBIOTICI - DIETA

CARATTERIZZAZIONE MICROBIOTA CELIACHIA

DIETA GLUTEN-FREE NON RESTITUISCE EUBIOSI

TERAPIA ADD-ON CON PROBIOTICO SPECIFICO E DIETA ADEGUATA

PREVENZIONE: MICROBIOTA-CARE ?

Beati quelli di
Houston
che hanno solo
un problema.
LE PERLE DI
SNOOPY

Grazie!