MONDAY, DECEMBER 2, 2019 (08:30 - 20:00)

Healthy Life And Longevity

Centenarians In Italy And Israeli Lifestyle, Nutrition, Clinical, and Genetics

The impact of Nutrition on health and longevity

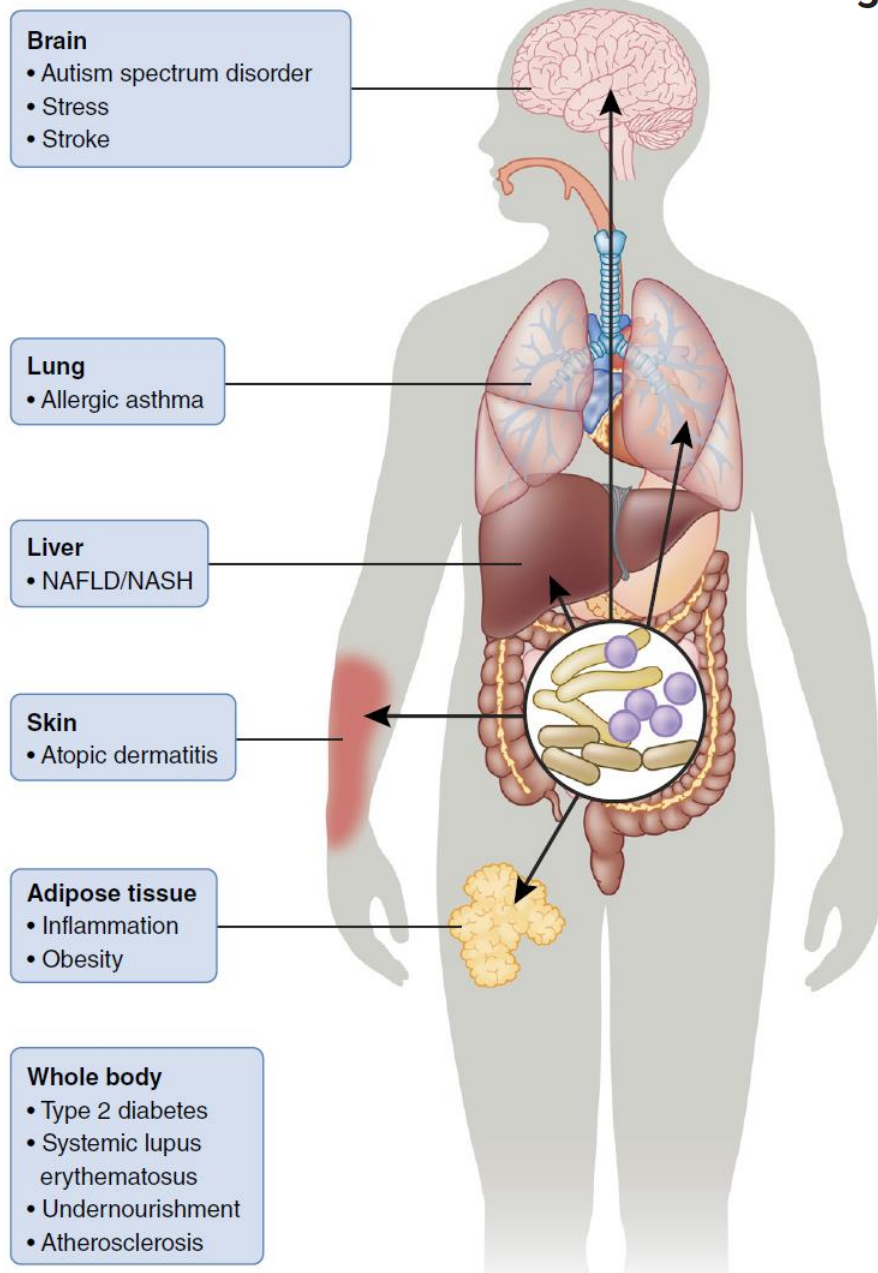**Santoro Aurelia**

Alma Mater Studiorum- University of Bologna

aurelia.santoro@unibo.it

Unexpected INCREASE of GM DIVERSITY in Italian, Chinese and Japanese centenarians

Diversity	GM diversity in Centenarians according to:			
	Biagi et al., 2016	Wang et al., 2015	Kong et al., 2016	Odamaki et al., 2016
Simpson reciprocal index of diversity	↑			
Alpha diversity (Chao index)	↑	↑	↑	↑
Shannon index	↑	=	↑	↑

In chronic age-associated diseases the GM diversity decreases

Santoro *et al*., 2017

Brain
- Autism spectrum disorder
- Stress
- Stroke

Lung
- Allergic asthma

Liver
- NAFLD/NASH

Skin
- Atopic dermatitis

Adipose tissue
- Inflammation
- Obesity

Whole body
- Type 2 diabetes
- Systemic lupus erythematosus
- Undernourishment
- Atherosclerosis

gut–brain axis in health and disease

Healthy CNS function

Abnormal CNS function

Healthy gut function

Abnormal gut function

The gut-joint axis

Infections
Stress
Shared genes
Gender
Food additives
Nutrients

Increased intestinal permeability

Dysbiosis

Immune stimmulation

tTg mTg

intestinal PAD microbial PAD

Amidation / Cross linking

Citrullination

Immunogenic neo-epitopes

anti tTg
anti neo tTg
anti mTg
anti neo mTg

anti CCP
ACPA

Pathogenic pathways activation

Autoimmunity

Schroeder et al., 2016

Signals from the gut microbiota to distant organs in physiology and disease
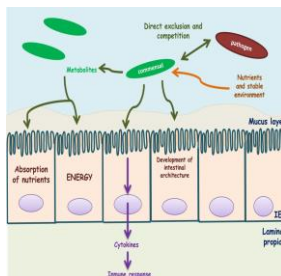
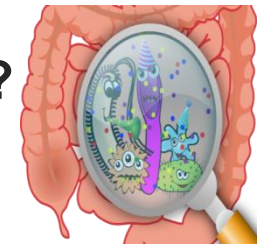# Can we modulate gut microbiota by diet in the elderly?

Human intervention study

NU-AGE   **MedDiet**

Gut microbiota composition?

Immune response?

THE NU-AGE PROJECT
EU-wide diet intervention

31 Partners

- 1. Alma Mater Studiorum Università di Bologna Research institution
- 2. University of East Anglia Research institution
- 3. Wageningen Universiteit Research institution
- 4. Institut National de la Recherche Agronomique Research institution
- 5. Spread European Safety Geie Stakeholder
- 6. University College Cork, Nat. Univ. of Ireland, Cork Research institution
- 7. Institute of Food Research Research institution
- 8. Szkola Glowna Gospodarstwa Wiejskiego Research institution
- 9. Confederation des Industries Agro-Alimentaires de L'UE Stakeholder
- 10. European Food Information Council Aisbl Stakeholder
- 11. Maa Ja Elintarviketalouden Tutkimuskeskus Research institution
- 12. Ethniko Idryma Erevnon Research institution
- 13. Straticell Screening Technologies SME
- 14. The University of Reading Research institution
- 15. Karolinska Institutet Research institution
- 16. Valio Enterprise
- 17. Orebro University Research institution
- 18. Lesieur Enterprise
- 19. Villani S.p.A. Enterprise
- 20. Pancrazio S.p.A. SME
- 21. Newsol SME
- 22. Wiesbauer Gourmet Gastro Gmbh Enterprise
- 23. Kanizsa Pékség Zrt. SME
- 24. VIDRERES LLET, S.L. Enterprise
- 25. Zeelandia Enterprise
- 26. MEVGAL Enterprise
- 27. Yoruk Sut Urunleri Hayvancılık Gıda San. Ve Tic. Ltd. Şti. SME
- 28. Kraft Foods R&D Inc., Zweigniederlassung München Enterprise
- 29. NEDERLANDSE ORGANISATIE VOOR TOEGEPAST NATUURWETENSCHAPPELIJK ONDERZOE Research institution
- 30. CRNH Auvergne Research institution
- 31. Nestec Enterprise

A total of **1294 volunteers aged 65-79 years** **i**ncluded in the project and **classified** as **NON frail** and **PRE-FRAIL** according to Fried Criteria for Frailty status

UK
POLAND
The Netherland
FRANCE
ITALY

Coordinated by Prof. Claudio Franceschi
Scientific Manager: Aurelia Santoro

Habitual Diet

Med Diet

n = 570 controls

n = 571 MedDiet

Diet Intervention 12 months

Gut microbiota and longevity

OPINION ARTICLE

Gut microbiota as a candidate for lifespan extension: an ecological/evolutionary perspective targeted on living organisms as metaorganisms

E. Ottaviani · N. Ventura · M. Mandrioli ·
M. Candela · A. Franchini · C. Franceschi

Gut microbiota tranplants extend lifespan in animal models

ANNUAL REVIEWS

- **100+ have a peculiar GM**
- **GM composition largely depends on diet**
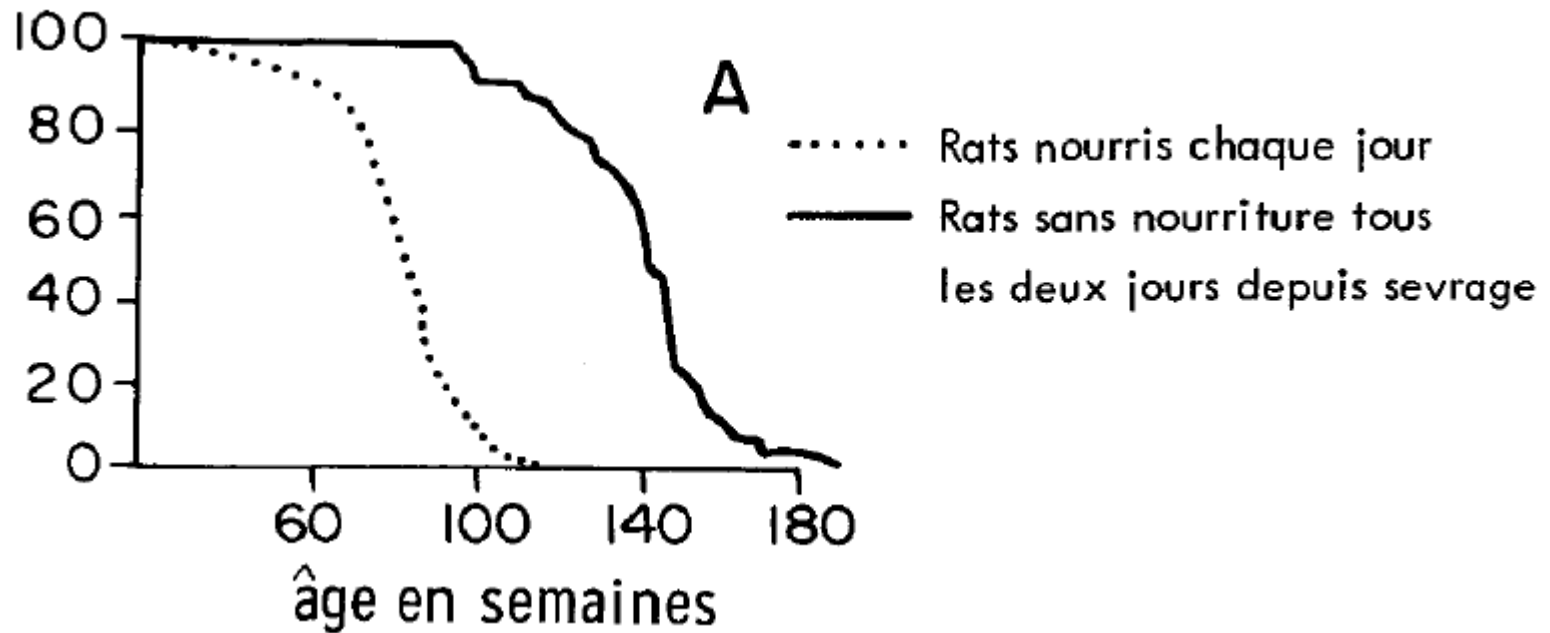- **What are the 100+ eating ?**

Nutrition and Inflammation: Are Centenarians Similar to Individuals on Calorie-Restricted Diets?

Claudio Franceschi,[1] Rita Ostan,[2] and Aurelia Santoro[2]

[1] IRCCS Institute of Neurological Sciences of Bologna, 40139 Bologna, Italy; email: claudio.franceschi@unibo.it

[2] Department of Experimental, Diagnostic, and Specialty Medicine (DIMES) and Interdepartmental Centre "L. Galvani" (CIG), Alma Mater Studiorum, University of Bologna, 40126 Bologna, Italy; email: rita.ostan3@unibo.it, aurelia.santoro@unibo.it

The most studied model to increase non genetically the lifespan across species and taxa is
CALORIE restriction (CR)

Legend:
- ...... Rats nourris chaque jour
- ——— Rats sans nourriture tous les deux jours depuis sevrage

CR-animals live longer and are healthier than *ad libitum*-fed controls (with several caveats !)

Walford RL 1985

100+ are similar to CR persons in terms of inflammatory, metabolic, hormonal and phenotypical adaptation
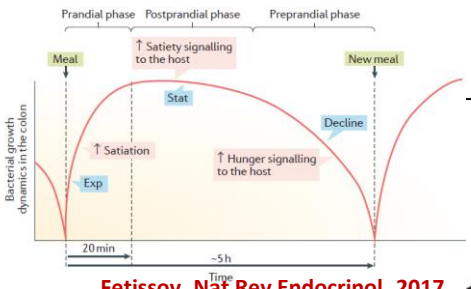
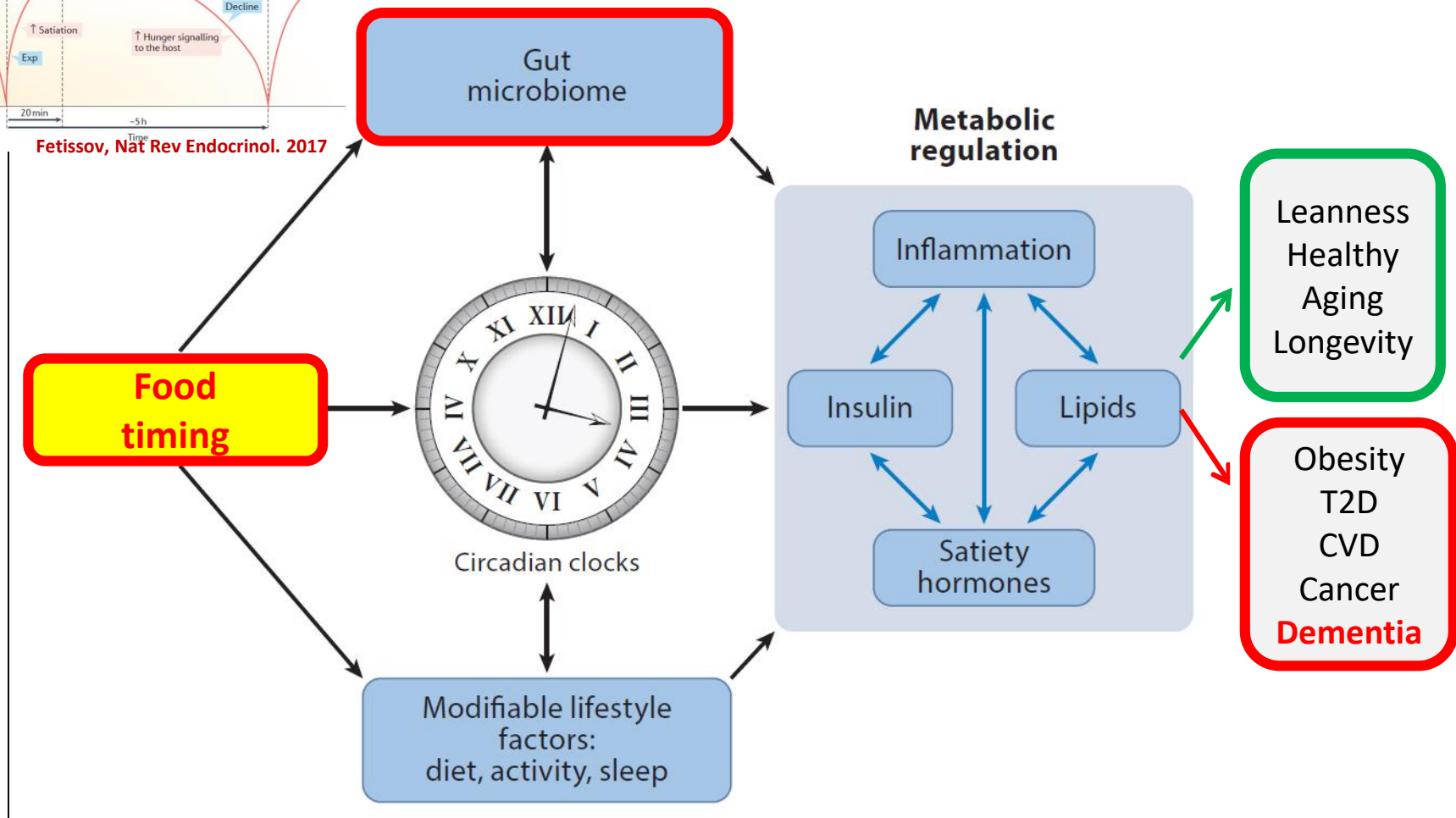| Adaptation	Parameter	Calorie-restricted diet (people aged 21–60 years)	Centenarians (>100 years)
Concordant			
Glucose metabolism	Glucose	↓	↓
	Insulin	↓	↓
	Insulin sensitivity	↑	↑
Blood pressure	Systolic	↓	↓
	Diastolic	↓	↓
Thyroid	T3	↓	↓
Lipid profile	Total cholesterol	↓	↓
	LDL cholesterol	↓	↓
	Triglycerides	↓	↓
Body composition	BMI	↓	↓
	Fat-free mass	↓	↓
	Bone mineral density	↓	↓
Metabolism	Cortisol	= or ↑	↑
	Adiponectin	↑	↑
	Leptin	↓	↓
	Tryptophan	↓	↓

What are the 100+ eating ?

Table 2 Summary of six detailed interviews conducted with centenarians (born between 1914 and 1916) with extraordinarily intact cognitive and health status, describing their familial situation, life experiences, body shape, physical activity, and nutritional habits when younger and as adults

Sex, birth year, age at time of interview	Family background	Education and occupation	Body shape	Physical activity	Diet	Meal timing and portion size
Male, 1915, 101 years	Parents were farmers, 7 siblings, living in the countryside. After the Second World War, he moved to the city (Bologna)	5 years of education, primary school certificate. Farmer until he was 25, then soldier for 5 years during World War II. After the end of the war, railway worker	Thin	Daily walking	Pasta, white bread, vegetables, fruit, cheese, pulses, potatoes, eggs, sweets once a week; meat (pork, poultry, and rabbit) 2–3 times a week; little red wine at meals. During the war, he suffered from hunger	Very regular, 2 meals/day, early dinner
Female, 1914, 102 years	Parents were a butcher (the father) and housewife (the mother), no siblings, living in the city (Bologna)	8 years of education, low secondary school certificate. Clerk for the family's business	Curvy	Daily walking or cycling	Pasta, meat (red meat until 20 years previously, then only white meat), eggs, white bread, vegetables, beans, sweets once a week, fish once a week, milk, cheese, fruit	Regular, 3–4 meals/day
Female, 1916, 100 years	Parents owned grocery shop, 8 siblings, living in a village in the Apennines (altitude, 900m). When she was 17 years old, she moved to the city (Rome and then Bologna)	5 years of education, primary school certificate. She took care of her younger siblings, was a maid for a family, and then left her job to take care of her disabled son	Curvy	Daily long-distance walking, housework	In her infancy and adolescence: pasta, meat (pork, poultry), eggs, white bread, potatoes, vegetables, pulses, nuts, fruit, cheese (cow and sheep). She suffered from hunger during her youth and the first years after she married	Very regular, 3 meals/day, small portions
Male, 1913, 103 years	Parents were farmers, 3 siblings, living in the countryside. When he was 17 years old, he moved to the city (Bologna)	4 years of education. Artisan, mechanic, warehouse worker	Thin	Daily long-distance walking or cycling, physical work	Pasta, white bread, milk, tomatoes, beans, eggs. Rarely: sweets, butter, cheese, poultry, and pork	Very regular, early dinner, 3 meals/day, small portions
Female, 1915, 101 years	Father died during the First World War. Lived with mother (seamstress), grandparents, and 2 sisters in a small village near the city (Bologna)	6 years of education, primary school certificate. Laborer for 20 years and then office worker for 15 years	Curvy and strong	Daily cycling, housework	Pasta, milk, white bread, meat (pork and poultry), parmesan cheese, beans, butter, olive oil, vegetables, fruit, and a little white wine; sweets once a week	Very regular, 3 meals/day, small portions
Female, 1916, 101 years	Farmer (mother) and carpenter (father), 5 siblings, living in the countryside. After wedding spent 2 years in Germany and 4 years in Belgium with her husband (miner), then she moved to city (Bologna)	5 years of education, primary school certificate. Farmer until wedding, then cook, greengrocer, and maid for a family	Medium	Walking, physical work	Pasta, milk, white bread, little meat (pork and poultry), little cheese, few eggs, pulses, vegetables, little wine; sweets once a week	Very regular, 3 meals/day, small portions

Food timing is critical for health

Fetissov, Nat Rev Endocrinol. 2017

Gut microbiome

Food timing

Circadian clocks

Modifiable lifestyle factors: diet, activity, sleep

Metabolic regulation

Inflammation

Insulin

Lipids

Satiety hormones

Leanness
Healthy
Aging
Longevity

Obesity
T2D
CVD
Cancer
Dementia

Gut microbiota and Body Composition

nature

Open

npg

ARTICLES

ORIGINAL ARTICLE

Obesity-associated gut microbiota is enriched in *Lactobacillus reuteri* and depleted in *Bifidobacterium animalis* and *Methanobrevibacter smithii*

nicrobiome
energy harvest

Elaine R. Mardis[1,2] & Jeffrey I. Gordon[1]

nature
COMMUNICATIONS
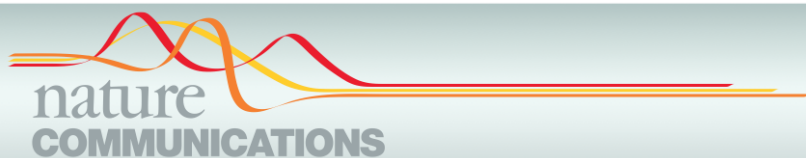
ARTICLE

OPEN

ced by Gender

Sex-specific association between gut microbiome and fat distribution

Yan Min[1,2,6], Xiaoguang Ma[3,4,6], Kris Sankaran[5], Yuan Ru[3,4], Lijin Chen[3,4], Mike Baiocchi[1,2,5] & Shankuan Zhu[3,4]

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Aging and imaging assessment of body composition: from fat to facts

Federico Ponti[1], Aurelia Santoro[2*], Daniele Mercatelli[1], Chiara Gasperini[1], Maria Conte[2], Morena Martucci[2], Luca Sangiorgi[1], Claudio Franceschi[2], Alberto Bazzocchi[1]

BODY COMPOSITION OF CENTENARIANS
DXA SCAN

T-score

- +1.0 / 0.0 normal bone density
- -1.0 / -2.0 / -2.5 low bone mass
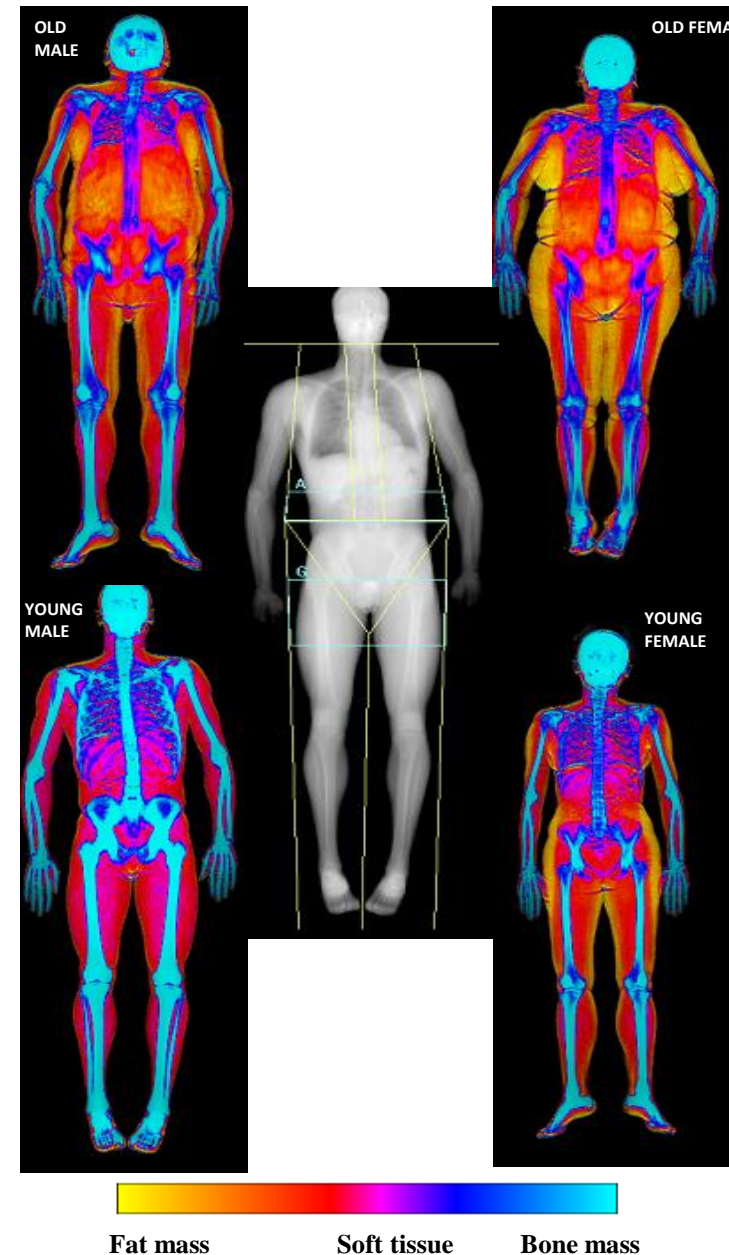- -3.0 / -4.0 presence of osteoporosis
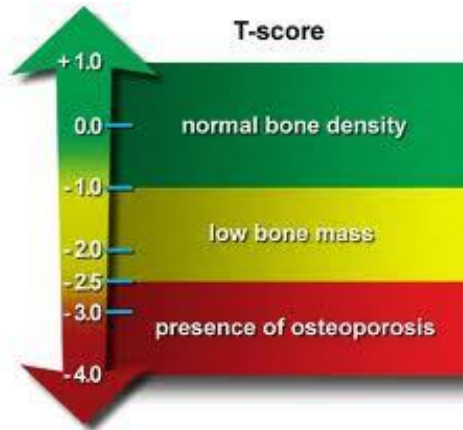
BODY COMPOSITION:

- FAT MASS
- LEAN MASS
- BONE MASS (MINERAL CONTENT AND DENSITY)

BODY COMPOSITION INDEXES:

- FAT MASS INDEXES: **fat weight** in kg /height in m^2
- SKELETAL MASS INDEX: **arms+legs lean mass**/weight

OLD MALE   OLD FEMA

YOUNG MALE   YOUNG FEMALE

Fat mass   **Soft tissue**   **Bone mass**

CONCLUSIONS

- **Centenarians** have a **high gut microbiota diversity**

- **Mediterranean Diet** is able to **modulate Gut Microbiota in elderly**

- **Centenarians are similar to Calorie Restricted like persons** in terms of glucose and lipid profile, metabolism, blood pressure, thyroid, BMI and BMC

- **Centenarians** followed a **strict FOOD TIMING** lifelong

- **Gut Microbiota** is **associated** with **Body composition**

- **Centenarians** have **LOWER BMI**, **WHOLE BODY FAT**, **LEAN AND BONE MASS** than 65-79 years old individuals

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NU-AGE

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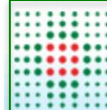- Willem de Vos
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- Federico Ponti
- Daniele Mercatelli

**YOU
for the attention!**