

IUNS 21st ICN International Congress of Nutrition “From Sciences to Nutrition Security”



Sociedad Argentina de Nutrición



IUNS

INTERNATIONAL UNION OF
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Conflict of Interest Disclosure

I have no conflict of interest to report in relation to this presentation.

The role of microbiota in nutrient metabolism and bioavailability

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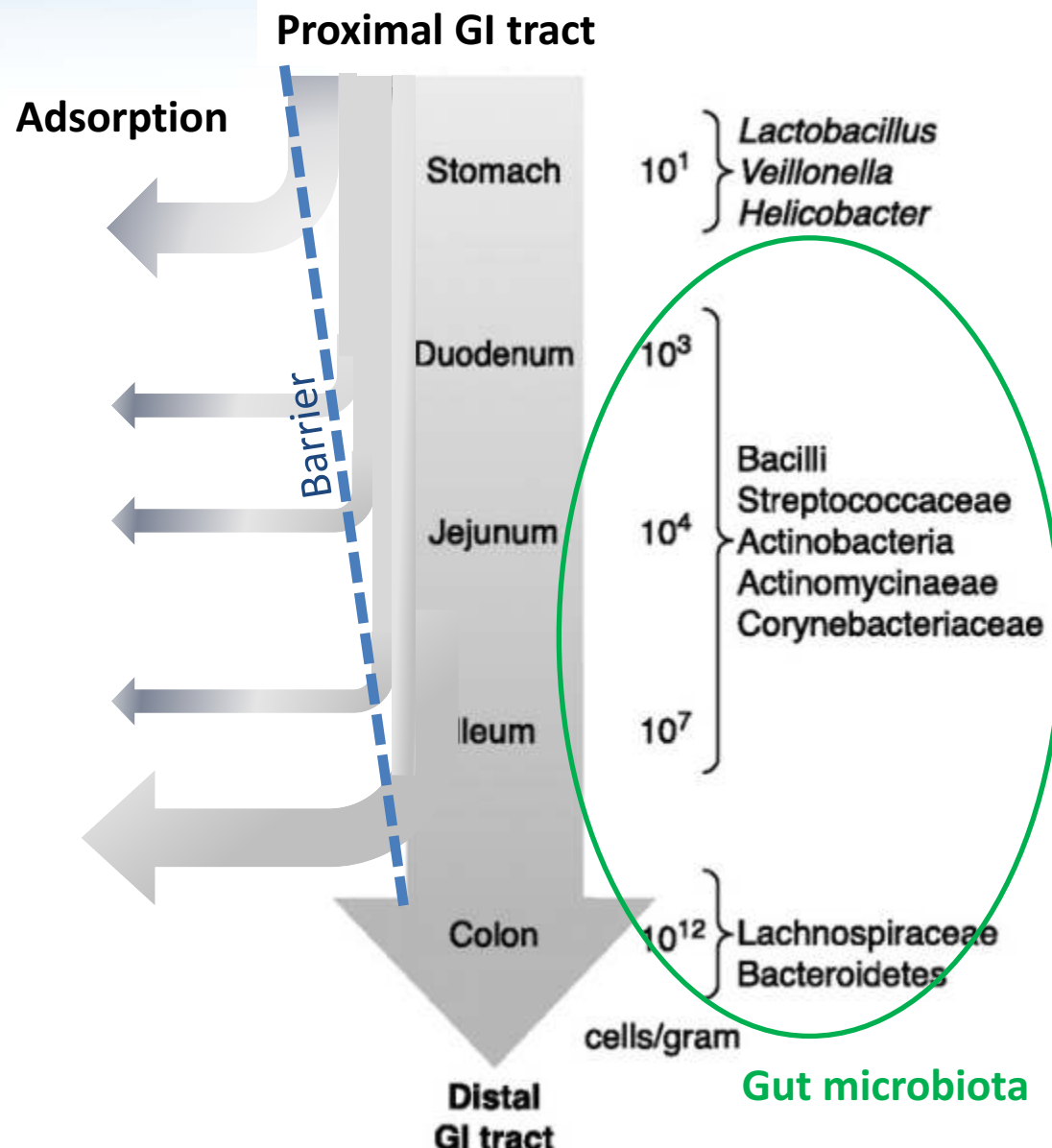
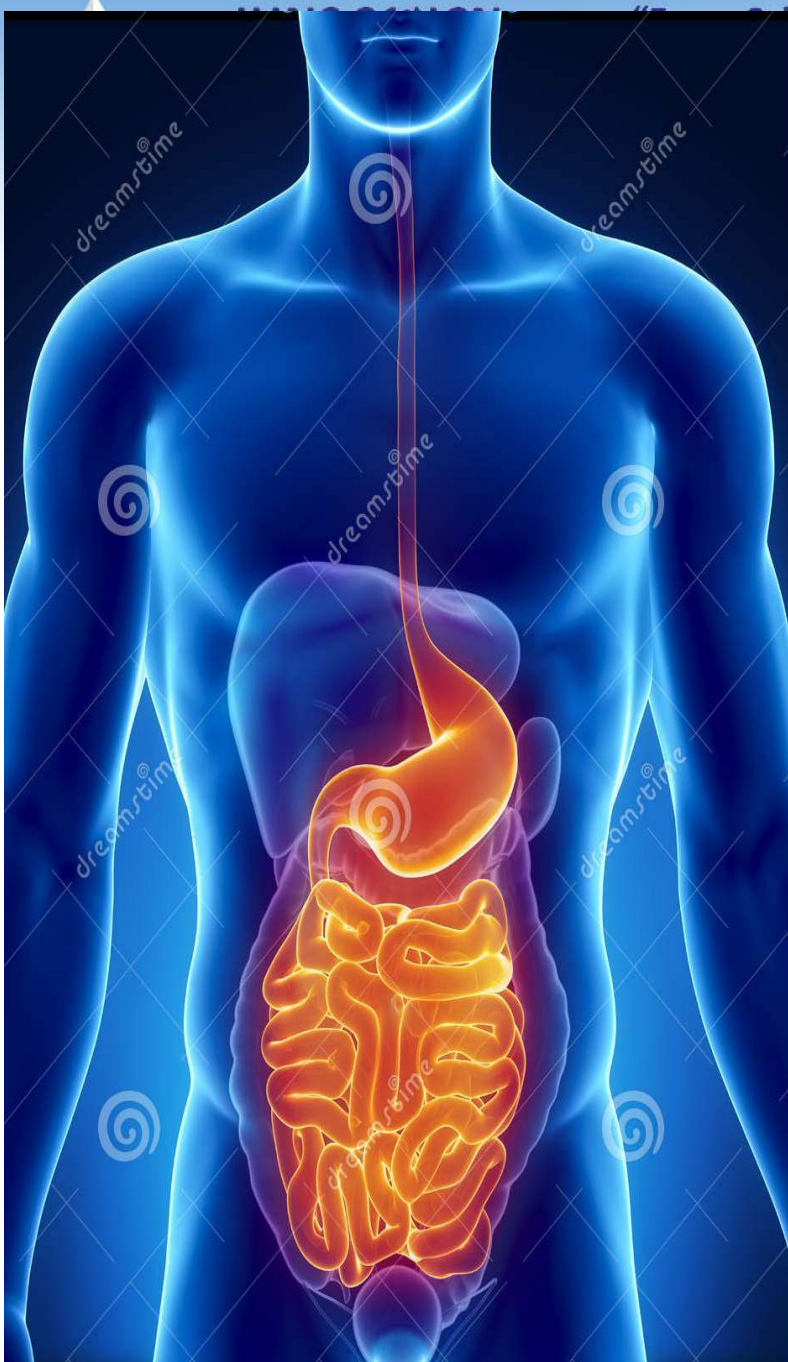


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Importance of microbiota



Definition of bioavailability in nutrition science

There are many different definitions of bioavailability in nutritional science, that differs from the accepted definition in pharmacology.

The concept of bioavailability incorporates: (i) availability for the **absorption** or “bioaccessibility”; (ii) **absorption; metabolism** (iii), tissue distribution (iv) bioactivity (v) and **excretion (vi)**. Stahl et al., Molecular Aspects of Medicine, 2002, 23, 39

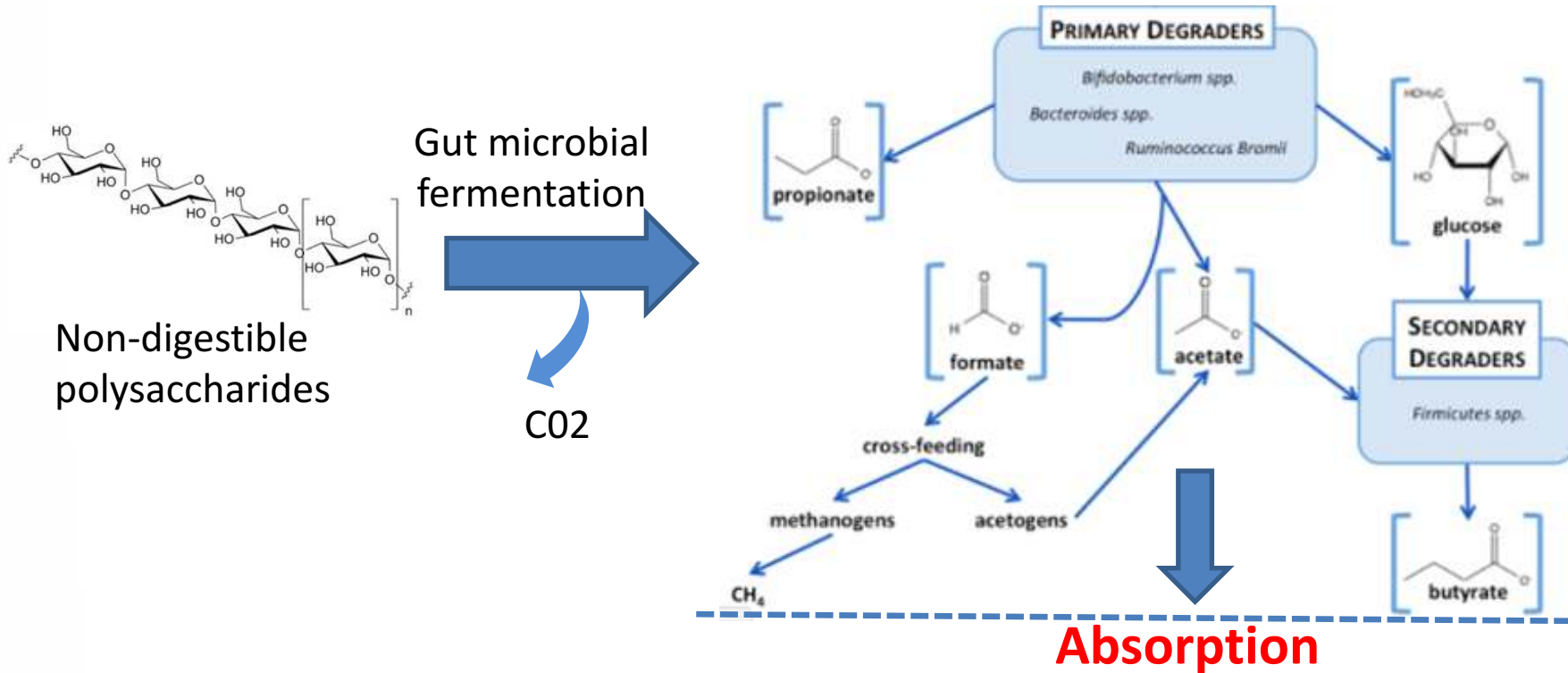
ADME concept : Absorption, distribution, metabolism, and excretion (ADME) patterns of the main plant food bioactives



Microbiota enhance bioavailability of some food nutrients

The contribution of gut microbiota to human nutrition, through the production of more bioavailable food compound is essential

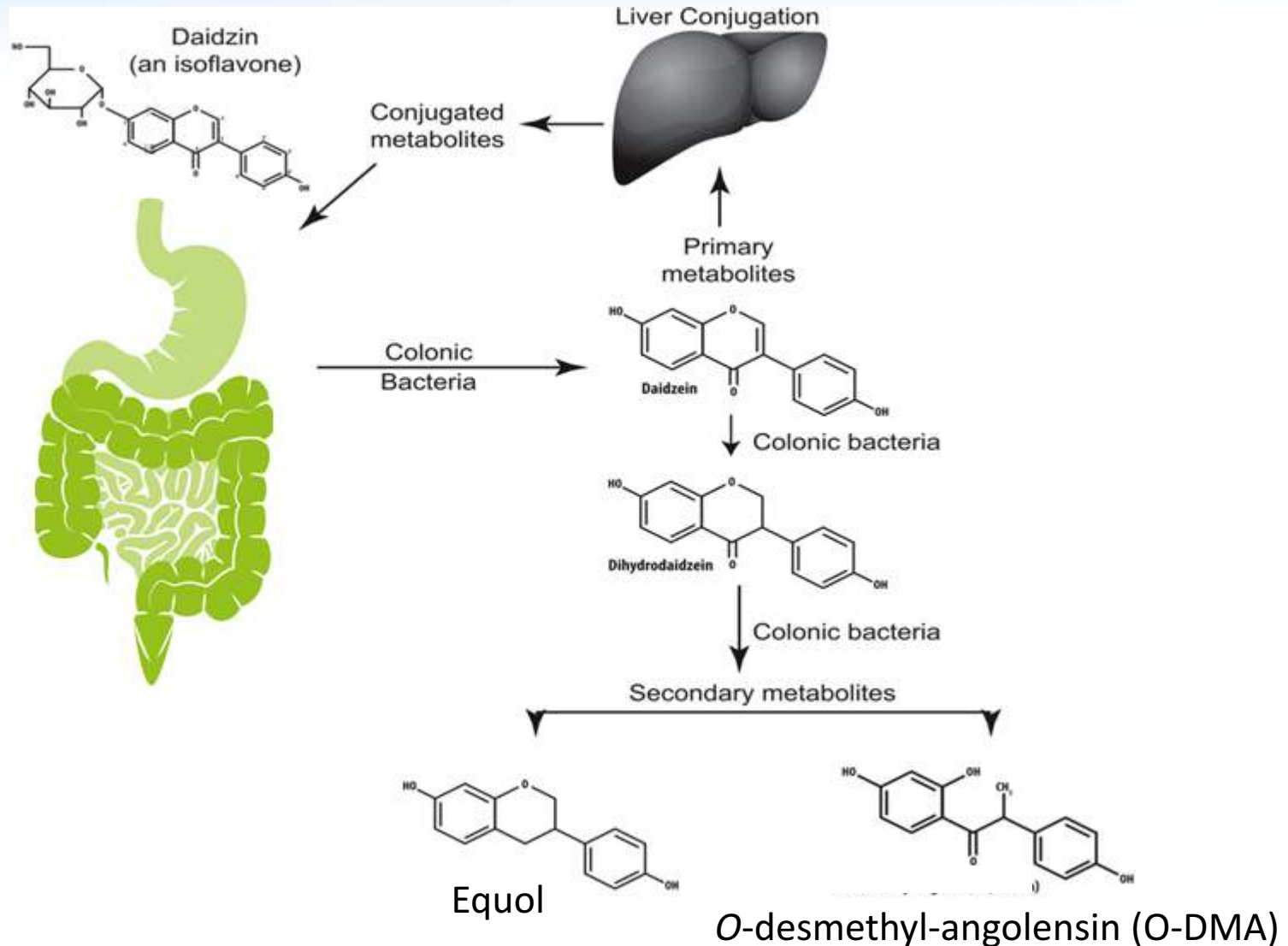
Synthesis of short chain fatty acids (SCFAs) from dietary fibres



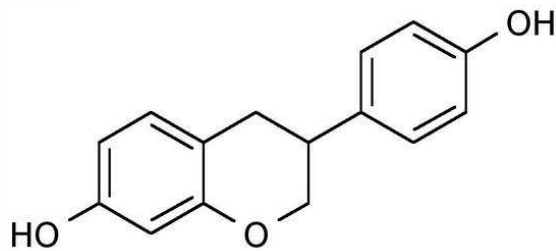
Are dietary fibers bioavailable ? At least partially

The importance of the conversion into SCFA depends on microbiota composition and as a consequence there is a high inter-individual variability

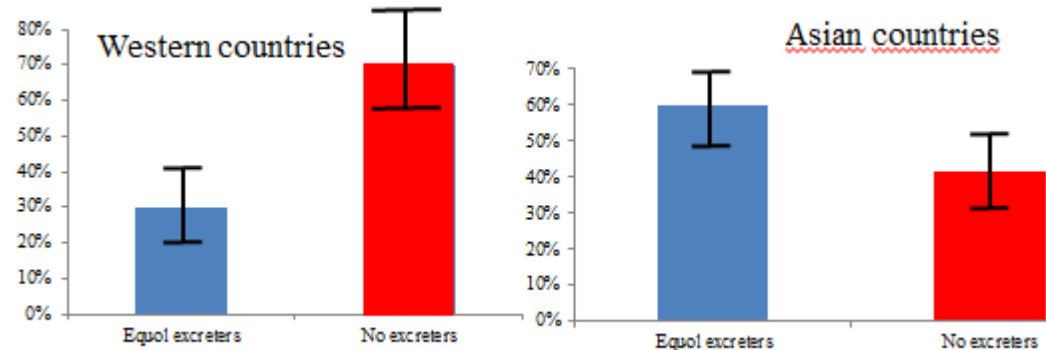
In-vivo metabolism of Isoflavones



Equol and O-DMA metabotype

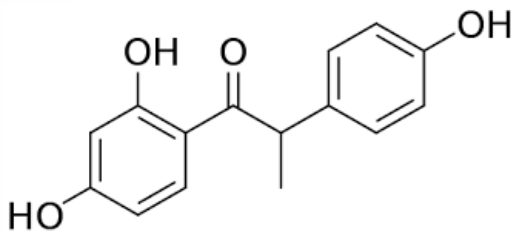


equol

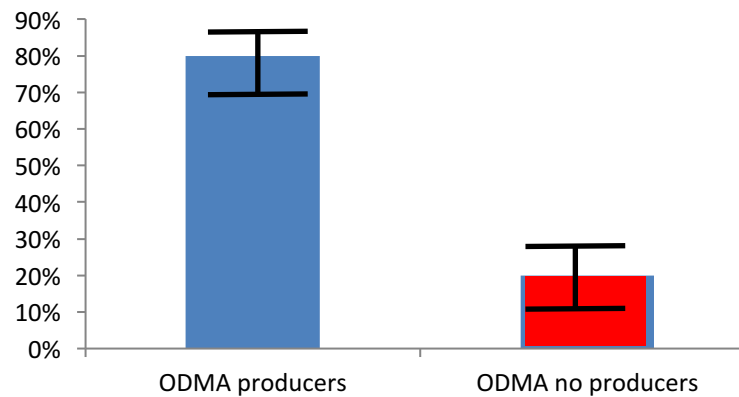


(Kenneth D. R. Setchell and Carlo Cleric; Equol: History, Chemistry, and Formation, *J Nutr.* 2010 Jul; 140(7))

(Kenneth D. R. Setchell and Carlo Cleric; Equol: History, Chemistry, and Formation, *J Nutr.* 2010 Jul; 140(7))



O-desmethyl-angolensin (O-DMA)



Gut-microbial phenotypes from Daizin

Gut metabotypes with specific polyphenol metabolism patterns can be differentiated

Probably up to 4 metabotypes for Daizin metabolism

- 1-ODMA and Equol-producer
- 2-No-ODMA- producer and Equol Producer
- 3-ODMA producer and no-Equol Producer
- 4- No-ODMA and equol producer

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The Clinical Importance of the Metabolite Equol—A Clue to the Effectiveness of Soy and Its Isoflavones¹

Kenneth D. R. Setchell², Nadine M. Brown, and Eva Lydeking-Olsen^{*}

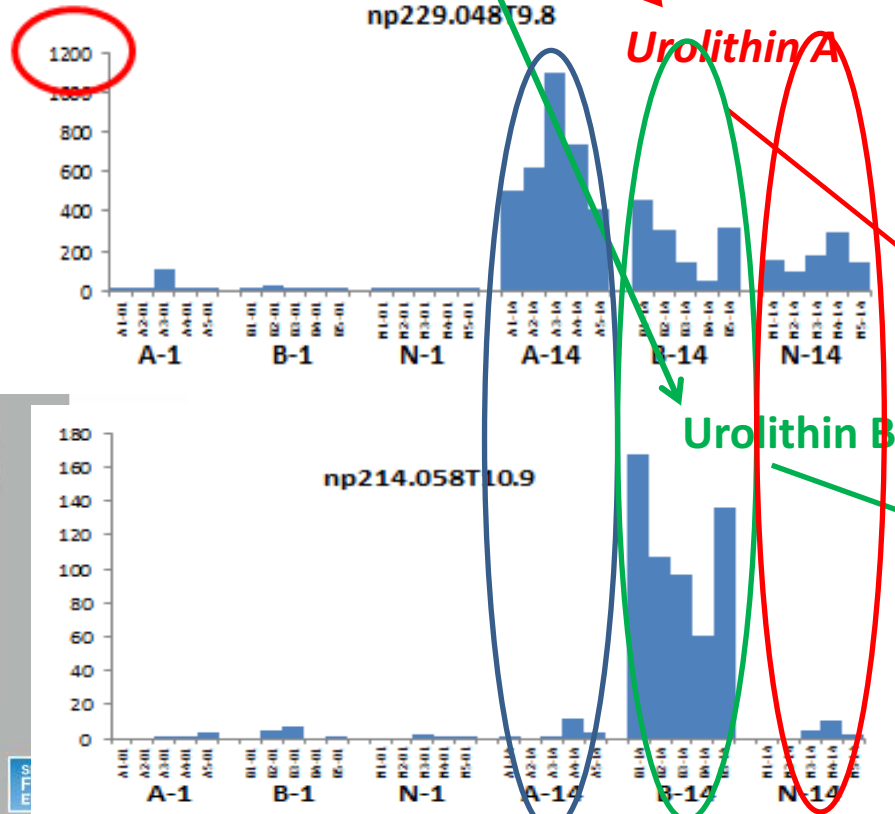
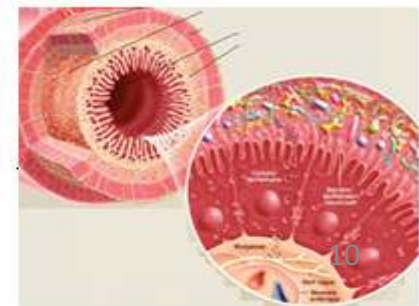
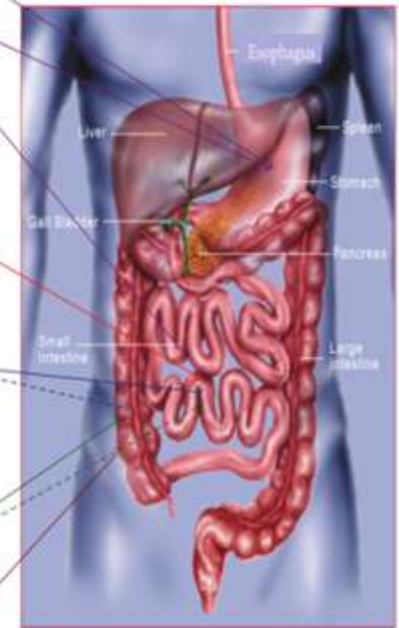
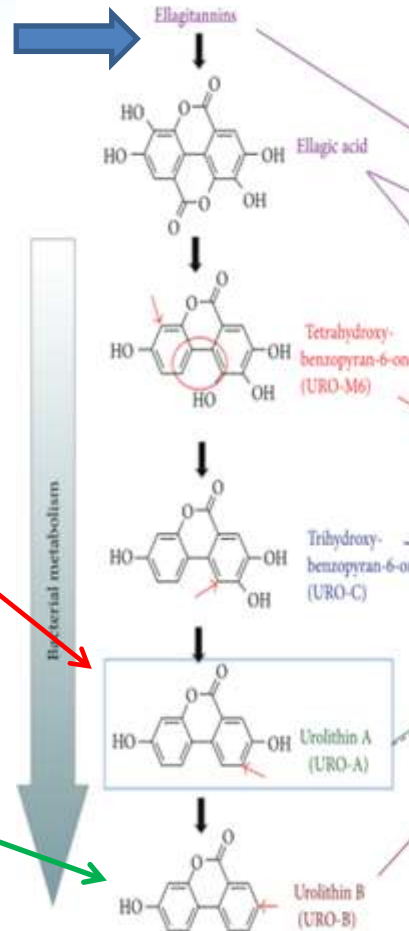
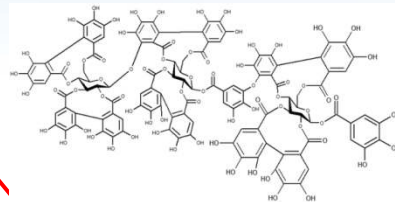
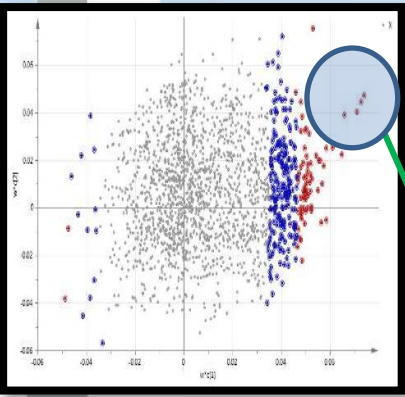
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Microbial and Dietary Factors Are Associated with the Equol Producer Phenotype in Healthy Postmenopausal Women¹⁻³

Selin Bolca^{4,6}, Sam Possemiers⁴, Annelies Herregat⁴, Inge Huybrechts⁵,

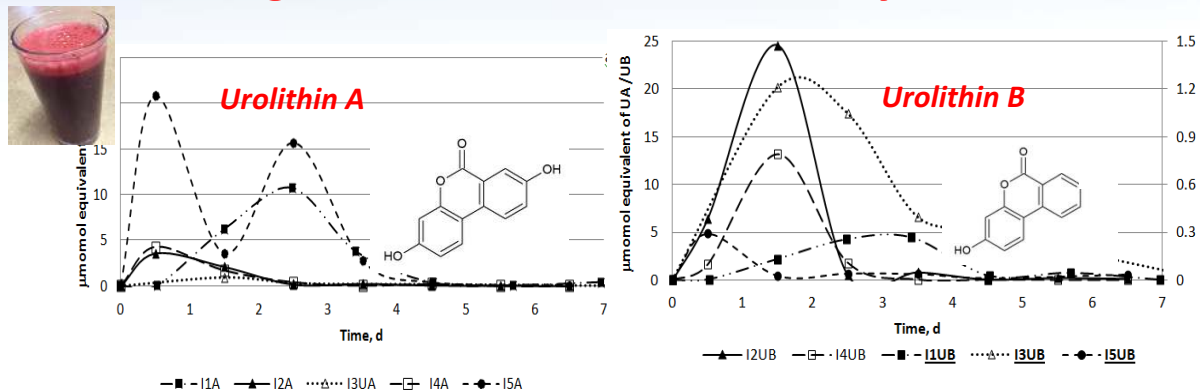
The interindividual differences in metabolizing the isoflavone daidzein to equol or *O*-desmethyl-angolensin (ODMA) might explain the discrepancy of the soy/isoflavones effects on human health (cardiovascular, obesity, bone density, etc.).

In-vivo metabolism of ellagitannins

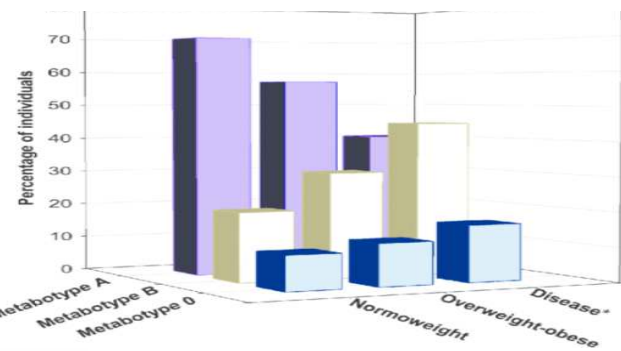
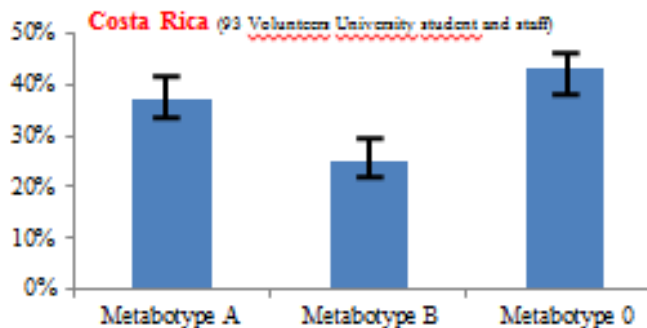


Urolithin excretion: High inter-individual variability

After one single shot of Andean blackberry juice



Large inter-individual variability, low intra-individual variability



Mol Nutr Food Res. 2017 May;61(5). doi: 10.1002/mnfr.201600830.

Clustering according to urolithin metabolite explains the interindividual variability in the improvement of cardiovascular risk biomarkers in overweight-obese individuals consuming pomegranate: A randomized clinical trial.

González-Sarrías A¹, García-Villalba R¹, Romo-Vaquero M¹, Alasalvar C², Örem A³, Zafrilla P⁴, Tomás-Barberán FA¹, Selma MV¹, Espín JC¹.

PUBLIC RELEASE: 27-APR-2017

Amazentis announces successful phase 1A/1B study results for urolithin A in healthy elderly subjects

J Cachexia Sarcopenia Muscle. 2017 Aug;8(4):583-597. doi: 10.1002/jcsm.12190. Epub 2017 Mar 1.

Urolithin B, a newly identified regulator of skeletal muscle mass.

Rodriguez J^{1,2}, Pierre N¹, Naslain D¹, Bontemps F³, Ferreira D⁴, Priem F², Deldicque L¹, Francaux M¹.

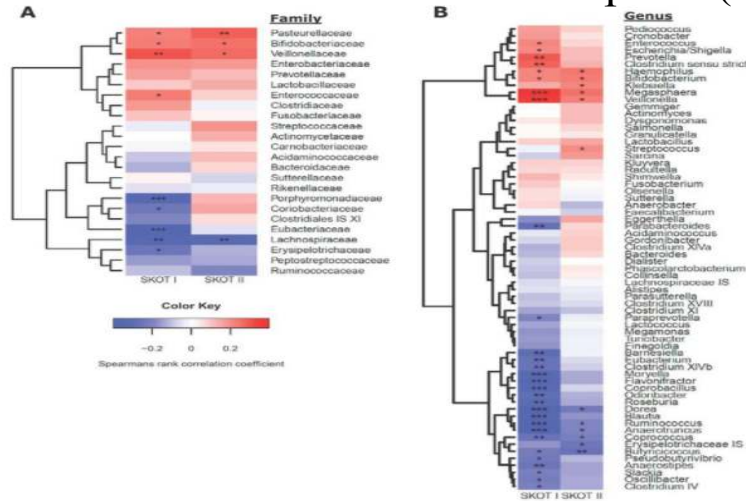
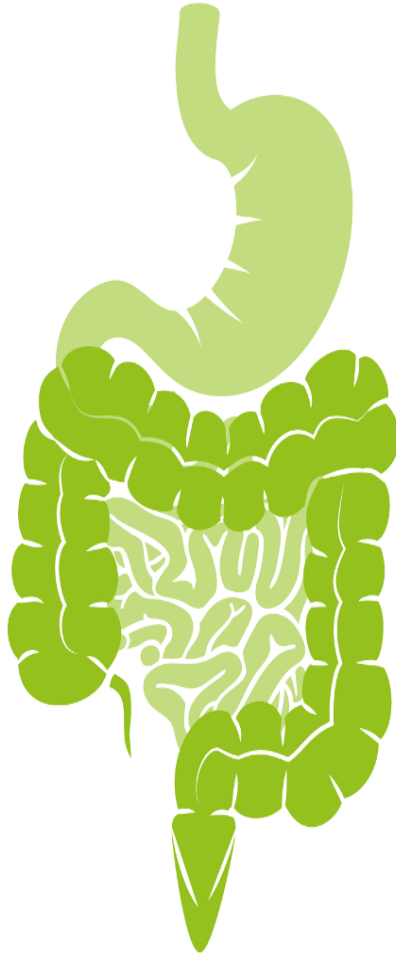
Spain: Tomás- Barberán et al. 2014

List of some bioactive compounds known to be metabolized by gut microbiota

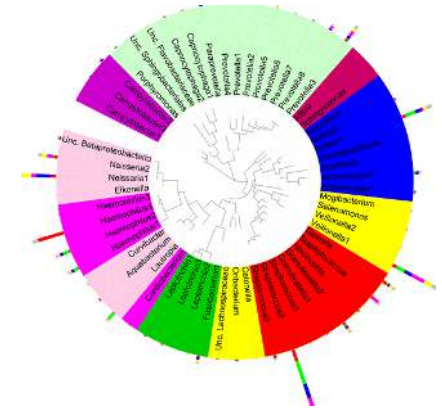
Dietary compound	Main food source	Gut microbial metabolite
Dietary fibbers	Whole grains	Short Chain Fatty Acids (SCFA) (butyrate, propionate, etc...)
Isoflavone	Soybean	Equol, O-DMA
Ellagitannins	Blackberry, walnuts, pomegranate	Urolithin A and B
Secoisolariciresinol	Flaxseed, sesame	Enterolactone, enterodiol
Linoleic acid	Vegetable oil	Conjugated linoleic acid (CLA)
Isoxanthohumol	Hop (beer)	8-prenylnaringenin
Resveratrol	Grape skin	dihydro-resveratrol
caffeoylisocitric acid	Amaranth	Hydroxyphenyl-propionic acid
Etc.....		

Characterization of gut microbiota

- From the taxonomic viewpoint (metagenomic)



Phylogenetic stratification



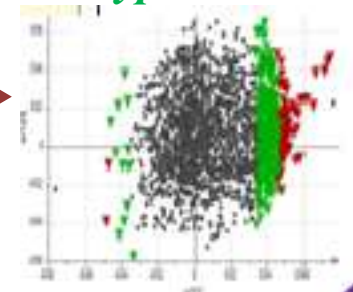
- From the functional viewpoint (metabolomic)

Functional stratification into metabolotypes

Food Nutrient



Microbiota



Metabolites

How phenotyping and stratifying individuals according to gut-microbiota functionality

□ Designing challenging tests

At the University of Costa Rica, was developed a standardized food supplement that contains blackberries (Ellagitanins), Soy flour (isoflavones) and flaxseed (lignan)



world's longest-lived people



Test: After ingestion of 100 ml of the standardized beverage during 3 days, urinary excretion of equol, urolithin, enterodiol and enterolactone is monitored on a fasting spot of urine on the 4th day. According to concentration (measured by UPLC-MS), individuals could be stratified according to each metabotypes.

➔ Try to correlate health status with gut metabotype of world's longest-lived people in a blue zone, Nicoya, Costa Rica.



conclusion

- ❑ The stratification of volunteers according to their microbiota metabotype could reduce the large variability of “health biomarkers” often observed in clinical trials assessing functional food effects
- ❑ Functional stratification in addition to phylogenetic stratification of gut-microbiota profile is required.
- ❑ Challenge test approach should allow stratifying individual according to microbiota metabotype

Thank you



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