

### Study Protocol: A 2-Month Cross-Over Controlled Feeding Trial Investigating the Effect of Animal and Plant Protein Intake on the Metabolome and Cardiometabolic Health

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# Study protocol: a 2-month cross-over controlled feeding trial investigating the effect of animal and plant protein intake

## on the metabolome and cardiometabolic health

Study design: 2-month cross-over randomized trial

2 weeks

(wash-out)

**D42** 

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**Post-prandial** 

follow up

Transcriptomics



### **Context:**

- A dietary shift from animal protein (AP) to plant protein (PP) advocated for sustainability and health reasons (lower cardiovascular and diabetes risk)
- Mechanistic bases underlying these associations still poorly characterized and involving numerous metabolic pathways.

### **Objective:**

This protocol aims at characterizing the metabolic reorientations induced by AP  $\rightarrow$  PP dietary shift and understanding their health effects in a population at cardiometabolic risk, combining a highly controlled feeding trial and "omics" analytical approaches (NCT04236518)

### 1. A population at cardiometabolic risk

This ongoing study targets the hyper-triglyceridemic enlarged waist circumference phenotype

### Inclusion criteria

- Men
- Age: 25 to 55 years
- BMI: 25-35 kg/m<sup>2</sup>

Age (y)

BMI  $(kg/m^2)$ 

- Waist circumference > 94cm
- Plasma triglycerides > 1,5g/L

# Recruitment objective: n=20 subjects

### 3. AP-rich and PP-rich diets

AP-rich diet ←→ western omnivore diet (65% AP:35% PV)

Body composition

Vascular function

■ PP-rich diet ←→ flexitarian diet including small amounts of meat and dairy (36% AP:64% PV)

4 weeks

**PP-rich diet** 

**D14** 

Both diets mixed all the major animal and plant sources, without any exclusion

Dairy

Fish

SFA

Fiber

Sugar

Intake (g/d)

White meat

Legumes

Red and processed meat

Fruits and vegetables

Grains and potatoes

### AP-rich diet (2106 kcal) Waist circumference (cm) 102.8 (5.5) Plasma triglycerides (g/L) 1.96 (0.57) **Table 1:** Description of the sample already included 2. A control feeding trial in a free living environment

Mean (SD)

44.2 (8.0)

29.4 (2.8)



- Ready-to-eat lunches and diners freshly prepared by a catering service
- **Dietary advices** regarding breakfast and snacks
- Compliance follow-up with dietary dairies and blood measurement of natural abundance of nitrogen isotope (AP and PP have distinct natural isotopic signatures)
- **3-day weighted food records** (before intervention and during wash-out) for characterization of habitual food intake

# Carbohydrates PP-rich diet (2017 kcal)

**Figure 1:** Mean daily macronutrients contribution to total energy intake provided by ready-to-eat meals

<u>Table 2</u>: Mean dietary composition of ready-to-eat meals provided in AP and PP-rich diets

### 4. Assessing metabolic flexibility following a high-fat meal

4 weeks

**D56** 

**AP-rich diet** 

Challenge meal

2H

Postprandial follow-up after a high-fat challenge (identical in each crossover arm) allows to measure adaptation capacity under challenging postprandial conditions (high influx of saturated fatty acids and sugar) and is expected to reveal subtle differences induced by the dietary intervention which could not be visible at the fasted state, when tight homeostatic processes still prevail.



**AP-rich** 

diet

166.4

158.6

58.6

98.6

35.7

64.3

580.0

461.4

30.4

29.2

70.7

PP-rich

diet

10.0

115.7

22.9

40.0

41.4

225.7

638.6

432.9

31.5

37.7

72.1

Challenge meal composition: 900kcal (80% lipid, 13% carbohydrate, 7% protein) Cream 30% fat (267g) + white sugar (20g) + whole milk protein isolate (11,5g)

### What is new about this study?

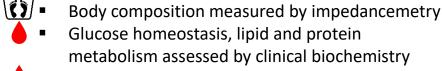
Very little is known regarding the metabolomics signature associated to AP and PP intakes in humans (see poster P11-019-21) and up to day, no RCT has specifically investigated the effects of the AP->PP dietary shift using a combination of "omics" approaches. This study will bring new hypotheses regarding the metabolic pathways affected by AP and PP-rich diets and associated biomarkers and will characterize with high-end methods the effects on endothelial function.





### Effects on cardiometabolic health

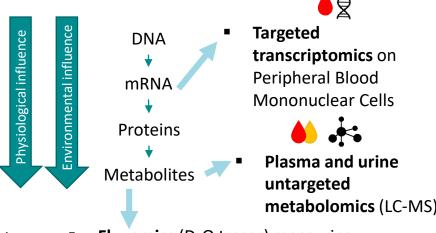
### 5. Overall health outcomes



Inflammation status (cytokines)

### 6. Multi-omics phenotyping

The combination of omics approaches, providing a multilevel phenotyping, will give the possibility to characterize very subtle metabolic reorientations induced by dietary changes.



**D70** 

D<sub>2</sub>O

**Post-prandial** 

follow up

6H /

Fluxomics (D<sub>2</sub>O tracer) measuring postprandial fluxes in lipogenesis de novo and protein synthesis pathways.

### 7. Measurement of endothelial function

- Circulating markers of endothelial function: plasma nitrite and nitrosothiols
- Flow Laser Doppler (FLD): measurement of hand microcirculation
- Flow Mediated Dilatation (FMD): measurement of brachial artery dilatation induced by blood flow changes

