**Combination of catheterized minipigs and high throughput «omics» methodologies: For new paradigms in the kinetics of development of insulin-resistance**

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**Aim:**

Study of the nutritional transition leading to the installation of insulin resistance: **EARLY PHASES**

1. **Investigation of the metabolic shift (insulin resistance installation) usually measured in plasma in the fasting state (glucose and insulin)**
2. **Idea:** Analysis of the subtle and early changes of the metabolic trajectories using an integrative approach: metabolomics in a compartment integrating fasting and fed states: urine

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**1/ Detection of insulin resistance with the « classical plasma biomarkers »: fasting glucose and insulin**

Detection of insulin resistance based on classical biochemical markers at 15 days following HF-HS diet. After 7 days, these biochemical markers remained unchanged and allow to conclude for a normal glucose homeostasis and insulin sensitivity.

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**2/ Metabolic trajectories following HF-HS diet: Analysis of targeted metabolites in urine**

Analysis including D0, D7, D14, D30, D60

Analysis focused on D0, D7 and D14

**Molecules related to the transient short term adaptations (D0-D7)**

**Molecules related to the new homeostatic state (D7-D14)**

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1. **Combination of urinary metabolome and new targeted plasma metabolites (other than glucose and insulin):** highlight key early time points involved in metabolic adaptations to the high fat – high sucrose diet

2. Some specific metabolites (urinary and other plasma metabolites) have been identified and described to explain these early adaptations

3. **These preliminary results will be the basis for experiments aiming at investigating the mechanisms explaining the metabolic flexibility/inflexibility involved in the early phases of insulin resistance development**