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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 :

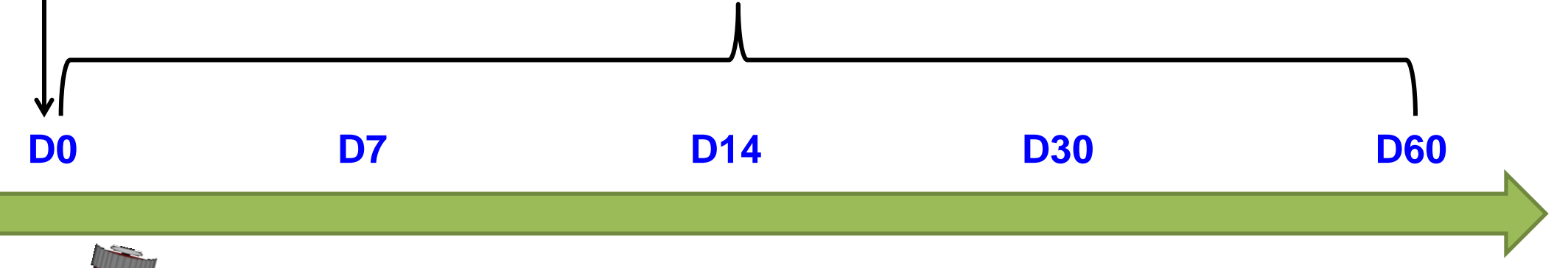
Study of the nutritional transition leading to the installation of insulin resistance : EARLY PHASES

- 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

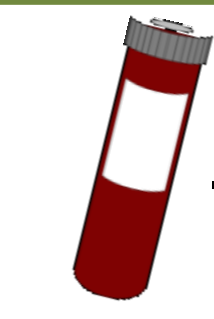
Control diet (C)
Diet : EM/kg : 13.3 MJ/kg feed
Daily ingested ME : 5.3 MJ

High fat / high sucrose diet (HF-HS)
Diet : ME/Kg : 15.6 MJ/Kg feed
Daily ingested ME : 13.3 MJ

6 adult Yucatan minipigs



Fasting blood sampling



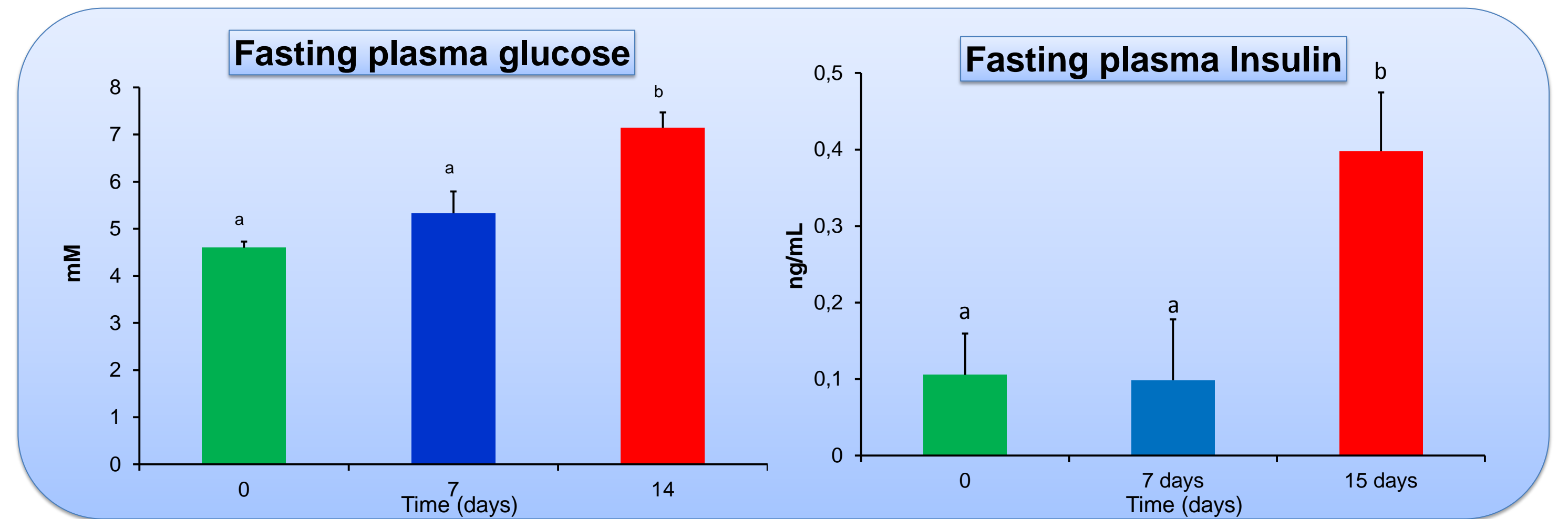
Plasma biochemical analysis

Urine collection over the postprandial period (0-8h after the meal)

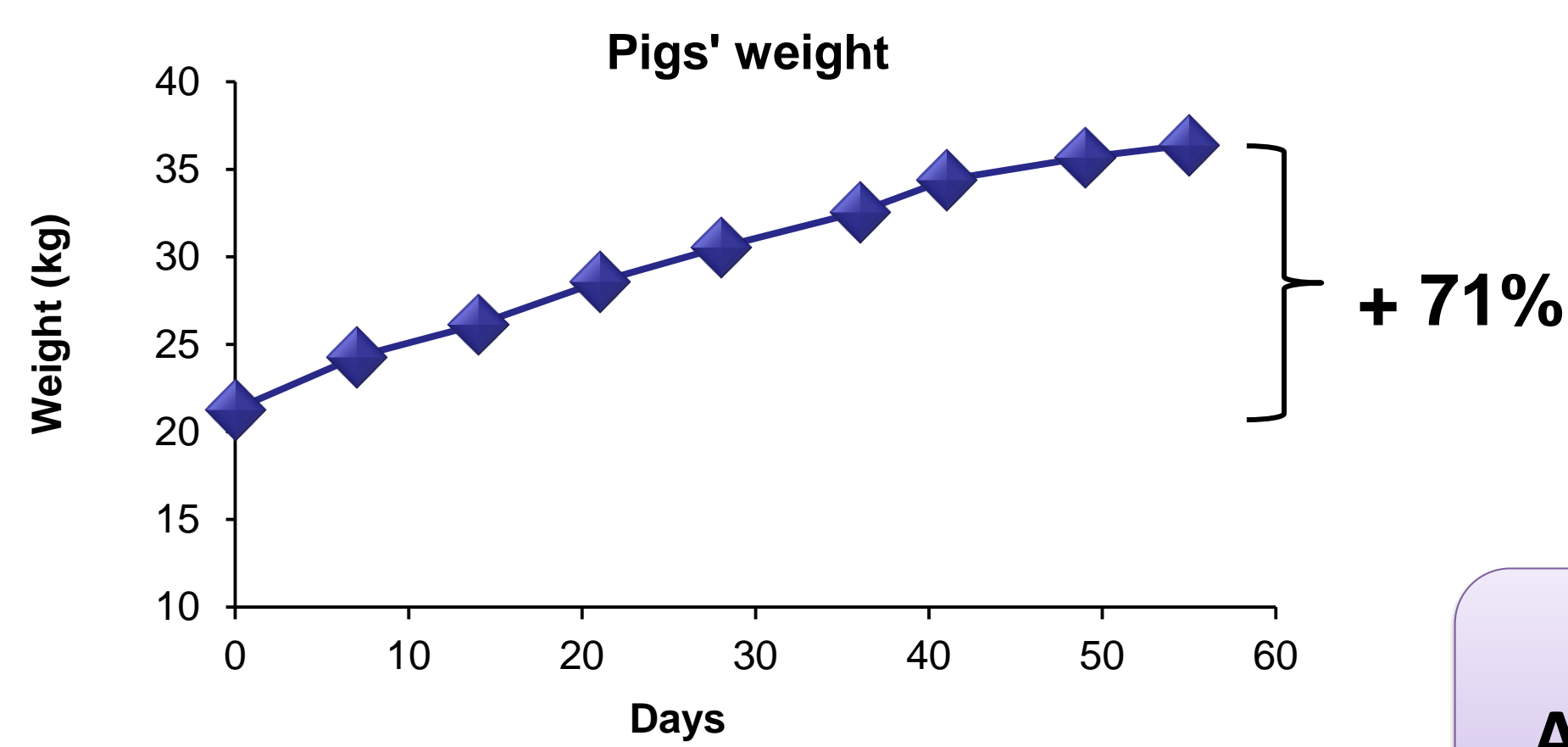
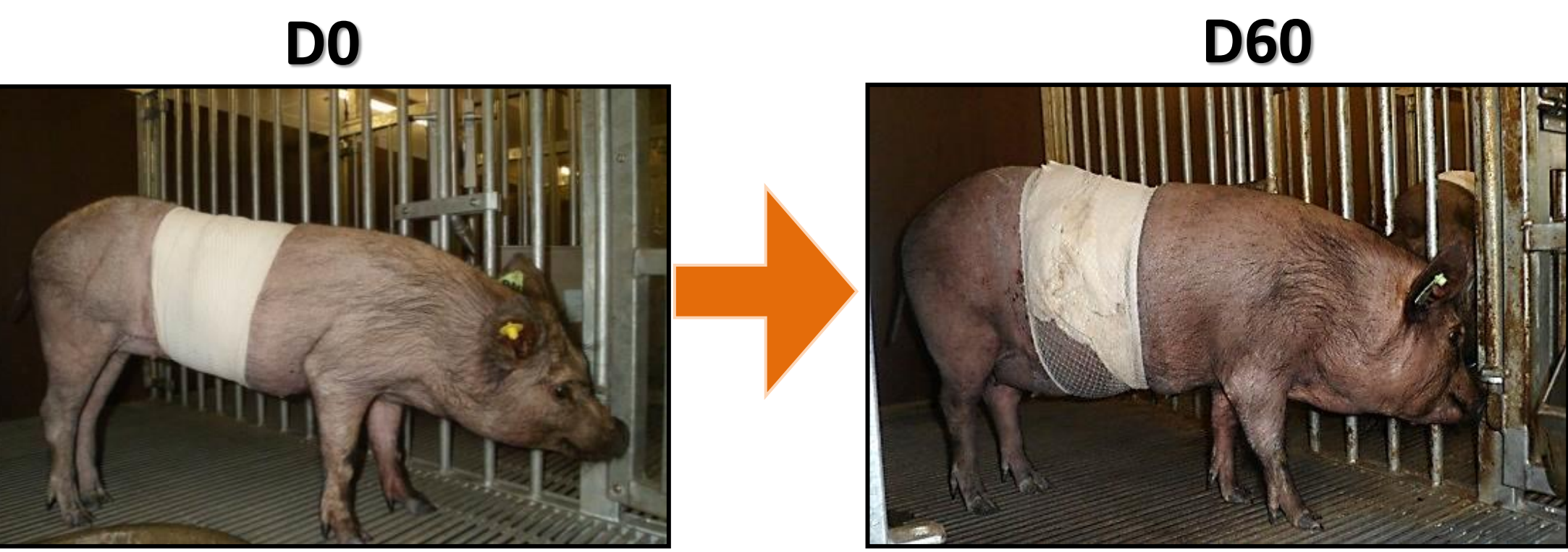


Urinary metabolomics analysis (UPLC-QToF)

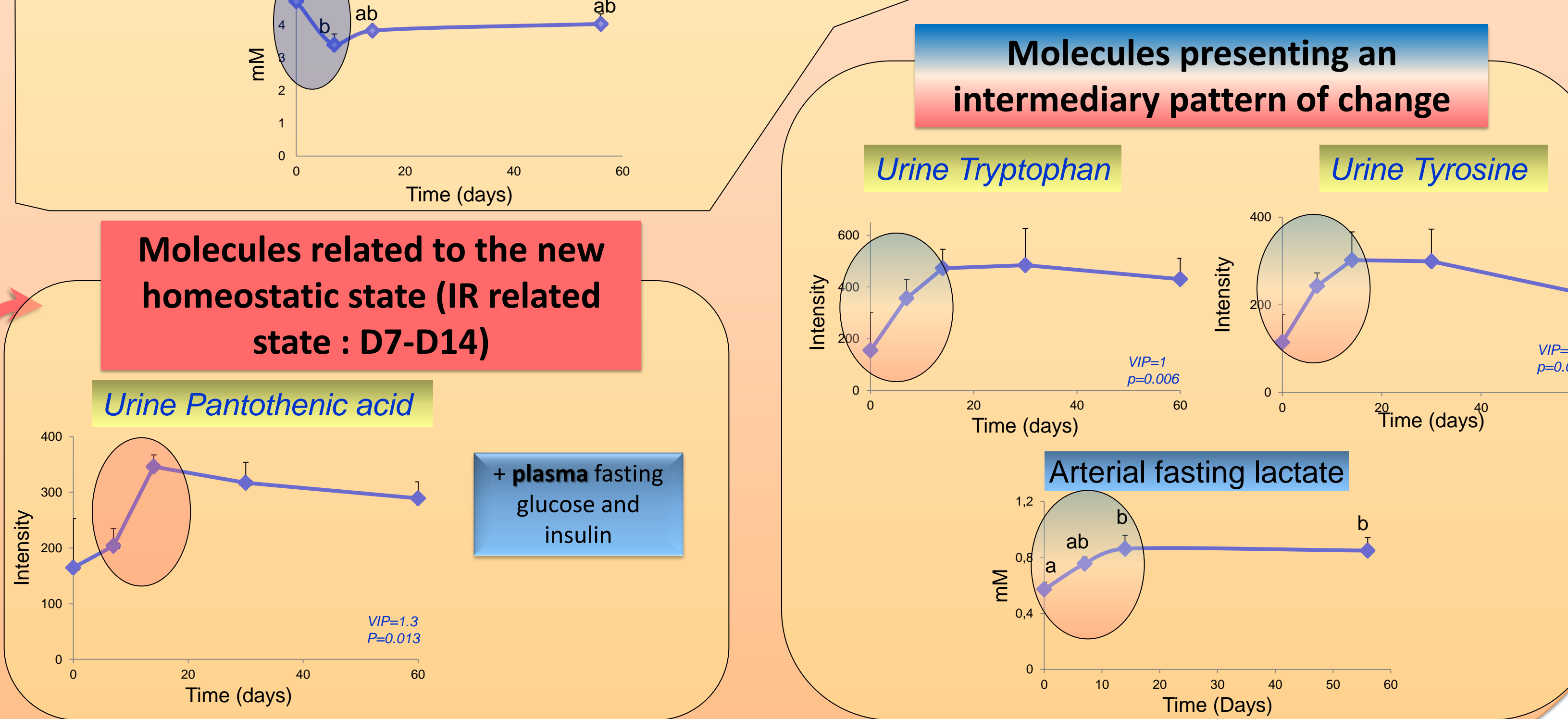
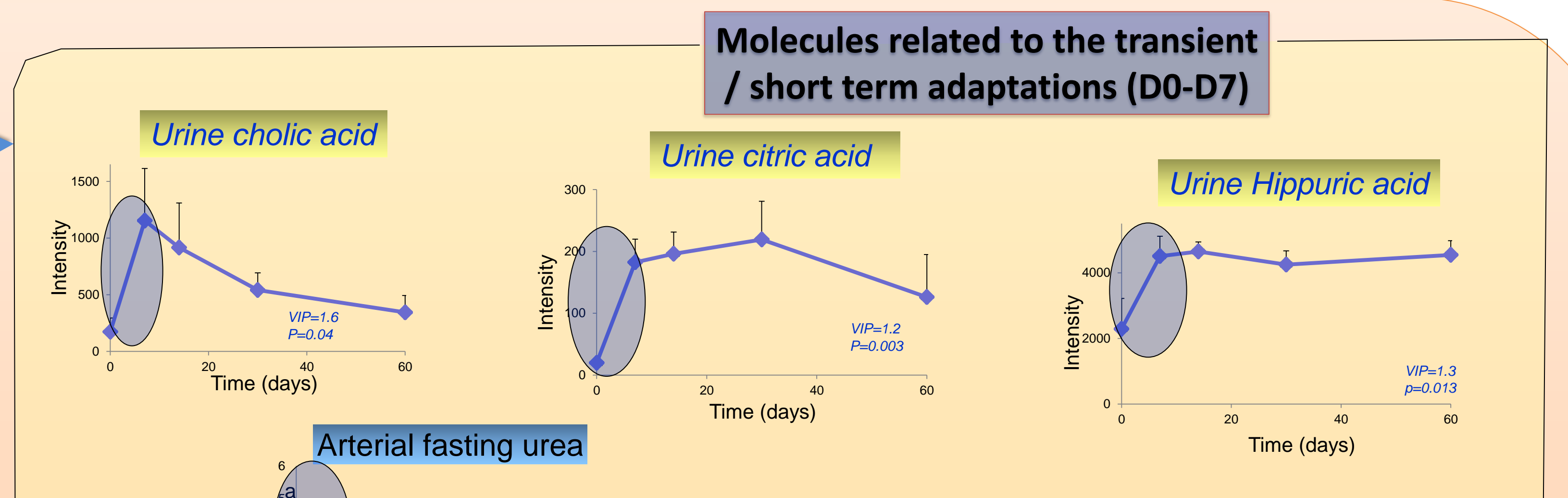
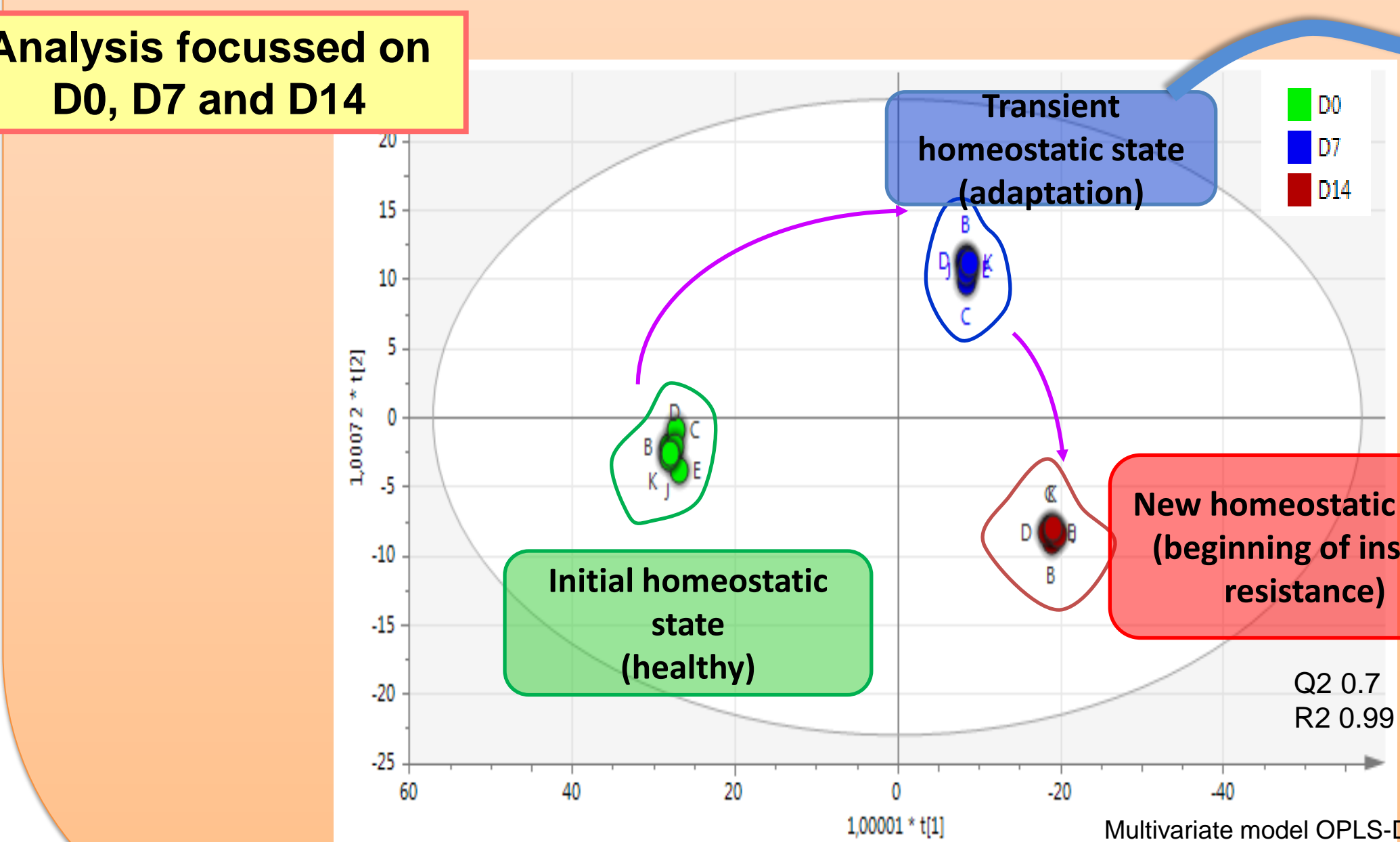
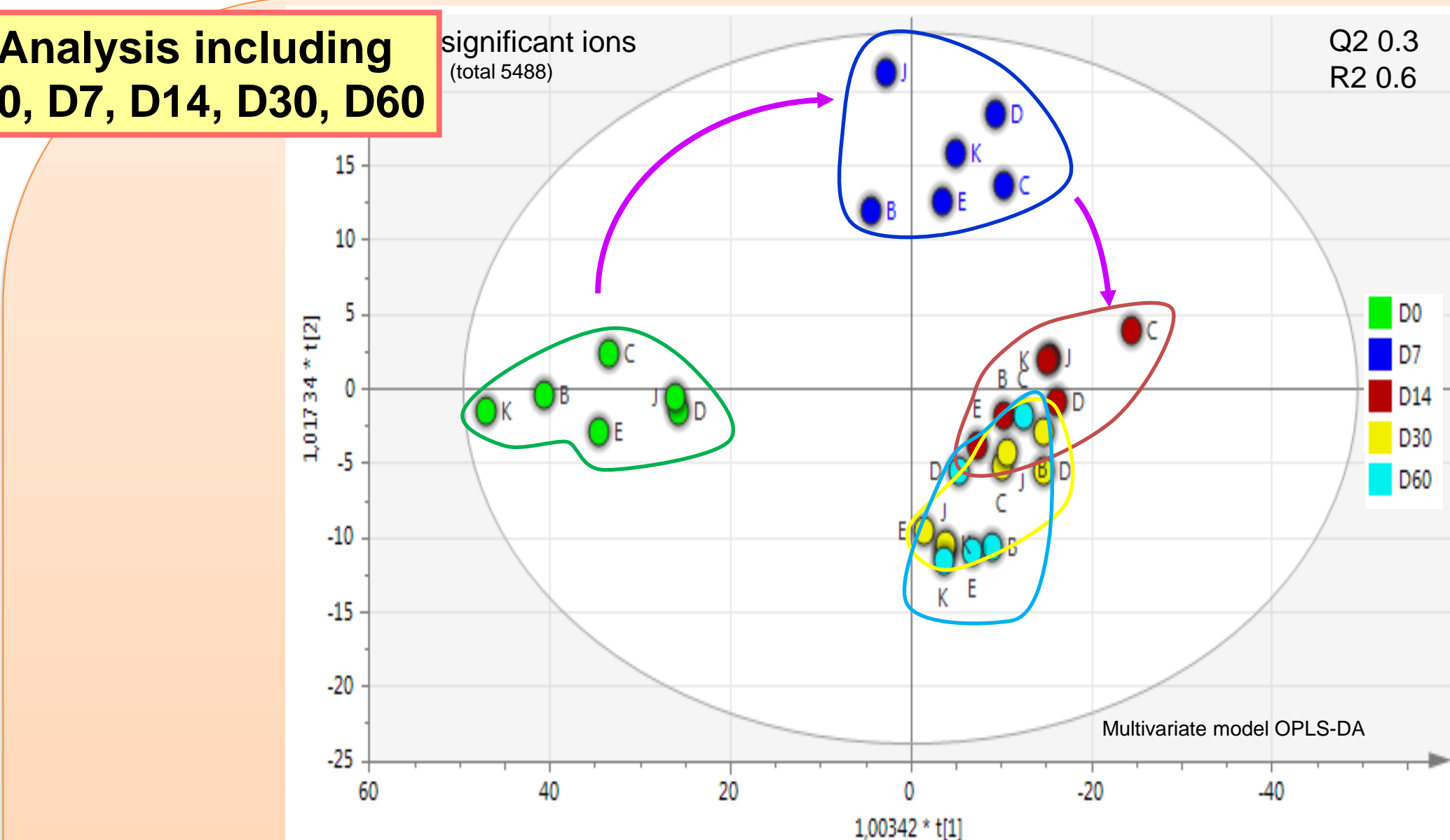
1/ Detection of insulin resistance with the « classical plasma biomarkers » : fasting glucose and insulin



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.



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



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

Urine Pantothenic acid

+ plasma fasting glucose and insulin

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