

# Glycaemic Response in Pigs Derived from Assisted Reproductive Technologies: a Long Term Follow-Up Study

Raquel Romar<sup>1</sup>, Jon Romero-Aguirregomezcorta<sup>1</sup>, Sonia Heras<sup>1</sup>, Evelyne Paris-Oller<sup>1</sup>, Cristina Soriano-Úbeda<sup>2</sup>, Joaquín Gadea<sup>1</sup>, Pilar Coy<sup>1</sup>, Sebastián Cánovas<sup>1</sup>

1.Department of Physiology, Universidad de Murcia, International Excellence Campus for Higher Education and Research (Campus Mare Nostrum), Murcia, Spain  
Institute for Biomedical Research of Murcia (IMIB), Murcia, Spain

2.Department of Veterinary Medicine, Surgery, and Anatomy, Veterinary School, University of León, León, Spain

Emerging evidence suggests that assisted reproductive technologies (ART) may predispose individuals to an increased risk of metabolic disorders including diabetes. Previous studies have reported a different glycaemic response in growing pigs derived from ART, but it is unknown whether these differences persist into adulthood and old age. The aim of the present work was to gain insight into the evolution of glycaemic response of ART-derived pigs across their life.

Pigs born through artificial insemination (AI group) and transfer of *in vitro*-produced embryos (IVP group) underwent a glucose challenge at young age (45 days), adulthood (365 days), and old age (1250 days). The number of animals, respectively for AI and IVP groups, were 16 and 29 (young), 13 and 21 (adult), and 9 and 13 (old). Oral glucose tolerance test (OGTT; 1.75g/kg body weight) was performed after overnight fasting and 1h water withdrawn. Blood samples were obtained from auricular vein prior (T=0 min) and 15, 30, 45, 60, 90, 120, 150 min following glucose intake. Glycemia was immediately determined by glucometer test strips (GlucoMenLX Plus). The area under the curve analysis was used to identify differences ( $p < 0.05$ ) between age and experimental groups.

Minimum and maximum glycemia recorded during the three OGTT tests were 22.0 and 319.0 mg/dl respectively. Both the origin of the animals (AI vs. IVP) and the age (young-adult-old) significantly affected the glycaemic response ( $p < 0.05$ ). At a similar age, there were no differences in fasting glucose between AI and IVP groups (young:  $81.70 \pm 4.67$  and  $90.25 \pm 8.27$  mg/dl; adult:  $91.13 \pm 7.41$  and  $87.70 \pm 7.14$  mg/dl; old:  $65.12 \pm 3.50$  and  $59.93 \pm 4.12$  mg/dl) being all data within the physiological range for pigs (60.00-100.00 mg/dl). Mean glycaemia during OGTT was 25-30 mg/dl higher in young and adult animals compared to old pigs ( $p < 0.05$ ). Evolution of glycemia curves showed a monophasic pattern during youth in both groups, as it is commonly observed in young pigs and we have previously described. Interestingly, the response pattern shifted into a biphasic curve in adult-AI pigs, returning to a monophasic response during old age, whereas in IVP animals the biphasic response appeared only during old age. The lack of studies in older pigs makes difficult to interpret the biphasic response which in other species is associated with a certain resistance to insulin.

Moreover, differences between origin of animals were observed at young and old ages ( $p < 0.05$ ). Therefore, young-IVP animals had higher AUC during the initial response to glucose challenge (15, 30 and 45 min) than young-AI pigs. However, old-IVP had lower AUC than old-AI pigs at the intermediate time of 60 min due to the biphasic glucose peak around this time. No differences between groups were observed during adulthood.

In conclusion, naturally and artificially conceived pigs show different responses to glucose challenge across life. The clinical relevance and implications of such differences should be further studied.

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