

## Invited Speaker Plenary 5: Obesity/Diabetes/Metabolic Syndrome

### Use of the pig and obese minipig in nutritional and obesity research

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**Background** - To develop preventative and treatment strategies to control obesity and resultant metabolic syndrome it is necessary to have animal models to study the aetiology of the metabolic syndrome. Obese minipigs are thought to be a good model for studying metabolic syndrome as they display insulin resistance and exhibit impaired glucose and amino acid utilisation. In this paper data supporting the use of the pig as a model for nutritional and obesity studies will be presented as will studies investigating some interventions, such as high protein diets.

**Review** - The pig is considered to be very similar to the human with respect to many aspects of intermediary metabolism allowing us to study how dietary factors may reduce the risk factors for a number of diseases.<sup>1-3</sup> More recently, our attention has turned to obesity and the possibility that high protein diets, particularly those of dairy origin, may be beneficial in satiety and weight control.<sup>4</sup> The major proteins present in milk include  $\beta$ -lactalbumin,  $\alpha$ -lactoglobulin, immunoglobulin, bovine serum albumin, and the caseins:  $\kappa$ -casein,  $\beta$ -casein, and the  $\alpha$ -caseins. In addition, they contains glycomacropeptide (GMP) that is cleaved from  $\kappa$ -casein during casein precipitation. Some whey protein isolates (WPI) are relatively high in GMP, which is thought to have intrinsic satiating effects. In a study conducted to demonstrate the relative differences in insulin sensitivity between lean and obese pigs 8 obese mini (141 kg, 50% body fat) and 8 conventional lean (111 kg, 27% body fat) female pigs were offered diets containing two sources of protein (WPI vs soy protein isolate (SPI)) formulated to provide 100% of CP requirements for at least 10 wk. The WPI contained 46, 30, and 8%  $\beta$ -lactalbumin, GMP and  $\alpha$ -lactoglobulin, respectively. Pigs were infused i.v. with insulin at 0.6 and 6.0 mU/(kg.min) and blood glucose and amino acids clamped at pre-infusion values by i.v. infusion of dextrose and amino acids. Pigs were also injected with epinephrine (3.0  $\mu$ g/kg) and the metabolic responses measured. Dextrose (11.8 vs 9.2 mg/(kg.min),  $P = 0.08$ ) and amino acids (1.42 vs 0.80 mg/(kg.min),  $P = <0.001$ ) required to maintain glycemia and plasma lysine were higher in lean pigs. Also, the plasma NEFA response to epinephrine was muted in the minipigs (0.48 vs -0.28 mM.min,  $P < 0.001$ ). Next, to test whether dietary protein could influence metabolism, 16 obese adult female minipigs (133kg, 50% body fat) were allocated to a 2x2 factorial design with the respective factors being source of protein (WPI vs SPI) or level of dietary protein (11 (LP) vs 22% (HP) CP). After consuming their respective diets *ad libitum* for 10 weeks insulin infusions as outlined above were conducted. Feed intake was lower in pigs fed the HP diet (2070 v. 2352 g/d,  $P < 0.001$ ), particularly in pigs fed WPC (1951 v. 2408 g/d) as indicated by an interaction ( $P = 0.027$ ) between source and level. Pigs consuming the HP diet deposited less weight (231 v. 382 g/d,  $P = 0.045$ ) and had a lower ratio of fat:lean in the ham (0.70 vs 0.76,  $P = 0.026$ ) at 8 weeks than those fed the LP diet. Protein source had no effect on the amount of dextrose infused to maintain euglycemia (108 v. 115 mL/h  $P = 0.59$ ) but the amount infused was lower in the minipigs fed the LP diet (101 v. 125 mL/h,  $P = 0.048$ ). Protein source had no effect on the amino acid infusion rate required to maintain plasma lysine concentrations (50 v. 50 mL/h,  $P = 0.98$ ) but the amount infused was lower in pigs fed the LP diet (45 v. 55 mL/h,  $P = 0.030$ ).

**Conclusions** - Obese minipigs exhibit insulin and epinephrine resistance. A HP diet reduces feed intake, weight gain and fat deposition and reduced insulin resistance in obese minipigs. The HP diet containing WPI that was enriched in GMP had the greatest effect upon feed intake and weight gain.

#### References

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