CHANGES IN GLUCOSE TRANSPORTER REGULATION IN THE LACTATING MOUSE

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The need to understand the factors that influence nutrient partitioning are central to the development of strategies to improve the biosynthetic capacity of the high producing cow. Due to the invasive nature of these studies, we use a highly fecund strain of mice, the QSI5 line, as a model for the high producing cow. Unlike the cow, however, this mouse appears to conserve bodyweight despite the metabolic drain that is associated with supporting sufficient milk for litters of up to 18 pups (Muhammad *et al*. 2003). Clearly the supply of glucose is central to milk lactose biosynthesis and milk volume. In this study, we investigated the relative importance of 2 key cellular glucose transporters, the non-insulin dependent Glut 1 and the insulin-dependent Glut 4, in order to understand how glucose is partitioned between the muscle and mammary tissues over the lactation cycle.

Multiparous QSI5 mice (n=13) were maintained at 21^{o}C in a 12:12 h light:dark cycle and euthanased by CO_2 asphyxiation when pregnant (day 16 of gestation; n=4), lactating (day 10 post-partum; n=4) or at involution (day 20 post-partum with pups removed at day 18; n=5). Abdominal mammary tissue (gland 4) and a sample of *M. longissimus* muscle were collected and frozen in liquid N_2 and stored at -80^{o}C pending analysis. Total RNA was extracted from mammary tissue using an integrated phenol/guanidine thiocyanate-based lysis with RNA on a silica gel membrane (Qiagen, Valencia, USA), and from muscle using an acid guanidinium thiocyanate phenol chloroform extraction method (Tri Reagent, Sigma, St Louis, USA). The cDNA was prepared by reverse transcription and specific primers designed for Glut 1 and Glut 4. Specific transcript expression was quantified by real time PCR (RotorgeneRG-3000; Corbett Scientific, Sydney) using specific primers for the highly stable house keeping gene, acidic ribosomal protein (ARP) for normalisation of analyses (Table 1).

Table 1. Changes in Glut 1 and Glut 4 expression over the murine lactation cycle (mean ± s.e.m. fold changes in expression relative to late pregnant tissue).

Tissue	Glut 1			Glut 4		
	Late pregnancy	Peak lactation	Involution	Late pregnancy	Peak lactation	Involution
Muscle	1.00 ± 0.68 ^{a}	0.92 ± 0.58 ^{a}	1.39 ± 1.26 ^{a}	1.00 ± 0.33 ^{a}	1.96 ± 0.40 ^{a}	2.10 ± 0.33 ^{a}
Mammary	1.00 ± 0.14 ^{a}	12.02 ± 1.21 ^{b}	2.92 ± 1.15 ^{a}	1.00 ± 0.54 ^{a}	3.27 ± 0.26 ^{b}	1.34 ± 0.32 ^{a}

Means with different superscripts within tissue are significantly different (P<0.05).

The expression of ARP (the number of cycles for a signal to reach an arbitrary threshold) was significantly (P<0.05) up-regulated in mammary tissue at peak lactation (14.2 ± 0.21) and involution (14.5 ± 0.36) relative to late pregnancy (13.4 ± 0.20). No changes, however, were recorded in muscle tissue over the cycle. Although this will influence expression levels in Table 1, it does not detract from the relative importance of the insulin independent Glut 1 transporter relative to the insulin dependent Glut 4 to meet the increased demand for glucose during lactation. Given that insulin is an obligatory member of the lactogenic hormonal complex, it is likely that its role in amino acid transport may be more important than in the stimulation of glucose uptake. In contrast, insulin plays a more important role in glucose uptake in muscle. Since peripheral insulin resistance is an important mechanism for nutrient partitioning, it is clear that the greater dependency on Glut 1 for glucose supply in lactation ensures that this mechanism is unable to alter glucose supply for osmolar lactose synthesis, thus ensuring milk volume is not affected. In contrast, insulin resistance has the potential to decrease glucose uptake in muscle through Glut 4 down-regulation, thereby, partitioning glucose for lactogenesis.

By the conduct of this experiment, we have provided evidence for 1 possible mechanism for the enhancement of milk output through preferential nutrient partitioning to the mammary gland.

MUHAMMAD, Z., WYNN, P.C., THOMSON, P.C. and SHEEHY, P.A. (2003). *Rec. Adv. Anim. Nutr. Aust.* **14**, 10A.

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