The Tammar Wallaby: A Model Organism for Fetal-Stage Growth Manipulation

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The developing mammal is incredibly plastic in its ability to cope with diminished or excessive resources, and to modify its growth trajectory and developmental progress accordingly. Possibly the best example of this are the classic experiments of Walton and Hammond [1] and later by Allen et al. [2] that demonstrate the rapid and excessive growth of ponies gestated in thoroughbred horses and the opposite effect of horses gestated in ponies. Camel-Llama hybrids are also smaller at birth and then recover to normal adult sizes during post-natal life [3]. These effects are not only the result of extended or shortened gestation periods but also of uterine space, placental investment and altered nutrient and oxygen exchange [2]. While there is a genetic contribution to ones size at birth, much of the natural variation within species can be accounted for by the size of the mother [4,5]. This is because larger mothers can contribute a greater relative level of nutrition during maternally supported development (placentation and lactation).

The endocrine effects of early mammalian growth perturbations are poorly understood yet the trajectory of growth during fetal and post-natal life is important predictors of future health and disease [6]. Low birth weight in particular, is associated with a range of adult diseases including obesity, stroke, diabetes and cardiovascular disease. For this reason, mammalian models of growth manipulation are increasingly relevant for human medicine as well as basic science. Current models use mainly sheep or rodents, and rely on alterations to the maternal diet (under/over-nutrition or supplementation) or surgical ligation of the uterine vessels during pregnancy to reduce or enhance the birth weight of the offspring [7]. In rodents, neonates can also be cross-fostered to mothers consuming higher calorie diets, thereby producing richer milks. Using this strategy, various combinations of pre and post-natal nutrient restrictions and/or enhancements can be implemented [8].

While eutherian mammals, particularly the sheep, have the advantage that the chronology of their reproduction (the length of gestation, size at birth and developmental maturity) is very similar to the human system, there are also some limitations. Placentation must balance the metabolic needs of the mother, placenta and fetus all of which can be influenced by hormones and growth factors in the bloodstream that may reflect either the stage of pregnancy or the response to a particular nutritional or surgical manipulation. Further complexity exists in models of maternal over-nutrition where animals may eat variable quantities of a calorie enhanced feed, of which the placenta may extract a variable amount of additional nutrients, thereby targeting the fetus only indirectly.

Marsupial mammals offer a more targeted model for fetal-stage growth manipulation because birth occurs at a much earlier stage of development relative to eutherian mammals, and the quantity and quality of milk changes progressively as development proceeds in the pouch. These changes in milk composition are species specific and controlled by the mother according to an intrinsic genetic program [9,10]. Therefore, the composition cannot be altered by changes in the sucking regimen of the pouch young or the volume of milk removed.

The tammar wallaby, *Macropus eugenii*, is highly plastic in its growth and developmental response to nutrient manipulation. Pouch young cross-fostered to the mammary glands of conspecific females, even at moderately advanced lactational stages, have dramatically increased rates of growth and development [9,11]. In contrast, the pouch young of small/juvenile females, pouch young cross-fostered to mothers at earlier lactational stages, or to the pouches of different species can have significantly retarded growth trajectories [10-12].

We hypothesize that nutrition alone is driving the changes observed in these marsupial young that have altered diets but there is also the possibility that it is the result of changes in hormones in the milk like insulin-like growth factor-I (IGF-I), which increases in concentration in the milk as lactation proceeds peaking at 200 days post-partum [13]. Nevertheless, the tammar wallaby may be a vital mammalian model going forward to clarify how dramatic variations in nutrition lead to growth acceleration or retardation of the young.

References


