Maternal nutrition and skeletal muscle development in the offspring: long-term impact on health

S.A. Bayol, Centre for Physical Activity and Nutrition Research, School of Exercise and Nutrition Sciences, Faculty of Health, Deakin University, VIC, 3125, Australia.

Skeletal muscle plays a central role in metabolic health. It accounts for about 40% of body mass, 20% of energy expenditure and is a major site for post-prandial glucose uptake. Furthermore, skeletal muscle mass is associated with better recovery from cardiac failure and cancer (reviewed by Wolfe, 2006) and muscle force is a predictor of longevity (Srikanthan & Karlamangla, 2014). Therefore, establishing adequate muscle mass in early life is crucial for lifelong health.

It is well characterized that muscle fibre formation (myogenesis) is completed by birth in most mammals, including humans, and that fibre number, a determinant of adult muscle mass, can vary depending on maternal nutritional levels during pregnancy (reviewed by Bayol *et al.*, In Press and Brown, 2014). Specifically, several studies carried out across a broad range of mammalian species have shown that nutrient restriction *in utero* leads to a permanent reduction in the number of muscle fibres that form in the offspring. This is then strongly associated with reduced muscle mass and insulin resistance into adult life, which can initiate the development of the metabolic syndrome and cardiovascular disease (reviewed by Brown, 2014). Growing evidence suggests that maternal obesity and/or excessive gestational weight gain are just as detrimental as undernutrition to muscle development (Bayol *et al.*, In Press). We and others have begun to bring evidence that skeletal muscle of offspring born to obese mothers exhibits reduced fibre number and/or increased ectopic fat accumulation. This leads to impaired contractile function and metabolic disruptions into adult life (reviewed by Bayol *et al.*, In Press). The underlying cell and molecular mechanisms by which this is mediated remain to be fully established. However, phenotypic and gene expression studies point to a stem cell differentiation shift away from myogenesis in favour of adipogenesis. This is further supported by a number of *in vitro* studies that have shown that excess lipids, insulin or glucose can inhibit myogenesis and/or favour differentiation of common precursor cells down the adipogenic lineage at the expense of myogenesis. Furthermore, muscle regeneration, which involves the activation of resident stem cells and their differentiation along a multistep process that is similar to myogenesis, is impaired in obese individuals (Akhmedov & Berdeaux, 2013). Therefore, high fat, high glucose and high insulin conditions brought in by maternal diet-induced obesity to the developing foetus may help explain the impaired myogenesis reported in offspring born to over-nourished mothers.

Taken together, evidence to date suggests that sub-optimal maternal nutrition during pregnancy, whether under- or over-nutrition, impedes skeletal muscle development in the offspring and its subsequent function into adult life. Given the importance of skeletal muscle in health, efforts should be targeted towards establishing the underlying mechanisms involved such that evidence-based targeted interventions can be developed. It is unclear if and to what extent early life exercise can reverse these defects.

Akhmedov D, Berdeaux R. (2013) *Frontiers in Physiology*, **4**: 371.
Bayol SAM, Bruce CR, Wadley GD. *Journal of Developmental Origins of Health and Disease*, In Press.
Brown L. (2014) *Journal of Endocrinology*, **221**: R13-29.
Gatford KL, Kaur G, Falcão-Tebas F, Wadley GD, Wlodek ME, Laker RC, Ebeling PR, McConell GK. (2014) *American Journal of Physiology. Endocrinology and Metababolism*, **306**: E999-1012.
Srikanthan P, Karlamangla AS. (2014) *American Journal of Medicine*, **127**: 547-53.
Wolfe RR. (2006) *American Journal of Clinical Nutrition*, **84**: 475-82.