

Supplementary Material

The tammar wallaby: a non-traditional animal model to study growth axis maturation

Jennifer A. Hetz^{A,B}, Brandon R. Menzies^{A,C}, Geoffrey Shaw^A and Marilyn B. Renfree^A

^ASchool of BioSciences, The University of Melbourne, Vic. 3010, Australia.

^BEscuela de Agronomía, Pontificia Universidad Católica de Valparaíso, Casilla 4-D, Quillota, Región de Valparaíso, Chile.

^CCorresponding author. Email: menziesb@unimelb.edu.au

Table S1. Growth alterations resulting from genetic disruptions in growth factors

| Gene | Function | Deficiency | Reference |
|--------|--|---|--|
| GH | Stimulates post natal growth | Excess of birth weight relative to length; progressive postnatal growth failure; slow muscle development, and altered body composition | Gluckman <i>et al.</i> 1992 |
| GHR | Regulates GH actions in target tissues | Short stature, truncal obesity; low plasma IGF1; elevated serum GH; absent, low, or dysfunctional serum GH binding protein (GHBP); and resistance to GH | Laron 1993; Zhou <i>et al.</i> 1997 |
| IGF1 | Stimulates pre and post natal tissue growth | Severe intrauterine and postnatal growth retardation; perinatal lethality; developmental defects in bone and muscle; increased serum GH levels, increased weight of kidney, heart, liver, and brain | Liu <i>et al.</i> 1993; Woods <i>et al.</i> 1996; Liu and LeRoith 1999 |
| IGF2 | Stimulates prenatal growth | Intrauterine growth restriction | DeChiara <i>et al.</i> 1990; Baker <i>et al.</i> 1993 |
| IGFALS | Increases half life and controls IGF1 bioavailability in adults Forms a ternary complex with IGFBP3 | No effects on survival rates and birth weights, but postnatal growth deficiency and reduction | Ueki <i>et al.</i> 2000; Domené <i>et al.</i> 2004 |

| | | | |
|--------|--|--|--|
| | | in IGF1 and IGFBP3 plasma concentration | |
| IGFBP3 | One of the major carrying protein for IGF1 and IGF2 in circulation, also modulator of IGFs bioactivity | No effects on circulating IGF1 | Lofqvist <i>et al.</i> 2007 |
| IGFBP2 | One of the principal binding proteins for IGF1 and IGF2 during development, controls bioactivity IGFs, widely expressed in fetal tissues | No phenotypic alterations, only reduction in spleen weight 30% | Wood <i>et al.</i> 1993; Schneider <i>et al.</i> 2000 |

Table S2. Effect of nutritional environment on growth factors during fetal and early post-natal life

| Gene | Under-nutrition | Over-nutrition | Species | Reference |
|--------|---|---|----------------------------------|--|
| GH | Higher concentration plasma. GH resistance. | Decreased plasma concentrations | Human, sheep, | Bauer <i>et al.</i> 1995; Albertsson-Wikland <i>et al.</i> 1997; Yasunaga <i>et al.</i> 1998 |
| GHR | Decreased hepatic abundance (in severe nutritional restriction). Reduction GH specific binding | Increased hepatic abundance and GH specific binding | Rat, sheep | Woodall <i>et al.</i> 1996; Rhoads <i>et al.</i> 2000a; Hyatt <i>et al.</i> 2004; Hyatt <i>et al.</i> 2007 |
| IGF1 | Decreased local expression, decreased hepatic expression and plasma concentration | Increased hepatic abundance and plasma concentration | Rat, sheep and mice | Oliver <i>et al.</i> 1993; Muaku <i>et al.</i> 1995; Woodall <i>et al.</i> 1996; Brameld <i>et al.</i> 2000; del Mar Plata <i>et al.</i> 2014 |
| IGF2 | Increased hepatic abundance | Increased hepatic abundance | Sheep, mice | Brameld <i>et al.</i> 2000; del Mar Plata <i>et al.</i> 2014 |
| IGFALS | Decreased hepatic abundance (in placental insufficient) | Increased hepatic abundance | Sheep | Rhoads <i>et al.</i> 2000a |
| IGFBP3 | Severe nutritional restriction decreased plasma concentration | Fat-enriched diets in neonates increased expression in subcutaneous fat | Human, sheep, guinea pig and pig | Gallaher <i>et al.</i> 1998; Carter <i>et al.</i> 2005; Verkauskiene <i>et al.</i> 2007; Sabin <i>et al.</i> 2011 |
| IGFBP2 | Increased plasma concentration and hepatic abundance (in severe chronic under-nutrition) | Fat diet in neonate increased expression in muscle | Rat, guinea pig and pig | Kampman <i>et al.</i> 1993; Woodall <i>et al.</i> 1996; Carter <i>et al.</i> 2005; Sabin <i>et al.</i> 2011 |