There is a significant increase in adult and childhood obesity in the United States with a

prevalence of over 39.8% and 18.5%, respectively (Hales *et al.*, 2015; Flegal *et al.*, 2016). Of concern, pre-pregnancy obesity has been increasing in tandem (Branum *et al.*, 2014). Maternal obesity has a long-term effect on the health of the mother (Sebire *et al.*, 2001) and the offspring (O’Reilly & Reynolds, 2013). Offspring of obese mothers are at a higher risk of developing insulin resistance (Samuelsson *et al.*, 2008; Mingrone *et al.*, 2008), which increases their risk of developing diabetes (Catalano *et al.*, 2009). Fetuses of obese mothers have a significantly higher HOMA-IR index compared to fetuses of lean mothers indicating that offspring insulin resistance can develop during gestation (Catalano *et al.*, 2009).

The underlying mechanisms by which maternal obesity influences offspring insulin resistance remain unclear. We propose to review the hypothesis that maternal obesity influences the offspring health through altering the maternofetal interface and placental transport capacity. The placenta is highly regulated to ensure adequate growth of the fetus in normal pregnancies (Gude *et al.*, 2004), but in obesity, placental transport capacity is modified. We will focus on the role of the placenta in modulating altered offspring outcomes, recent findings on placental micro- and macronutrient transport, and the underlying mechanisms and metabolic pathways that result in the impaired placental function.

The placenta is the rate-limiting step for fetal nutrient acquisition, and hence, fully understanding the placental nutrient transport will help develop future treatments that limit the effects of maternal obesity on the offspring. This review will also help bridge the gap in knowledge between potential mechanisms that alter the placental nutrient transport and the offspring risk of disease.

This review will include the following sections:

# Introduction

* Associations between maternal obesity and offspring obesity and metabolic disease

# Defining the placenta

* Overall structure and function of the human and animal placenta
* Placental differentiation and growth processes throughout gestation
* Placental responses to maternal endocrine and nutritional signals in lean and obese mothers

# Altered placental transport capacity in obesity

* Key nutrient transporters present on the placental maternal and fetal membranes
* How micro- and macronutrient placental transporters are altered in obesity and how this affects nutrient flux and macronutrient accretion in the fetus
* Alterations in metabolic and signaling pathways that result in altered nutrient transport at the placental level
* Emerging evidence on the role of placenta in determining offspring risk of disease in human and animal models

# Future directions

* Current gaps in our understanding of mechanisms of disrupted placental transport
* The effect of placental impaired function on offspring risk of disease
* Discussing the mechanisms by which altered transport could affect susceptibility to chronic disease in the offspring

# References

Branum AM, Kirmeyer SE & Gregory ECW (2014). National Vital Statistics Reports Prepregnancy Body Mass Index by Maternal Characteristics and State: Data From the Birth Certificate, 2014. Available at: https://www.cdc.gov/nchs/data/nvsr/nvsr65/nvsr65\_06.pdf [Accessed December 8, 2017].

Catalano PM, Presley L, Minium J & Hauguel-de Mouzon S (2009). Fetuses of Obese Mothers Develop Insulin Resistance in Utero. *Diabetes Care* **32,** 1076–1080.

Flegal KM, Kruszon-Moran D, Carroll MD, Fryar CD & Ogden CL (2016). Trends in Obesity Among Adults in the United States, 2005 to 2014. *JAMA* **315,** 2284.

Gude NM, Roberts CT, Kalionis B & King RG (2004). Growth and function of the normal human placenta. *Thromb Res* **114,** 397–407.

Hales CM, Carroll MD, Fryar CD & Ogden CL (2015). Prevalence of Obesity Among Adults and Youth: United States, 2015–2016 Key findings Data from the National Health and Nutrition Examination Survey. Available at: https://www.cdc.gov/nchs/data/databriefs/db288.pdf [Accessed December 8, 2017].

Mingrone G, Manco M, Mora MEV, Guidone C, Iaconelli A, Gniuli D, Leccesi L, Chiellini C & Ghirlanda G (2008). Influence of maternal obesity on insulin sensitivity and secretion in offspring. *Diabetes Care* **31,** 1872–1876.

O’Reilly JR & Reynolds RM (2013). The risk of maternal obesity to the long-term health of the offspring. *Clin Endocrinol (Oxf)* **78,** 9–16.

Samuelsson A-M, Matthews PA, Argenton M, Christie MR, McConnell JM, Jansen EHJM, Piersma AH, Ozanne SE, Twinn DF, Remacle C, Rowlerson A, Poston L & Taylor PD (2008). Diet-Induced Obesity in Female Mice Leads to Offspring Hyperphagia, Adiposity, Hypertension, and Insulin Resistance: A Novel Murine Model of Developmental Programming. *Hypertension* **51,** 383–392.

Sebire N, Jolly M, Harris J, Wadsworth J, Joffe M, Beard R, Regan L & Robinson S (2001). Maternal obesity and pregnancy outcome: a study of 287 213 pregnancies in London. *Int J Obes* **25,** 1175–1182.