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The Placental Phenotype Adapts to Chronic Hypoxia and Mitochondria-Targeted Antioxidant (MitoQ) Therapy in Rat Pregnancy

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Introduction: The placenta responds to adverse environmental conditions, such as maternal glucocorticoid over-exposure and dietary manipulation, by adapting its capacity for substrate transfer to maintain appropriate fetal growth and development (Fowden et al. *J Neuroendocrinol* 20(4):439, 2008). Comparatively little is known about placental adaptations to hypoxia and/or oxidative stress. Here, we determined the effect of maternal chronic hypoxia on placental morphology and established whether maternal treatment with MitoQ protected against hypoxia-induced alterations in placental structure.

Methods: Wistar dams were exposed to normoxia (N, 21% O₂) or hypoxia (H, 13% O₂) from days 6-20 of pregnancy +/- MitoQ (500µM in drinking water). On day 20, animals were sacrificed and weighed and the placentae were processed for stereology. One placenta per litter per group was used. This model does not affect maternal food intake.

Results: Neither hypoxic pregnancy or mitoQ treatment affected fetal growth (N: 3.6 ± 0 ; H: 3.4 ± 0 ; HM: 3.6 ± 0 ; NM: 3.4 ± 0 g). Relative to normoxia, the placental absolute volume and the labyrinthine fetal capillary surface area were significantly increased in hypoxic pregnancy (Fig. 1 A and B, $P < 0.05$). Maternal MitoQ treatment in hypoxic pregnancy additionally increased the maternal blood space surface area (Fig. 1C, $P < 0.05$).

Conclusions: The data show that the placenta adapts to chronic hypoxic pregnancy by increasing the fetal capillary surface within the labyrinthine transport zone to maintain fetal growth. Maternal mitochondrial targeted antioxidant therapy during hypoxic pregnancy improves perfusion on the maternal side of the placenta.

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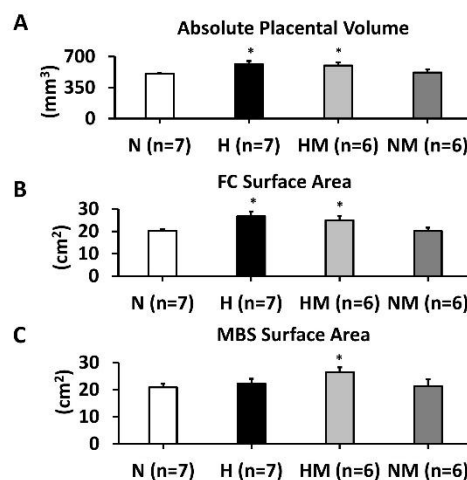


Figure 1. Placental morphology following chronic hypoxic pregnancy. Mean + S.E.M. for (A) absolute placental volume, (B) labyrinthine zone surface area of fetal capillaries (FC) and (C) maternal blood spaces (MBS). N, normoxia, H, hypoxia, HM, hypoxia+MitoQ, NM, normoxia+MitoQ. * $P < 0.05$ vs. N, General Linear Model. *n* numbers in parenthesis.

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