MICRONRNA SIGNATURE IN CARDIAC HYPERTROPHY PROGRAMMED BY MATERNAL DIET-INDUCED OBESITY

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BACKGROUND Gestational exposure to maternal obesity in humans and animals increases the risk of cardiovascular disease (CVD) in the offspring. We and others have shown that poor maternal nutrition alters tissue-specific microRNA profiles in the offspring and this may contribute to later disease predisposition.

HYPOTHESIS We hypothesised that differential expression of microRNAs mediates the effects of maternal diet-induced obesity on offspring cardiac structure and function.

METHODS A well-established mouse model of maternal diet-induced obesity where dams are fed a high fat/high simple carbohydrate diet was used to define consequences of exposure to maternal over-nutrition during pregnancy and lactation.

RESULTS Dams fed the obesogenic diet were significantly heavier on the day of mating, and remained heavier throughout pregnancy and at weaning compared to controls. Obese dams gave birth to smaller litters than control fed dams (average control n=8.2 [n=17 litters] vs obese n=6.0 [n=14 litters]. Pups from obese mums were born smaller (1.43g ± 0.05 [16] vs 1.72g ± 0.04 [15]; P=0.007), but underwent catch up growth becoming significantly heavier than control pups by day 14 (obese litters [n=16] vs control litters [n=15]; P=0.002). At day 21 pups were divided into 4 experimental groups: male offspring of control mums weaned either onto a control chow diet (CC) or an obesogenic diet (CO), and male offspring of obese mothers weaned onto either a control chow diet (OC) or an obesogenic diet (OO). Exposure to obesity during pregnancy programmed cardiac hypertrophy in OC offspring (CC vs OC, P=0.002), regardless of postnatal diet (CO vs OO, P=0.217). Profiling of microRNAs in the cardiac tissue of OC mice by array technology, revealed up regulation of two clusters, miR-15b/16-2 and miR-144/451.

CONCLUSIONS Collectively, these findings suggest that maternal diet-induced obesity during pregnancy programs changes in the cardiac miRNA profile in the offspring, which may contribute to their increased risk of CVD in later life.

Key Words: developmental programming, cardiovascular diseases (CVD), microRNA

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