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SAT-158 Offspring Exposed to Maternal High Fat Diet Exhibits Systemic Inflammation and Pancreatic Islet Dysfunction

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Abstract

Offspring born to overweight mothers are more likely to develop dysregulated immune response[1], obesity[1] and pancreatic islet dysfunction[2]. These offspring have increased inflammation at birth[3] and at least until childhood[4]. We hypothesize that heightened inflammation in offspring of overweight mothers increases offspring risks of pancreatic islet dysfunction. We induced maternal overweight by providing 45% high fat diet (HFD) to female mice 2 - 4 weeks before pregnancy until weaning. When compared to controls, P21 weanlings of HFD mothers had impaired glucose tolerance in dose and gender dependent manner [GTT AUC: male 2-week HFD* 30 ± 6% higher; male 4-week HFD* 37± 3% higher: 9-11/group; female 2-week HFD 13 ± 5% higher; female 4-week HFD* 22 ± 3% higher: 3-9/group, *p<0.05 compared to controls]. Glucose intolerance persisted in 8-week-old male from 2-week HFD mothers (p<0.05, n=6-9/group), with decreased pancreatic islets glucose induced calcium response measured using Fura-2AM calcium imaging (F1/F0 Con:2.00 ± 0.06, HFD2W: 1.69±0.12*, HFD4w: 0.71±0.09*, n =3/group). Cytokines production in the serum, macrophage response and metabolic phenotypes of offspring were assessed on postnatal day 21 (P21) and at 8 weeks old. Compared to control pups, weanling of HFD mothers had elevated serum/plasma IL-1b level along with increased polarization of M1 macrophages and decreased M2 macrophages, as well as an increase of IL-1b secretion in LPS-stimulated macrophages. At 8 weeks of age, HFD male offspring had increased activation markers of splenic dendritic cells indicating a development of systemic inflammatory response early in life. Taken together, our findings suggest that mice offspring from HFD mothers have pancreatic dysfunction, and an inflammatory response. This work is funded by the Riley Children's Foundation. 1. Kelishadi, R., Roufarshbaf, M., Soheili, S., Payghambarzadeh, F. & Masjedi, M. Association of Childhood Obesity and the Immune System: A Systematic Review of Reviews. Child. Obes. Print 13, 332-346 (2017). 2. Graus-Nunes, F. et al. Pregestational maternal obesity impairs endocrine pancreas in male F1 and F2 progeny. Nutrition 31, 380-387 (2015). 3. Dosch, N. C. et al. Maternal Obesity

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