Nephron Endowment is Influenced by Maternal Macronutrient but not Caloric Intake in the Early Postnatal Period, and is Principally Driven by Fat and Protein

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Background: Low nephron endowment is associated with greater risk of high blood pressure and chronic kidney disease. Nephrogenesis in humans is complete before term birth but continues for 2-3 days after birth in mice. Here we examined the influence of maternal macronutrient balance on postnatal nephrogenesis in mice.

Methods: At 15.5dpc pregnant Swiss mice were allocated to donor or foster groups. Donor dams were fed a macronutrient ratio similar to that of AIN93G (21% protein, 63% carbohydrate, 16% fat as a percentage of total energy). Foster dams were fed one of 10 diets varying in protein (8-42%), carbohydrate (20-76%) and fat (16-60%) content, replicated across two energy (caloric) densities (10.4MJ/kg and 14.7MJ/kg), yielding 20 different diets. At birth, pups from foster dams were replaced with pups from donor dams. From weaning (40dpc), all mice were fed a Barastoc diet until tissue collection at 6 months. Individual and interactive effects of maternal macronutrient intake on nephron endowment were analysed using the Geometric Framework of Nutrition.

Results: Nephron endowment ranged from 9,101 to 19,719 per kidney across the 20 diets. Nephron number was augmented with increasing maternal fat intake (coupled with moderate protein), with 250-350kJ fat and 125-150kJ protein during the postnatal nephrogenic period producing the highest nephron endowment. Caloric intake did not influence nephron number.

Conclusion: These findings demonstrate the marked and rapid effect of postnatal maternal nutrition, delivered via milk, on the final stages of nephrogenesis. We are currently investigating whether maternal nutrition can rescue nephron endowment in premature mice.