

LINLI LUO : FEEDING BROODSTOCK NILE TILAPIA (*Oreochromis niloticus*) WITH HIGH LEVEL OF CARBOHYDRATES: IMPACT ON METABOLISM AND EPIGENETICS OF OFFSPRING.
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Nutritional programming (NP) using hyperglucidic stimuli through high carbohydrate (CHO) feeding in broodstock may lead to modulation of CHO metabolism in the offspring. This study, therefore, aimed to analyze the long-term effects of NP induced by high CHO (HC) feeding in broodstock on CHO metabolism and epigenetic modulation in juvenile and adult offspring, as well as the effectiveness of plant-based diet utilization. The study included two experimental broodstock groups: one fed a high CHO/low protein (HC/LP) diet and the other fed a low CHO/high protein (LC/HP) diet. Offspring from both experimental groups were cultured through the juvenile stage for dietary challenge with the HC/LP diet (Experiment I) and through the adult stage for dietary challenge with the HC/LP diet (Experiment II). In addition, Experiment III involved dietary challenging the offspring of both groups with a plant-based diet.

In Experiment I, broodstock feeding with an HC diet could modulate CHO metabolism and related metabolic pathways in their offspring at the juvenile stage (week 17), including increased hepatosomatic index (HSI) and hepatic triglyceride levels, induction of muscular glycolysis (*pfkma* and *pfkmb*), and suppression of hepatic gluconeogenesis (*g6pca1*) and amino acid catabolism (*alat*). When juvenile offspring were challenged with the HC diet for 4 weeks (week 18–21), more pronounced intermediary metabolism and CHO metabolic responses were observed, including: 1) increased plasma glucose and triglyceride levels and decreased plasma protein levels, 2) increased hepatic and muscular fat, glycogen, and triglyceride contents, 3) induction of hepatic glycolysis (*gck* and *pkfr*), lipogenesis (*fasn* and *g6pd*), muscular glucose transport (*glut4*), and glycolysis (*hk1* and *hk2*), and 4) suppression of hepatic gluconeogenesis (*g6pca2* and *pck2*) and amino acid catabolism (*asat*). In addition, HC feeding in broodstock led to modulation of mRNA expression levels of enzymes associated with hepatic and muscular DNA (de)methylation, histone (de) methylation,

and (de)acetylation in juvenile offspring.

In Experiment II, the long-term NP effects of dietary HC stimulus in broodstock on the modulation of CHO metabolism persisted into adulthood (week 25). Parental HC stimulation increased HSI, induced muscular glycolysis (*pfkma* and *pfkmb*), and decreased hepatic amino acid catabolism (*alat*). Furthermore, during the dietary challenge phase (weeks 26–29), parental HC stimulation improved growth performance. The NP effects of parental HC stimulation also modulated several CHO metabolic responses in adult offspring, including the induction of hepatic glycolysis and lipogenesis, as well as muscular glucose transport, and the suppression of gluconeogenesis and amino acid catabolism in the liver. At the molecular level, parental HC stimulation modulated several enzymes related to DNA and histone (de)methylation and histone de(acetylation) in the liver and muscle, suggesting that epigenetic modifications are involved in the long-term NP effects of CHO in Nile tilapia.

In Experiment III, the long-term NP effects of dietary HC stimulus in broodstock on the modulation of CHO metabolism persisted into harvestable adult offspring (week 56), including the suppression of gluconeogenesis (*g6pca1* and *g6pca2*) and amino acid catabolism (*asat* and *alat*) in the liver, and the induction of glycolysis (*pfkma*) in muscle. After the offspring were exposed to high plant-based diets, irrespective of the NP effects of CHO in broodstock, the plant-based HC diet inhibited growth performance and increased hepatic and muscular fat, glycogen, and triglyceride levels, as well as whole-body fat content in fish. However, a history of broodstock HC stimulation improved growth performance and modulated CHO metabolism. Again, at the molecular level, parental HC stimulation modulated several enzymes related to epigenetics.

In conclusion, dietary HC stimulation in broodstock could exert long-term beneficial NP effects that improve the adaptability of the offspring to HC diets. This study suggests that parental nutritional regulation of CHO could serve as a tool to improve the efficient use of dietary CHO and plant-based diets in Nile tilapia.

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