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ChREBP in Response to Carbohydrates in Glucolipid Metabolism of Fish

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Abstract: Protein, as the most important nutrient in fish compound feed, however, due to the limited utilization ability of carbohydrate in fish, fish are "born with diabetes constitution". Inappropriate intake of sugars will disturb the normal glucolipid metabolism of fish and affect the growth and development of fish. Against this background, this review integrates the current research contents on the response of glucolipid metabolism to carbohydrate. Through the role of transcription factors such as ChREBP in carbohydrate, the regulation of related glucolipid metabolic pathways is explained from the perspective of molecular mechanism.

1. Introduction

Carbohydrate is an important ingredient in fish feed. Adding an appropriate amount of carbohydrate into the feed can reduce protein consumption of fish. Studies have shown that carbohydrate has an obvious effect on protein conservation in fish such as cachama (*Piaractus Brachypomus*) [1], Richardson(*Pelteobagrus Vachelli*) [2] and Common Sea perch(*Lateolabrax Japonicus*) [3],In addition, the feed utilization rate and protein retention Atlantic salmon(*Salmo salar*)[4],cod (*Gadus morhua*)[5] and different kinds of carp[6]of different species have been improved,However, other studies have shown that high carbohydrate intake of fish can reduce the growth rate, feed efficiency, immune response and the nutritional quality of fish fillets [7].Some studies have shown that high dietary carbohydrate levels lead to liver hypertrophy and increased glycogen levels in red snapper(*Lutjanus argentimaculatus*) [8] and Ridged-eye flounder(*Pleuronichthys cornutus*)[9]High sugar diet can make the body grow and accumulate fat. Studies have shown that carbohydrate can be converted into fat cells in the liver of fish such as Atlantic cod(*Gadus morhua*)[10] and Atlantic salmon(*Salmo salar*)[11].

Thus, while carbohydrates have important utility values, they can have adverse effects on fish, and the role of carbohydrates in fish needs to be further elaborated. Glucose metabolism and lipid metabolism are closely linked through glycolysis and lipid synthesis, Glucose and lipid metabolic pathways are regulated by transcription factors such as CHREBP.

2. Structure and Function of ChREBP

It was found in the study that transcription factor carbohydrate-reponsive -element-binding protein (ChREBP) plays a major role in the regulation of liver glycolysis and lipid formation.

ChREBP has a molecular weight of about 90kD and contains four phosphorylation sites closely related to its activity.

The by-pass product of glucose metabolism, Xylose-5-phosphate (XU-5-P), can activate protein phosphatase 2A, which promotes dephosphorylation of ChREBP. Dephosphorylated ChREBP enters the nucleus and forms a heterodimer, ChREBP/MLX, with the Max-like protein (MLX). ChREBP/MLX binds to the ChRE in the promoter region of the target gene and activates transcription of the target gene. The target genes of ChREBP are mainly some enzymes involved in glycolysis and lipid synthesis, so the activation of ChREBP can promote the transformation of glucose to lipid, in addition, it can maintain insulin sensitivity. Chrebp has two subtypes that are transcribed from different promoters,they are CHEBRAP-α and Chrebp -β, and both subtypes can be transcribed by glucose. ChREBP widely expressed in mammalian groups, it is highly expressed in liver, white fat, brown fat, small intestine, kidney and muscle, In addition, the liver can transform the excessive carbohydrate consumed by the body into fat through glycolysis and fat synthesis pathway, and transport it to the peripheral adipose tissue for storage, which is an important way for mammalian energy storage acquired in the evolutionary process [12].However, there is not much information about the presence of ChREBP in fish and its response to changes in the level of carbohydrates and other nutrients.

3. ChREBP Responds to Carbohydrate

At present, it is known that both fructose and glucose can activate ChREBP[13], but the relevant transcription mechanism is not clear from the current studies. In recent years, transcription factor ChREBP has become the main mediator of glucose to lipid gene expression, and is also a key determinant of lipid synthesis in vivo. Glucose can activate the expression of a large number of genes involved in glucolipid metabolism in the liver. According to gene chip analysis by Towle Laboratory, glucose can up-regulate the expression of 224 genes in liver cells, among which 139 are regulated by ChREBP[14].

Currently, glucose is known to induce ChREBP gene expression in liver both in vivo and in vitro [15].ChREBP is located in cytoplasm under low glucose condition, and in response to high glucose, it is concentrated in nucleus.Under the action of glucose, ChREBP is transferred from cytoplasm to nucleus, and through the formation of dimer and the activation of GRACE (Glucose response activation conserved element), it promotes the process related to glycolysis and lipid development.Correspondingly, Chrebp can also affect the uptake of glucose into adipose tissue by regulating the mRNA level of glucose transporter. Savanna et al. found in their study of Wuchang bream(*Megalobrama amblycephala* Yih)that high carbohydrate content significantly increased the expression level of chREBP-MLX heterodimer, and the high carbohydrate and high fat feed also significantly increased the expression level of ChREBP, indicating that high carbohydrate content increased the transport and synthesis of fatty acids in the body of Wuchang bream[16],However, other studies have found that the use of low or high carbohydrate does not change the phosphorylation degree of ChREBP, and ChREBP phosphorylation site mutation can still respond to glucose [17].

Although ChREBP is mainly a glucose reaction factor, recent observations in different animal models have shown that ChREBP plays a crucial role in fructose metabolism. Fructose has the same chemical formula as glucose. However, its metabolic effects seem to be more harmful than glucose, and it has been shown that excessive intake of fructose increases the generation of new fats and serum triglyceride levels ,leading to insulin resistance and dyslipidemia in the liver. Fructose can activate ChREBP transcriptional activity by increasing DNA binding, through XU-5-P phosphorylation, O-glycation, and acetylation.In both subtypes of ChREBP, the gene encoding

ChREBP-βis more sensitive to fructose. Recently, Kim M et al. showed that high-fructose diets significantly induced ChREBP- βexpression in the liver and intestines, followed by increased glycolysis, fructose decomposition, and lipogenesis gene expression [18].In the zebrafish study, it was found that high fructose could cause endoplasmic reticulum stress and oxidative stress, leading to a significant increase in the expression of ChREBP mRNA [19].Interestingly, no difference in Chrebp expression was found in rats fed glucose and fructose respectively [20].

4. Conclusion

The explanation for the low utilization capacity of carbohydrate in fish has not been unified, and the relevant regulatory mechanism is still unclear.

Therefore, deepening the fish to study the response of the lipid metabolism of carbohydrate, especially related transcription factors such as CHREBP and regulatory mechanism, and strengthen the biological functions of related regulatory factors, is a better use of carbohydrates, the key to solve the problem of protein are in short supply, and to promote healthy growth of fish and achieve the goal of preventing metabolic disorders.

References

[1] VSQUEZ TORRES W,ARIAS CASTELLANOS J A. Effect of dietary carbohydrates and lipids on growth in cacham a (Piaractus brachypomus) [J]. Aquacult Res,2013,44(11):1768-1776.

[2] Yang Y, Chen L q, LI Y C, et al. Effect of feed sugar level on growth, body composition and serum bio chemical indexes of pseudobagrus fulvidraco [J].Journal of Fudan University: Natural Science edition, 2011 (05):625-631.

[3] Dou Bing-shuai, Liang Meng-qing, Zheng Keke, et al. Effects of carbohydrate level in feed on growth, ph ysiological parameters and body composition of bass [J].Advances in fishery science, 2014,35 (1) : 46-54.

[4] Hemre G I , Sandnes K , Lie, et al. Carbohydrate nutrition in Atlantic salmon, Salmo salar L.: growth and feed utilization[J]. Aquaculture Research, 2010, 26(3):149-154.

[5] Kristin H . Nutrition in cod (Gadus morhua) larvae and juveniles[J]. Ices Journal of Marine ence, 2006(2):267-274.

[6] Erfanullah, Jafri A K . Growth rate, feed conversion, and body composition of Catla catla, Labeo rohita, and Cirrhinus mrigala fry fed diets of various carbohydrate-to-lipid ratios[J]. J.world Aquacult.soc, 2010, 29(1).

[7] Hemre G I , Mommsen T P , KROGDAHL. Carbohydrates in fish nutrition: effects on growth, glucose metabolism and hepatic enzymes[J]. Aquaculture Nutrition, 2015, 8(3):175-194.

[8] Furuchi, M. & Yone, Y. (1971) Studies on nutrition of red sea bream. 4. Nutritive value of dietary carbohydrate. Re p. Fish. Res. Lab., Kyushu Univ. (Japan), 1, 75–81.

[9] Cowey C B , Adron J W , Brown D A , et al. Studies on the nutrition of marine flatfish. The metabolis m of glucose by plaice (Pleuronectes platessa) and the effect of dietary energy source on protein utilizatio n in plaice[J]. British Journal of Nutrition, 1975, 33(2):219-231 [23]Postic C , Dentin R , Denechaud P D , et al. ChREBP, a transcriptional regulator of glucose and lipid metabolism.[J]. Annual Review of Nutr ition, 2007, 27(1):179-192.

[10] G.㊣. Hemre, Kahrs F . 14C-glucose injection in Atlantic cod, Gadus morhua, metabolic responses and excretion via the gill membrane[J]. Aquaculture Nutrition, 1997, 3(1):3-8.

[11] G-I. Hemre, Storebakken T . Tissue and organ distribution of 14C-activity in dextrin-adapted Atlantic salmon after oral administration of radiolabelled 14C1-glucose[J]. Aquaculture Nutrition, 2000, 6(4).

[12] Huo Ming, Yang Jichun, Guan Youfei. The role of ChREBP in glycolipid metabolism in hepatocytes [J].A dvances in Physiological Science,2009,(4).

[13] Lanaspa M A , Sanchez-Lozada L G , Cicerchi C , et al. Uric Acid Stimulates Fructokinase and Accelerates Fructose Metabolism in the Development of Fatty Liver[J]. Plos One, 2012, 7.

[14] [14] Ma L , Robinson L N , Towle H C . ChREBPMlx Is the Principal Mediator of Glucose-induced Gene Expression in the Liver[J]. Journal of Biological Chemistry, 2006, 281(39):28721.

[15] [15] Dentin R , Pegorier J P , Benhamed F , et al. Hepatic Glucokinase Is Required for the Synergistic Action of ChREBP and SREBP-1c on Glycolytic and Lipogenic Gene Expression[J]. Journal of Biological Chemistry, 2004,

279(19):20314-26.

[16] [16]Savanna. Effects of high-sugar and high-fat diet on liver structure and transcriptome of megalobrama amblycephala growth traits [D].Wuhan: Huazhong Agricultural University,2018.

[17] [17] Tsatsos N G,Towle H C. Glucose activation of ChREBP in hepato-cytes occurs via a two - step me chanism[J].Biochem Biophys Res Commun,2006,340: 449 - 456.

[18] Kim M S , Astapova I I , Flier S N , et al. Intestinal, but not hepatic, ChREBP is required for fructose tolerance[J]. JCI Insight, 2017, 2(24).

[19] Bo C , Yang-Min Z , Jing-Pu Z . Comparative Study of Different Diets-Induced NAFLD Models of Zebr afish[J]. Frontiers in Endocrinology, 2018, 9:366-.

[20] Koo H Y , Miyashita M , Cho B H S , et al. Replacing dietary glucose with fructose increases ChREB P activity and SREBP-1 protein in rat liver nucleus.[J]. Biochemical & Biophysical Research Communicati ons, 2009, 390(2):285-289.