Molecular Cloning of a Functional Fads2 Promoter from Zebrafish

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INTRODUCTION

Mammalian desaturases can be regulated by various transcription factors; however, two most prominent transcription factors affecting the expression of fatty acid desaturase 2 (FADS2) would be peroxisome proliferator-activated receptor α (PPARα) and sterol regulatory element-binding proteins 1c (SREBP-1c) [1,2]. Although, polyunsaturated fatty acids (PUFAs) are catalytic products of desaturases, its involvement in a feedback regulatory function via the PPARα and SREBP-1c on desaturases expression has been noted previously. Other than PPARα and SREBP-1c, key cis-acting elements and their corresponding trans-acting factors like nuclear transcription factor Y (NF-Y), specificity protein 1 (Sp1), GATA, CCAAT-enhancer-binding proteins (C/EBPα), retinoid X receptor (RXR) and carbohydrate-responsive element-binding protein (ChREBP) have been implicated in desaturases transcriptional activation. In fact, NF-Y and SREBP sites were remarkably conserved as previously identified in Salmon and Cod FADS2 promoter [3].

In teleost like zebrafish, localization of high level of transcript in the liver and intestine in adult suggested that these were the primary PUFAs biosynthesis sites [4]. In early embryonic stages, localization of fads2 transcripts in the primitive brain further proves the significance of PUFAs during early vertebrate neural development. As embryos progressed into the 72 hpf stage, the primary biosynthesis role was taken over by the now extensively differentiating hepatocytes in the primitive endodermal layer as shown through in situ hybridization [5]. This demands an extensive coordination among the brain, primitive liver and intestinal tissues. In this aspect, it is possible that different subsets of transcription factors are required to fully integrate the responses needed for tissue specific desaturation of PUFAs to occur in the continuously growing vertebrate.

In view of the apparent conservation of the biosynthesis pathway for PUFAs between mammals and teleost, it is reasonable to postulate that similar transcriptional regulation mechanism governs the expression of fads2 in zebrafish. Due to the many desirable features of using zebrafish as a model such as the optical transparency and non-invasive procedures in gene...