

Studies on the Tilapia (*Oreochromis mossambicus*) Hepatocyte Nuclear Factor-1 and -3 in the Regulation of Reproductive Sy

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ABSTRACT

Tilapia is the most general aquacultivating fish in the fresh water and has characteristics of fast growing and well disease resistance. Thus tilapia is an important animal model for relative aquaculture researches. Hepatocyte nuclear factors (HNFs) are liver-enriched transcription factors, which can activate the expressions of tissue-specific, growth and development related genes. The expression of HNFs was detected in the gonads of tilapia previously, and which could be regulated by steroid hormones. Therefore, the reproductive system in tilapia could exist a different endocrine pathway other than the traditional one. To identify this hypothesis and to find out the optimal steroid, concentration and culture period, gonads from tilapia were cultured in vitro in a time course manner (0, 6, 12, 18, 24, 32 and 36 hrs) with different kinds (?-estradiol and hydrocortisone) or concentrations (0, 0.1, 1, 10, 100 and 1000 nM) of steroid hormones, which were all performed after a 6-hr preculture without hormone supplement. The total RNA isolated from previous different groups was analyzed by RT-PCR and semi-quantified with an internal control of ?-actin. Though the expression of HNF-1? and -1? could not be induced by ?-estradiol and hydrocortisone, the expression of HNF-3? could be induced by these two steroids, and showed a dose-dependent manner. Beta-estradiol exerted a better induction result, and the optimal concentration and incubation period were 10 nM and 12 hours, respectively. The detection of HNF proteins in 1-, 2-week and one month old juvenile tilapia by immunohistochemistry showed that HNFs were found mainly in liver and epithelial cells of the digestive organs. According to the above results, the expression of HNF-3? in the gonads of tilapia can be regulated by the steroid hormone and could be involved in the development and gametogenesis of gonads in tilapia. Whether the growth and development of juvenile tilapia is affected by HNFs still needs further investigation.

Keywords : tilapia ; gonad ; hepatocyte nuclear factors (HNFs) ; steroid hormones

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REFERENCES

- 沈世傑 , 1990。台灣魚類檢索。南天書局。pp. 321-327。邵廣昭 , 1996。台灣常見魚貝類圖說。台灣省漁業局。pp. 125-146。高承志 , 1996。魚類生殖的內分泌基礎。漁業推廣。117: 15-23。施瓈芳 , 1994。魚類生理學。水產出版社。pp. 318-321。Allan, G., Flint, D. and Patel, K. 2001. Isulin-like growth factor axis during embryonic development. *J. Reprod. Fertil.* 122: 31-39. Baker, J. P., Robertson, E. J. and Efstratiadis, A. 1993. Role of insulin-like growth factors in embryonic and postnatal growth. *Cell* 75: 73-82. Baker, J., Hardy, M. P., Zhou, J., Bondy, C., Lupu, F., Bellve, A. R. and Efstratiadis, A. 1996. Effects of an Igf 1 gene null mutation on mouse reproduction. *Mol. Endocrinol.* 10: 903-918. Bell, G. I., Gerhard, D. S., Fong, N. M., Sanches-Pescador, R. and Rall, L. B. 1985. Isolation of the human insulin-like growth factor gene: Insulin-like growth factor II and Isulin genes are contiguous. *Proc. Natl. Acad. Sci.* 82: 6450-6454. Berger, R. R. and Sanders, M. 2000. Estrogen modulates HNF-3 mRNA levels in the developing chick oviduct. *DNA Cell Biol.* 19: 103-112. Bigsby, R. M. and Li, A. 1994. Differentially regulated immediate early genes in the rat uterus. *Endocrinology* 134: 1820-6. Billard, R., Fostier, A., Weil, C. and Breton, B. 1982. Endocrine control of spermatogenesis in teleost fish. *Can. J. Fish Aquat. Sci.* 39: 65-79. Binkley, S. A. 1995. Growth hormone from anterior pituitary. In " Endocrinology ". Ed. Binkley, S. A. HarperCollins College Div. pp. 107-126. Cao, Q. P., Duguay, S. J., Plisetskaya, E., Steiner, D. F. and Chan, S. J. 1989. Nucleotide sequence and growth hormone-regulated expression of salmon insulin-like growth factor I mRNA. *Mol. Endocrinol.* 3: 2005-2010. Cereghini, S., Ott, M. O., Power, S. and Maury, M. 1992. Expression patterns of vHNF-1 and HNF-1 homeoproteins in early postimplantation embryos suggest distinct and sequential developmental roles. *Development* 116: 783-797. Chang, C. F. and Yueh, W. S. 1990. Annual cycle of gonadal histology and steroid profiles in the juvenile males and adult females of the protandrous black porgy, *Acanthopagrus schlegeli*. *Aquaculture* 91: 179-196. Chang, C. F., Lau, E. L. and Lin, B. Y. 1995. Estradiol-17 β suppresses testicular development and stimulates sex reversal in protandrous black porgy (*Acanthopagrus schlegeli*). *Fish Physiol. Biochem.* 14: 481-488. Chen, J. Y., Tsai, H. L., Chang, C. Y., Wang, J. I., Shen, S. C. and Wu, J. L. 1998. Isolation and characterization of tilapia (*Oreochromis mossambicus*) insulin-like growth factors gene and proximal promoter region. *DNA Cell Biol.* 17: 359-376. Cirillo, L. A., McPherson, C. E., Bossard, P., Stevens, K., Cherian, S., Shim, E. Y., Clark, K. L., Burley, S. K. and Zaret, K. S. 1998. Binding of the winged-helix transcription factor HNF3 to a linker histone site on the nucleosome. *EMBO J.* 17: 244-254. Clark, K. L., Halay, E. D., Lai, E. and Burley, S. K. 1993. Co-crystal structure of the HNF-3/fork head DNA-recognition motif resembles histone H5. *Nature* 364: 412-420. Cohick, W. S. and Clemons, D. R. 1993. The insulin-like growth factors. *Annu. Rev. Physiol.* 55: 131-153. De Silva, S. S. and Sirisena, H. K. G. 1988. Observations on the nesting habits of *Oreochromis mossambicus* (Peters) (Pisces:Cichlidae) in Sri Lankan reservoirs. *J. Fish Biol.* 33: 689-696. Deryckere, F., McNair, A. and Gannon, F. 1996. Hepatocyte nuclear factor 4 (HNF4) binding sites in the salmon HNF1 promoter. *Gene* 175: 35-41. Duan, C. 1997. The insulin-like growth factor system and its biological action in fish. *Am. Zool.* 37: 491-503. Duguay, S. J., Swanson, P. and Dickhoff, W. W. 1994. Differential expression and hormonal regulation of alternatively spliced IGF-I mRNA transcripts in salmon. *J. Mol. Endocrinol.* 12: 25-37. Duguay, S. J., Lai-Zhang, J., Steiner, D. F., Funkenstein, B. and Chan, S. J. 1996. Developmental and tissue-regulated expression of IGF-I and IGF- mRNAs in *Sparus aurata*. *J. Mol. Endocrinol.* 16: 123-132. Froesch, E. R., Schmid, C., Schwander, J. and Zapf, J. 1985. Actions of insulin-like growth factors. *Annu. Rev. Physiol.* 47: 443-467. Greene M. W. and Chen, T. T. 1999. Quantitation of IGF-I, IGF-II, and multiple insulin receptor family messenger RNAs

during embryonic development in rainbow trout. Mol. Reprod. Dev. 54: 348-361. Hayashi, Y., Wang, W., Ninomiya, T., Ohta, K. and Itoh, H. 1999. Liver enriched transcription factor and differentiation of hepatocellular carcinoma. Mol. Pathol. 52: 19-24. Hines, G. A., Boots, L. R., Wibbels, T. and Watts, S. A. 1999. Steroid levels and steroid metabolism in relation to early gonadal development in the tilapia (*Oreochromis niloticus*). Gen. Comp. Endocrinol. 114: 235-248. Hirose, K., Adachi, S. and Nagahama, Y. 1985. Changes in plasma steroid hormone levels during sexual maturation in the ayu *Plecoglossus altivelis*. Bull. Jpn. Soc. Sci. Fish. 51: 399-403. Holly, J. M. and Wass, J. A. 1989. Insulin-like growth factors autocrine, paracrine or endocrine ? New perspectives of the somatomedin hypothesis in light of recent developments. J. Endocrinol. 122: 611-618. Huang, W. T., Gong, H. Y., Lin, C. F., Weng, C. F., Chen, M. C. and Wu, J. L. 2001. Hepatocyte nuclear factors-1, -1, and 3, expressed in the gonad of tilapia (*Oreochromis mossambicus*). Biochem. Biophys. Res. Comm. 288: 833-840. Huang, W. T., Yu, H. C., Yang, H. C., Lin, C. J. F., Gong, H. Y., Weng, C. F. and Wu, J. L. 2004. Studies on the expression and localization of hepatocyte nuclear facotrs (HNFs) in the gonads of tilapia (*oreochromis mossambicus*). In " Proc. Symp. of the 5th Congress of Asian and Oceanian Society for Comparative Endocrinology ", Nara, Japan. P-054. Hull, K. L. and Harvey, S. 2001. Growth hormone: roles in female reproduction. J. Endocrinol. 168: 1-23. Imae, M., Inoue, Y., Fu, Z., Kato, H. and Noguchi, T. 2000. Gene expression of the three members of hepatocyte nuclear factor-3 is differentially regulated by nutritional and hormonal factors. J Endocrinol. 167: 1-5. Kaestner, K. H. 2000. The hepatocyte nuclear factor 3 (HNF3 or FOXA) family in metabolism. Trends Endocrinol. Metab. 11: 281-285. Katsu, Y., Yamashita M, and Nagahama, Y. 1999. Translational regulation of cyclin B mRNA by 17alpha, 20beta-dihydroxy-4-pregnen-3-one (maturation-inducing hormone) during oocyte maturation in a teleost fish, the goldfish (*Carassius auratus*). Mol. Cell. Endocrinol. 158: 79-85. Kaufmann, E. and Knochel, W. 1996. Review article Five years on the wings of fork head. Mech. Dev. 57: 3-20. Kavsan, V. M., Koval, A. P., Grebenjuk, V. A., Chan, S. J., Steiner, D. F., Roberts, C. T. Jr and Le Roith, D. 1993. Structure of the chum salmon insulin-like growth factor I gene. DNA Cell Biol. 12: 729-737. Kermouni, A., Mahmoud, S. S., Wang, S., Moloney, M. and Habibi, H. R. 1998. Cloning of a full-length insulin-like growth factor-I complementary DNA in the goldfish liver and ovary and development of a quantitative PCR method for its measurement. Gen. Comp. Endocrinol. 111: 51-60. Khan, I. A. and Thomas, P. 1999. Ovarina cycle, teleost fish. In " Encyclopedia of reproduction ". Eds. Knobil, E. and Neill, J. D. Academic Press. pp. 552-564. Kim, S. J., Ogasawara, K., Park, J. G., Takemura, A. and Nakamura, M. 2002. Sequence and expression of androgen receptor and estrogen receptor gene in the sex types of protogynous wrasse, *Halichoeres trimaculatus*. Gen. Comp. Endocrinol. 127: 165-173. Kulik, V. P., Kavsan, V. M., Schaik, F. M., Nolten, L. A., Steenbergh, P. H. and Sussenbach, J. S. 1995. The promoter of the salmon insulin-like growth factor I gene is activated by hepatocyte nuclear factor 1. J. Biol. Chem. 270: 1068-1073. Lai, E., Prezioso, V. R., Smith, E., Litvin, O., Costa, R. H. and Darnell, Jr., J. E. 1990. HNF-3, a hepatocyte-enriched transcription factor of novel structure is regulated transcriptionally. Genes Dev. 4: 1427-1436. Le Gac, F., Loir, M., le Bail, PY. and Ollitrault, M. 1996. Insulin-like growth factor (IGF-I) mRNA and IGF-I receptor in trout testis and in isolated spermatogenic and Sertoli cells. Mol. Reprod. Dev. 44: 23-35. Le Menn, F. and Burzawa-Gerard, E. 1985. Effect of carp gonadotropin (cGTH) and a fraction unabsorbed on concanavalin A-Sepharose obtained from cGTH on vitellogenesis in the hypophysectomized marine teleost *Gobius niger*. Gen. Comp. Endocrinol. 57: 23-36. Matsubara, T., Adachi, S., Ijiri, S. and Yamauchi, K., 1995. Changes of lipovitellin during in vitro oocyte maturation in Japanese flounder *Paralichthys olivaceus*. Fish. Sci. 61: 478-481. McCormick, SD., Sakamoto, T., Hasegawa, S. and Hirano, T. 1991. Osmoregulatory actions of insulin-like growth factor-I in rainbow trout (*Oncorhynchus mykiss*). J. Endocrinol. 130: 87-92. Meton, I., Boot, E. P. J., Sussenbach, J. S. and Steenbergh, P. H. 1999. Growth hormone induces insulin-like growth factor- gene transcription by a synergistic action of STAT5 and HNF-1 . FEBS Lett. 444: 155-159. Mirua, T. 1996. Molecular control mechanisms on spermatogenesis in fish. Nippon Suisan Gakkaishi 62: 547-550. Moriyama, S., Ayson, F. G. and Kawauchi, H. 2000. Growth regulation by insulin-like growth factor- in fish. Biosci. Biotechnol. Biochem. 64: 1553-1562. Moyle, P. B. and Cech, J. J. 1996. Fishes: " An Introduction to Ichthyology. " 3rd ed. Eds. Moyle, P. B. and Cech, J. J. Prentice Hall. pp. 137-171. Murphy, L. J., Bell, G. I., Duckworth, M. L. and Friesen, H. G. 1987. Identification, characterization, and regulation of a rat complementary deoxyribonucleic acid which encodes insulin-like growth factor-I. Endocrinology 121: 684-691. Nagahama, Y. 1997. 17 , 20 -dihydroxy-4-pregnen-3-one, a maturation-inducinghormone in fish oocytes: Mechanisms of synthesis and action. Steroids 62: 190-196 Oshiro, T. and Hibiya, T. 1981. Relationship of yolk globules fusion to oocyte water absorption in the plaice, *Limanda yokohamae* during meiotic maturation. Bull. Jpn. Soc. Sci. Fish. 47: 1123-1130. Ott, M. O., Rey, C. J., Cereghini, S. and Yaniv, M. 1991. vHNF1 is expressed in epithelial cells of distinct embryonic origin during development and precedes HNF1 expression. Mech. Dev. 36: 47-58. Oyadomari, S., Matsuno, F., Chowdhury, S., Kimura, T., Iwase, K., Araki, E., Shichiri, M., Mori, M. and Takiguchi, M. 2000. The gene for hepatocyte nuclear factor (HNF)-4alpha is activated by glucocorticoids and glucagon, and repressed by insulin in rat liver. FEBS Lett. 478: 141-146. Palamarchuk, A., Gritsenko, O., Holthuizen, E., Sussenbach, J., Caelers, A., Reinecke, M. and Kavsan, V. 2002. Complete nucleotide sequence of the chum salmon insulin-like growth factor II gene. Gene 295: 223-230. Palamarchuk, A. Y., Kavsan, V. M., Sussenbach, J. S. and Holthuizen, P. E. 1999. The chum salmon IGF-II gene promoter is activated by hepatocyte nuclear factor 3 . FEBS Lett. 446: 251-255. Perez-Sanchez, J., Weil, C. and Lebail, P. Y. 1992. Effects of human insulin-like growth factor- on release of growth hormone by rainbow trout (*Oncorhynchus mykiss*) pituitary cells. J. Exp. Zool. 262: 287-290. Peter, R. E., Trudeau, V. L. and Sloley, B. D. 1991. Brain regulation of reproduction in teleosts. Bull. Inst. Zool. Acad. Sin. 16: 89-118. Pinter, J. and Thomas, P. 1999. Induction of ovulation of mature oocytes by the maturation-inducing steroid 17, 20?, 21-trihydroxy-4-pregnen-3-one in the spotted seatrout. Gen. Comp. Endocrinol. 115: 200-209. Reber, M. and Cereghimi, S. 2001. Variant hepatocyte nuclear factor 1 expression in the mouse genital tract. Mech. Dev. 100: 75-78. , K. L., Halay, E. D., Lai, E. and Burley, S. K. 1993. Cocrystal structure of the HNF-3/fork head DNA-recognition motif resembles histone H5. Nature 364: 412-420. Riley, L. G., Hirano, T. and Grau, E. G.

2004. Estradiol-17beta and dihydrotestosterone differentially regulate vitellogenin and insulin -like growth factor-I production in primary hepatocytes of the tilapia *Oreochromis mossambicus*. *Comp. Biochem. Physiol.* 138: 177-186. Rinkerknecht, E. and Humbel, R. E. 1978. The amino acid sequence of human insulin-like growth factor I and its structural homology with proinsulin. *J. Biol. Chem.* 253: 2769-2776. Rotwein, P., Pollock, K. M., Didier, D. K. and Krivi, G. G.. 1986. Organization and sequence of the human insulin-like growth factor I gene. Alternative RNA processing produces two insulin-like growth factor I precursor peptides. *J. Biol. Chem.* 261: 4828-4832. Rouiller-Fabre, V., Leref, L., Gautier, C., Saez, J. M. and Habert, R. 1998. Expression and effect of insulin-like growth factor I on rat fetal Leydig cell function and differentiation. *Endocrinology* 139: 2926-2934. Sakai, N., Iwamatsu, T., Yamauchi, K. and Nagahama, Y. 1987. Development of the steroidogenic capacity of medaka (*Oryzias latipes*) ovarian follicles during vitellogenesis and oocyte maturation. *Gen. Comp. Endocrinol.* 66: 333-342. Sakai, N., Ueda, H., Suzuki, N. and Nagahama, Y. 1989. Steroid production by amago salmon (*Oncorhynchus rhodurus*) testes at different developmental stages. *Gen. Comp. Endocrinol.* 75: 231-240. Sakamoto, T. and Hirano, T. 1993. Expression of insulin-like growth factor I gene in osmoregulatory organs during seawater adaptation of the salmonid fish: possible mode of osmoregulatory action of growth hormone. *Proc. Natl. Acad. Sci.* 90: 1912-1916. Shimatsu, A. and Rotwein, P. 1987. Mosaic evolution of the insulin -like growth factors. Organization, sequence, and expression of the rat insulin-like growth factor I gene. *J. Biol. Chem.* 262: 7894-7900. Simpson, E. R. and Waterman, M. R. 1988. Regulation of the synthesis of steroidogenic enzymes in adrenal cortical cells by ACTH. *Annu. Rev. Physiol.* 50: 427-440. Smit, L. S., Meyer, D. J., Billestrup, N., Norstedt, G., Schwartz, J. and Carter-Su, C. 1996. The role of the growth hormone (GH) receptor and JAK1 and JAK2 kinases in the activation of Stats 1, 3, and 5 by GH. *Mol. Endocrinol.* 10: 519-533. Sourdive, D. J. D. and Yaniv, M. 1997. The hepatic nuclear factor1 . In " Transcription factors in eukaryotes. " Ed. Paparassiliou, A. G. Landes Bioscience. pp. 189-209. Spiliotis, B. E. 2003. Growth hormone insufficiency and its impact on ovarian function. *Ann. NY Acad. Sci.* 997: 77-84. Stenson, C., McNair, A., Byrnes, L., Murphy, M., Smith, T. and Gannon, F. 2000. Atlantic salmon HNF-3/forkhead: cDNA sequence, evolution, expression, and functional analysis. *DNA Cell Biol.* 19: 59-68. Stenson, C., McNair, A., Curley, M., Smith, T. and Gannon, F. 2002. A role for HNF-3 in the regulation of the HNF-1 gene of the Atlantic salmon. *Mol. Genet. Genomics* 266: 832-837. Ueda, H., Kambegawa, A. and Nagahama, Y. 1984. In vitro 11-keto- teatosterone and 17?, 20?-dihydroxy-4-pregnen-3-one production by testicular fragments and isolated sperm of rainbow trout, *Salmo gairdneri*. *J. Exp. Zool.* 231: 435-439. Ueda, H., Nagahama, Y., Tashiro, F. and Crime, L. W. 1983. Some endocrine aspects of precocious sexual maturation in the amago salmon, *Oncorhynchus rhodurus*. *Bull. Jpn. Soc. Sci. Fish* 49: 587-596. Wang, J., Stromstedt, P., O ' brien, R. and Granner, D. 1996. Hepatic nuclear factor 3 is an accessory factor required for the stimulation of phosphoenolpyruvate carboxykinase gene transcription by glucocorticoids. *Mol. Endocrinol.* 10: 794-800. Weigel, D., Jurgens, G., Kuttner, F., Seifert, E. and Jackle, H. 1989. The homeotic gene fork head encodes a nuclear protein and is expressed in the terminal regions of the *Drosophila* embryo. *Cell* 57: 645-658. Yoshikuni, M. and Nagahama, Y. 1991. Endocrine regulation of gametogenesis in fish. *Bull. Inst. Zool. Acad. Sin.* 16: 139-172.