腦垂體腺?・釋穭?▼E活?扣顜d郭魚體外培養性腺組織之表現及調控研究

李佳榮、黃尉東

E-mail: 9706774@mail.dyu.edu.tw

摘 要

腦垂體腺?酸環化?激活?(pituitary adenylate cyclase activating polypeptide, PACAP)為一神經胜?（neuropeptide），屬於血管活性腸?(vasoactive intestinal peptide, VIP)/胰泌素(secretin)/昇醣素(glucagon)/生長激素釋放素(growth hormone releasing hormone, GHRH)家族成員之一。PACAP於生物體內具有兩種不同構形，其胺基酸序列從N端組成38個及27個胺基酸兩種構形，分別命名為PACAP38與 PACAP27，二者於哺乳類具有調控細胞凋亡、代謝、內分泌及免疫系統等重要之功能，PACAP及其受體於斑馬魚（zebrafish）、薩克愛鮭（sockeye salmon）、泰國鯰（Thai catfish）、彩虹鱒魚（rainbow trout）及紅鰭東方豚（fugu rubripes）等其他魚種器官之分佈已有探討，但於吳郭魚除腦外，於其他各器官並無相關之研究。本研究除將針對tPACAP38及PAC1-R於吳郭魚各臟器及組織之分佈與表現進行分析外，另以dibutyryl-cAMP、ovine PACAP38、forskolin及H89等藥物對體外培養之吳郭魚性腺組織(精巢及卵巢)進行劑量及時間相關之試驗，以探討此些藥物對性腺 tPACAP38分泌之影響。以半定量反轉錄?-聚合?鏈鎖反應（semi-quantitative RT-PCR）及PCR雜合反應（PCR hybridization）分析發現tPACAP38及PAC1-R，除肝臟外，於吳郭魚之腦、膽囊、鰓、心臟、腸、腎臟、肌肉、胃、精巢及卵巢等組織中皆有表現，且於雄、雌魚腦中tPACAP38及其受體之表現量均顯著高於其他組織者（P ? 0.05），於其他組織之表現量則無顯著之差異（P ? 0.05）。另以免疫組織化學染色法（immunohistochemistry）分析PACAP及其受體蛋白質表現與分佈所得之結果，與前述各組織之表現相吻合。以不同濃度之cAMP (dibutyryl-cAMP; 0.25, 1.5 and 5 mM)誘導於體外培養之吳郭魚性腺組織2小時後，或以1.5 mM之cAMP濃度或5 nM ovine PACAP38誘導經不同培養時間(0, 2, 4 and 8 h)後，tPACAP38之mRNA表現量於2小時後之表現量較高，並隨著誘導時間增加其表現量則有明顯下降之趨勢。續以forskolin (1, 5 and 10 μM)及H89 (10 μM)進行誘導tPACAP38表現之結果顯示，發現forskolin雖為腺?環化?(adenylate cyclase)之活化劑，但其之誘導作用可受蛋白激?A (protein kinase A, PKA)抑制劑H89所抑制，因此tPACAP38之表現可能與cAMP-PKA之訊號傳遞路徑有關，推測tPACAP38可能於硬骨魚類扮演旁分泌或自分泌（paracrine/autocrine）調控者之角色。

關鍵詞 : 吳郭魚、腦垂體腺?酸環化?激活?、腦垂體腺?酸環化?激活?第一型受體、性腺、訊號傳遞

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