Synuclein 相關基因在斑馬魚之基因表現研究

Expression and characterization of synuclein-related genes in zebrafish

中文摘要

帕金森氏症(Parkinson''s disease, PD)是一種神經系統基底核黑質細胞退化性疾病，引起該疾病的可能原因可以大致區分成老化、環境因子及基因遺傳三大類，而在遺傳基因方面的研究已發現有十個以上的基因突變與該疾病的形成有關。其中α-synuclein 是最早被發現的致病基因，然而相關的致病機轉目前仍未清楚。先前有研究指出所有的 synuclein 異構型在胚胎發育早期即在中樞神經系統被大量表現，顯示這一類基因對中樞神經系統的發育可能是很重要的，但是研究 synuclein 在胚胎早期發育方面的相關研究則較少。因此在本研究中將人類、老鼠以及斑馬魚 synuclein 相關基因選殖出來，以斑馬魚作爲實驗動物模式，利用具有神經細胞專一性表現之啓動子經由顯微注射使其在斑馬魚的神經細胞中過量表現，分析這些基因在斑馬魚中樞神經系統早期發育過程中的基因表現特性，以期能更進一步的了解這些基因在神經系統中所具有的功能。實驗結果發現人類 A30P 突變型α-synuclein 顯微注射組之螢光強度有隨著成長天數增加而明顯降低之現象，而正常型及 A53T 突變型α-synuclein 則無此種現象。另外在本實驗中觀察人類正常型α-synuclein 於斑馬魚神經系統內表現情形，發現正常型α-synuclein 重組質體在神經元纖維的表現情形，呈現密集而不連續性的點狀分布，而該現象在人類 A30P 與 A53T 突變型α-synuclein 則僅各有 37%及 58%的發生率。此研究結果提供我們未來在研究該基因的致病機轉以及基因突變後所造成之蛋白質特性改變等兩方面一些新的研究方向。

英文摘要

Parkinson''s disease (PD) is a neurodegenerative motor disorder that is characterized by the loss of dopaminergic neurons from the substantia nigra. The pathological mechanism of Parkinson’s disease is categorized in aging, environmental factor, and genetic disorders. In genetic research, there were more than 10 genes mutations identified in this disease. The first pathogenetic gene identified is α-synuclein, but its phathological mechanism is unknown. In previous study, it’s demonstrated that all synuclein isoforms expressed massively in early embryologic development of the central nervous system. These results revealed that synuclein may be essential to neurogenesis. In our research, we cloned synuclein of human, rat, and zebrafish. Using constructs containing synuclein and green fluorescent protein (GFP) genes drived by the neural-specific promoter, HuC, over-expressed in zebrafish neural system. In our study, it’s demonstrated that the intensity of fluorescence in human

α-synuclein containing the A30P Parkinson''s disease mutation injected embryos decreased along with the growing days obviously, however, the same phenomenon was not found in human α-synuclein wild type and human α-synuclein containing the A53T Parkinson''s disease mutation injected embryos. Furthermore, we found that the expression of human α-synuclein wild type occurred dense and discrete dots in neurite, but the pattern found at the incidence of 37 % and 58 % in α-synuclein mutant A30P and A53T respectively. These results provided us some new directions in researches about the possible pathogenesis of PD and the property change in α-synuclein Parkinson''s disease mutation in the future.