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Skeletal Dysplasia Caused by FGFR3 Mutation in Taiwanese Patients
第三號纖母細胞成長因子受體基因突變引起的骨酪異化症

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Abstract

Background. The identification of a missense mutation (G380R) in the fibroblast growth factor receptor 3 (FGFR3) gene in patients with achondroplasia was followed by the detection of common FGFR3 mutations in two clinically related occurrences of skeletal dysplasia.: hypochondroplasia, and thanatophoric dysplasia. In this study, we investigated the FGFR3 mutation of achondroplasia, hypochondroplasia, and thanatophoric dysplasia in Taiwanese patients. Methods: There were 28 patients with achondroplasia, 18 with hypochondroplasia and two with thanatophoric dysplasia type I included in this study. Polymerase chain reaction (PCR), direct sequencing, and amplification created restriction site (ACRS) tests were performed to analyze the mutations on FGFR3 in these patients. Results: Genetic homogeneity of achondroplasia was demonstrated as recurrent G380R mutations in all patients hitherto reported. Although all detected mutations of hypochondroplasia were accounted for by a recurrent N540K mutation in the first tyrosine kinase domain of the receptor, a significant portion (45%) of our patients did not harbor the N540K mutation. Two patients with type I thanatophoric dysplasia were found to carry the R248C mutation. Conclusions: We used either a natural restriction enzyme site or ACRS to detect the recurrent G380R mutation of achondroplasia. The use of the ACRS was found to be more cost-effective and efficient than the use of the natural restriction enzyme digest.

Key words：Achondroplasia; Amplification created restriction site; ACRS; Fibroblast growth factor receptor3; FGFR3; Hypochondroplasia; Thanatophoric dysplasia

中文摘要

背景 第三號纖母細胞成長因子受體（FG FR3）基因上的突變會導致骨骼異化症是最近分子生物學的最重要發現之一。為了解台灣這類型疾病上的基因突變情形我們分析了 achondroplasia，hypochondroplasia 及 thanatophoric dysplasia 的病人其 FGFI 好的特殊點突變。方法 利用聚合酶連鎖反應、基因定序以及酵素內切法，找出骨骼異化症的突變。結果 所有的 achondroplasia 病人都帶有 G380R 的突變，而在 hypochondroplasia 病人身上則具有一常見的 N540K 的突變，但仍有 45%的病人不具此突變，另外兩名罕見的 thanatophoric dysplasia 病人都有 R248C 突變。結論 本研究證實利用 ACRS 的方法偵測 achondroplasia 比傳統的酵素內切法更其效力。

關鍵字：骨骼異化症；第三號纖母細胞成長因子受體基因