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Analysis of *FokI* Polymorphism of Vitamin D Receptor Gene in Intervertebral Disc Degeneration

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Aim: We have hypothesized a possible relationship between disc degeneration (DD) and *VDR FokI*/T2C polymorphism. *Methods:* A case–control study was performed comprising 121 Brazilian patients with confirmed DD by nuclear magnetic resonance and a control group consisting of 131 healthy patients without a history of disc cysts of the lumbar spine. Detection of *VDR FokI*/T2C polymorphism was performed using restriction fragment length polymorphism–polymerase chain reaction. The chi-square test was used to compare allele and genotype frequencies between groups, and a p-value of < 0.05 was considered statistically significant. *Results:* The results disclosed statistical difference between allele distribution among cases and controls ($p = 0.025$, odds ratio = 1.58, confidence interval = 1.07–2.32) considering *VDR FokI*/T2C polymorphism. *Conclusion:* The results showed a positive association between *VDR FokI*/T2C polymorphism and DD in Brazilian patients tested.

Introduction

The intervertebral disc is a fibrocartilaginous structure whose main function is to act as a buffer, transmitting compressive loads between vertebral bodies (Buckwalter, 1995; Miller *et al.*, 1988). The intervertebral disc consists of three main structures: the cartilaginous endplates, the central nucleus pulposus, and the annulus fibrosus located at the periphery of the disc. The intervertebral disc loses its hygroscopic properties with aging, leading to a progressive dehydration process, characterizing disc disease. From the intervertebral disc degeneration (DD), the spine begins to show progressive instability of the affected region (Inoue, 1981).

The process of DD is associated with many clinical conditions, including low back pain, which is one of the most common health problems in society, being a major cause of work absenteeism and use of health services. It is estimated that 15–20% of adults have back pain during a single year and 50–80% experience at least one episode of back pain during their lifetime (Rubin, 2007).

The precise etiology of DD is not fully understood. Until recently, it was exclusively attributed to the accumulation of environmental effects, primarily micro or macro, trauma, lifestyle, smoking, atherosclerosis, and the changes that occur in the disc with aging (Zawilla *et al.*, 2013). However, more recent research has demonstrated that the influence of these factors is moderate in DD, reinforcing the notion of genetic involvement in the etiology of the disease (Nunes *et al.*, 2007). Epidemiological studies on families and twins suggest that inheritance is the major determinant of DD (Battie *et al.*, 1995; Matsui *et al.*, 1998; Sambrook *et al.*, 1999). Several disease-associating variations have been found in a number of different genes, suggesting that intervertebral DD is a multigenetic entity (Ala-Kokko, 2002; Kalichman and Hunter, 2008; Zawilla *et al.*, 2013).

To date, several gene loci associated with human DD have been identified (Chan *et al.*, 2006). Variations in the genes involved in inflammation, extracellular matrix components, and protein metabolism have been reported as associating with DD (Kalichman *et al.*, 2008).

Vitamin D is known as a hormone that regulates calcium homeostasis and bone mineralization (Cantorna and Mahon, 2004) and can be found in two forms: ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3). Vitamin D, derived from the diet or the bioactivation of 7-deidrocalciferol, is inert and must be activated to exert the biological functions (Fraser and Kodicek, 1970). The hormonal form of vitamin D (1,25-2-hydroxyvitamin D3) has essential roles in endocrine functions: (1) mineralization process of bone, (2) absorption of calcium from the intestine, (3) control of calcium and phosphorus homeostasis, and (4) regulation of parathyroid hormone (Vilarino *et al.*, 2011), and it has shown antiproliferative

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