19. Could Estrogen Impact a New Pertinent Gene for Adolescent Idiopathic Scoliosis (AIS)?

Amani Hassan [1], Bagu E[2], Zaouter C[1], Patten S [1,3,] Moldovan F[1,]
Edward Baggu, Charlotte Zaouter, Kessen Patten
[1]CHU Sainte-Justine, Montreal, Canada; [2]Faculty of Dentistry-Stomatology, Université de Montréal, Montréal, QC.; [3]École Polytechnique de Montréal, Montréal, QC.

Introduction: Adolescent Idiopathic Scoliosis (AIS) is a complex rotational spinal deformity that occurs during the pubertal growth spurt. Recently, through a stepwise association study a new susceptibility locus on chromosome 6q24.1 was reported in Japanese population. The most significantly associated SNP, rs6570507, was in GPR126. In French Canadian sporadic cases of AIS, we identified variants in the gene coding for another GPR protein (GPR128). Both GPR 126 and 128, are orphan members of the adhesion subfamily of G-protein coupled receptors which are characterized by a long serine/threonine-rich N-terminus possibly regulated by hormones such as estrogens and consequently involved in the progression of AIS. To study the role of estrogen in AISwe investigated the regulation of the GPR128.

Methods: In-silico analysisfor potential ERE sites in the GPR128 promoter was done using MatInspector and ECR-Browserand then several promoter fragments were cloned in PGL3 vector upstream of the luciferase gene. Huh-7 cells were then transiently transfected with the GPR128 promoter constructs. The luciferase activity was measured in the presence or absence of estrogen (17 -□estradiol 10-7M). RNA was extracted and QPCR was performed on osteoblasts that is overexpressing the estrogen receptor hfob/ER9 as well as in Huh-7 cells that were either treated with estradiol or Vehicle.

Results: In Huh7 hepatic cell lines that were transfected with the GPR128 promoter constructs, treatment with estrogen (10 □M) over a period of 24 hours following over-expression of ER-□ led to a 2.5 fold increase in the promoter activity, confirming the regulation of GPR128 by estrogen. Likewise the expression of GPR128 mRNA was increased by 3-fold following treatment of Huh7 cells with estradiol.

Conclusion: Our study demonstrated that estrogen is involved in the expression of GPR128. These results could help to understand the molecular mechanisms involved in AIS pathogenesis.