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Campeau L[1], Gorbachinsky I[2], Stancill J[2], Rohozinski J[2], Andersson K[2], Ziegler J[3], Langefeld C[3], Badlani G[3]
1. *Wake Forest Institute for Regenerative Medicine,* ***2.*** *Wake Forest Institute for Regenerative Medicine,* ***3.*** *Wake Forest University Health Sciences*

CHARACTERIZATION OF SNPS WITHIN THE MMP-1 PROMOTOR REGION IN WOMEN WITH AND WITHOUT POP

Hypothesis / aims of study

Pelvic organ prolapse (POP) is a detriment to quality of life in many affected women. It has been proposed that decreased collagen content may weaken pelvic floor support, culminating in POP. One possible etiology is elevated activity of extracellular matrix collagen degrading enzymes such as Matrix Metalloprotinase-1 (MMP-1). Previously, we reported that an upregulating 2G single nucleotide polymorphism (SNP) in the -1607 position of the MMP-1 promoter region is significantly more common in women with POP versus non-POP controls. This promoter has other SNPs known to bind various transcription factors. Additionally, the specific combination of SNPs (haplotypes) has been shown to control MMP-1 expression in cancer cell lines from different tissues. A similar phenomenon might explain the pathogenesis of POP. We sought to determine if MMP-1 promoter SNPs and/or haplotypes were significantly correlated with the presence of POP.

Study design, materials and methods

Adult females with surgically corrected POP (n=63) and controls without POP (n=93) were identified in the Department of Urology and/or Obstetrics/Gynecology. DNA was isolated from blood cell lysates obtained via phlebotomy. MMP-1 SNPs were noted from prior literature. The MMP-1 promoter was sequenced and 8 SNPs identified and genotyped. Tests of association were computed assuming and dominant genetic model using a logistic regression model.

Results

For the -519, -755, and -839 SNPs, the number of POP and control specimens sequenced was 20 & 21, 19 & 16, and 23 & 18, respectively. All POP and control frequencies were consistent with Hardy-Weinberg equilibrium. Both the -519 A to G and -839 G to A SNPs were less common in POP populations (p= 0.024, OR=0.24, 95%CI=0.07-0.85, p=0.040, OR=0.27, 95%CI= 0.08-0.97, respectively). The -755 T to G SNP is more frequent in POP (p=0.025, OR =6.61, 95%CI=1.13-38.7). No significant haplotypes were noted among these SNP combinations.

Interpretation of results

The increased presence of the 519 A to G and/or -839 G to A SNPs in the control population may represent a protective effect on POP manifestation. On the contrary, the strong correlation of the -755 T to G SNP in the POP group suggests that this allele is associated with the POP phenotype. The identification of these three SNPs will allow to narrow down the area of interest in the MMP-1 promoter region involved in the pathophysiology of POP

Concluding message

Further studies with larger patient numbers will aid in recognition and characterization of these and other SNPs as well as possible haplotypes within the MMP-1 promoter region

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Is this a clinical trial?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Wake Forest University Office of Research and Sponsored Programs** **Institutional Review Board**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**