Polymorphic Variation of the COMT Gene in Patients Undergoing Surgical Treatment for Lumbar Degenerative Disc Disease
David Kim, MD¹, Julia Martha, BA¹, Robert Banco, MD², Louis Jenis, MD², Scott Tromanhauser, MD², Inga Peter, PhD², Carolyn Schwartz, ScD¹

BACKGROUND CONTEXT: Increasing evidence suggests that the experience of pain symptoms related to lumbar degenerative disc disease (DDD) is genetically determined. Potential candidate genes conferring greater risk for development of chronic pain include the catecholamine-O-methyltransferase gene (COMT). COMT codes for a critical enzyme in catecholamine metabolism and modulates dopamine, epinephrine, and norepinephrine-mediated neurotransmission as well as μ-opioid system responses. Human studies have demonstrated that common functional genetic polymorphisms in the COMT gene affects the response to sustained pain.

PURPOSE: To characterize the distribution of allelic variations in the COMT gene in patients undergoing surgery for lumbar DDD.

STUDY DESIGN/ SETTING: Prospective cohort study.

PATIENT SAMPLE: 100 patients presenting for surgical treatment of lumbar DDD based on clinical evaluation and MRI. Patients were 18 years and older with moderate to severe low back pain unresponsive to at least 6 months of non-operative treatment.

OUTCOME MEASURES: Genetic analysis.

METHODS: A sample of venous blood was obtained from each patient for DNA extraction and sequencing. Analysis of COMT was performed with respect to 5 single nucleotide polymorphisms in non-coding regions potentially associated with pain response. Allelic frequencies for all known polymorphisms were measured and the distribution of individual patient genotypes were compared to those predicted for the general population.

RESULTS: 5 of 5 COMT loci yielded informative results for the study population. Test for Hardy-Weinberg equilibrium (HWE) revealed 2 COMT loci that diverged significantly from expected distributions. Specifically, carriers of COMT rs6269 (minor allele frequency, MAF 50%) and rs4818 (MAF 46%), both in strong linkage disequilibrium, were less likely to be homozygous for minor allele and more likely to be heterozygous than expected under HWE. Chi-square analysis for these loci yielded p-values of 0.0488 and 0.0458, respectively.

CONCLUSIONS: As a group, patients presenting for surgical treatment of lumbar DDD demonstrate significant deviation from HWE for a set of
polymorphisms with respect to the pain-modulating COMT gene. These results might suggest that allelic variations in specific genes result in predisposition to chronic pain associated with DDD. Future research regarding such potential genetic risk factors may allow development of more effective selection criteria for surgical treatment of DDD.

FDA DEVICE/DRUG STATUS: This abstract does not discuss or include any applicable devices or drugs.