**Case selection.** The results shown here are based upon data generated by the TCGA Research Network: <https://www.cancer.gov/tcga>. Applicable patients were identified using simplified search criteria, filtering total cases (N=44,637) for those with mutations in *RBMX* (e.g., ‘GENE=RBMX’). This search yielded 116 cases corresponding to 6198 files (**Figure 1**). Filtering for *.maf* files reduced the number of files to 732 and additional filtering for ‘open’ data reduced the number of files to 122. To summarize, most cases were female (80.2%), White (69%), and diagnosed with Endometrioid adenocarcinoma, NOS (33.6%) (**Table 1**). The average age at diagnosis was 62 years old. Most *RBMX* mutations were non-synonymous single nucleotide polymorphisms (69.8%). Some cases had multiple mutations in the *RBMX* gene, resulting in a total of 140 mutations. For those cases, one mutation was randomly selected and included in the analysis. Regarding the SIFT variable, the number of tolerated (34.5%) and deleterious (35.3%) mutations were distributed equally and 30.2% were missing. For PolyPhen, 55.2% were benign or possibly damaging, 14.7% were probably damaging, and 30.2% were missing. Using the IMPACT categorization, most (91.4%) RBMX mutations were classified as ‘low, moderate, or modifier’ and 8.6% ‘high.’

**Statistical Analysis.** The impact of RBMX mutations was tested *in silico* using three variables: Sorting Tolerant From Intolerant (SIFT), Polymorphism Phenotyping (PolyPhen), and Variant Impact (IMPACT). To account for non-normality, we calculated Spearman's rank-order correlation between each pathogenicity variable and the number of C🡪T and G🡪A mutations, separately. Exact p-values were not computed in the presence of ties. Each pathogenicity variable describes the predicted impact of the mutations on protein function by incorporating information about sequence homology and/or physico-chemical properties of amino acids. Each of these protein-related fields denote pathogenicity along with an associated score derived from a bioinformatics algorithm [references: doi:10.1038/nprot.2009.86, doi: 10.1002/0471142905.hg0720s76, https://www.ensembl.org/Help/Glossary]. The SIFT algorithm uses a sequence homology-based approach to predict whether a single amino acid substitution resulting from a non-synonymous single nucleotide polymorphism will affect protein function. The algorithm is based on the degree of evolutionary conservation of amino acids within protein families, where proteins ‘intolerant’ to substitution comprise highly conserved positions and those deemed ‘tolerant’ are in regions of low conservation.We estimated the correlation between binary (0=tolerated; 1=deleterious) and continuous (0-1) categorizations of the SIFT variable and the number of mutations, where a deleterious categorization suggests the mutation results in a protein that is non-functional.The PolyPhen algorithm combines multiple protein sequence alignment and machine-learning classification to estimate the probability that a non-synonymous, single nucleotide polymorphism will be 'damaging,' or result in a non-functional protein. The algorithm produces a qualitative score (benign, possibly damaging, or probably damaging) along with a probability score. We estimated the correlation between binary (0=benign/possibly damaging; 1=probably damaging) and continuous (0-1) categorizations of the PolyPhen variable and the number of mutations. A probably damaging categorization suggests that the mutation results in a protein that is non-functional. Finally, the variant impact variable is based on the severity of the variant consequence. The Ensembl glossary defines them as High (assumed to have high (disruptive) impact in the protein, probably causing protein truncation, loss of function or triggering nonsense mediated decay), Low (assumed to be mostly harmless or unlikely to change protein behaviour), Moderate (non-disruptive, may change protein effectiveness), and Modifier (non-coding variants or variants affecting non-coding genes, where predictions are difficult or there is no evidence of impact). We calculated the correlation between a binary (0=Low/Moderate/Modifier; 1=High) categorization of the PolyPhen variable and the number of mutations because a numerical score is not provided. ‘High’ suggests that the mutation results in a protein that is non-functional. The total number of mutations (genome-wide) and those at loci corresponding to cancer genes are evaluated separately throughout the analysis. All statistical tests were performed in R.