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# The occurrence of reactive oxygen and nitrogen species in normal endometrial tissues might explain signature hotspot mutations found in the *PTEN* gene in endometrial adenocarcinoma

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Endometrial cancer is the most prevalently diagnosed gynecological cancer. The majority of type-I endometrial cancer cases are reported to have a mutated PTEN tumor suppressor gene. With respect to endometrial cancer cases, the PTEN suppressor gene, codon 130, is a hotspot for mutation involving a cytosine to guanine transversion mutation. The mechanism for the C to G transversion in endometrial cancer has not been previously explained. Codon 130 contains a CpG dinucleotide, which could be methylated to 5-methylcysoine. For the first time, we have shown that methylation is present on the coding and non-coding strand at codon 130 of the PTEN gene in normal endometrial tissues. The presence of 5-methylcytosine increases oxidation of the adjacent guanine. Oxidized guanine (8-oxo-G), in the presence of peroxynitrite, can form Guanidinohydantoin (Gh) and mispair with guanine. This mechanism may explain the unusually high level of codon 130 mutations in endometrial cancer cases. 8-oxo-G and peroxynitrite can be formed in tissues from Reactive Oxygen (ROS) and Nitrogen (RNS) Species. We have used immunohistochemistry and immunofluorescence to assess the presence of such markers of damage in benign human endometrial tissues. We show that markers of ROS and RNS damage are found in benign endometrial tissues. The generation of DNA damage in histologically normal endometrial tissue is in accord with the mutagenic mechanism described above. Further study will contribute to development of methods capable of diagnosing precursors of endometrial cancer and potentially reveal new pharmacological targets.

## Biography

Michaela Huynh is Current MD-PhD Student at Texas A&M University, and she did graduate Program in Biochemistry & Molecular Biology. She graduated at Magna Cum Laude, Texas A&M University and Century Scholars Scholarship Program, Texas A&M University. She is involved in a number of student organizations on campus, including Students Together for Service and the Graduate Student Organization. Her research interest includes Enzymology and DNA repair mechanisms.

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