Title: Detecting DNA Methylation using Surface Enhanced Raman Spectroscopy (SERS)

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One of the most important epigenetic event, DNA Methylation, often leads to various diseases such as- cancer, lupus, muscular dystrophy and several birth defects. Alkylation of various bases in the DNA are often responsible for the manifestation of the diseases. DNA methylation in guanine was found to be a vital cause for canine lymphoma. Here, we have performed surface enhanced Raman spectroscopy (SERS)-based experimental studies and density function theory (DFT)-based computational studies to analyze the methylated and non-methylated guanine structure. Methylation of guanine often occurs in the N7 and O6 positions of guanine structure with the addition of various adducts such as methyl, hydroxyethyl and methyl d3 groups. Based on the spectrum data Principle Component Analysis (PCA)-based method was used to complete the statistical analysis and differentiate the methylated samples from the non-methylated samples. Methylated samples were then distinguished based on their methylated positions and added adducts. In order to explain the experimental results, a complete optimization and frequency calculation were performed based on Density Functional Theory (B3LYP). The vibrational mode of the Raman spectrum from the experimental results were explained by comparing with DFT results with that of experiments. The highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) for each structures were also analyzed and the sensitivity of the electron transfer were identified for each cases. The electrostatic potential for each of the molecules were also observed to understand the charge distribution of the DNA adducts. The study will provide a label free technique to analyze epigenetic modification of DNA.