

# **Assessment of pH effect on mutation and perturbation of P53 gene by computational and modeling methods**

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## **Abstract**

**Aim and Background:** P53 tumor suppressor gene, also known as “genome guardian” is mutated in more than half of all kinds of cancers. P53 protein acts as a tetramer and is a transcription factor, controlling the transcription of genes that are necessary for apoptosis or cell proliferation arrest. Also it inhibits the transcription of genes that are responsible for cell growth.

Experimental researches revealed that acidic pH raised the rate of cancer and mutation in 248CGG codon of P53 gene. This may be due to protonation of this three-nucleotide codon. Mutation in this codon changes the encoding amino acid and subsequently produces a protein, which has oncogenic features instead of tumor suppressor characteristics of original p53 protein. In current study, we perform an investigation on the impact of protonation on stability of codon 248CGG in this gene.

**Materials and Methods:** Molecular mechanic methods used in this study to calculate energy levels. HYPERCHEM software used in AMBER, BIO<sup>+</sup>, MM<sup>+</sup> and OPLS.

**Results:** Obtained results from different force fields all suggest that acidic condition can increase molecular instability in given sequence in comparison with physiological pH.

**Conclusion:** Our results suggested a reliable answer about the effect of protonation on mentioned codon and its stability. From theoretical point of view, acidity can increase the instability of this specific codon. Along with the experimental investigations, our results can, to some extent, elaborate the mutagenesis of acidic pH.

**Keywords:** P53 gene, protonation, mutagenesis

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