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Identification of novel miRNAs that regulate OGG1 mediated DNA repair

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Reactive oxygen species induce modifications of the DNA bases that are implicated in cancer development and progression as well as aging and age-related neurological disorders. The base excision repair mechanism had evolved to repair the mutations induced by oxygen radicals. The objective of this study is to identify novel microRNAs that regulate the expression of 8-oxoguanine glycosylase (OGG1), an enzyme that plays an important role in the DNA base excision repair pathway. Altered expression of OGG1 leads to accumulation of modified bases, DNA damage, and increased rate of nucleic acid mutation. To simulate conditions of oxidative stress, human astrocytes were treated for 16 hours with 10 μ M sodium dichromate. OGG1 mRNA and protein expression levels were assessed via RT-qPCR and protein simple Wes® assay. Comet assay analysis were performed to assess the level of oxidative stress induced DNA damage. RNA extracted from treated and non-treated cells was sequenced using Ion Proton small RNA sequencing platform. OGG1 mRNA and protein expression levels were significantly reduced after treatment with sodium dichromate. Comet assay analysis confirmed high levels of oxidative stress induced DNA damages. MicroRNA sequencing revealed that large number of microRNAs are up regulated following treatment with sodium dichromate. Bioinformatics analysis was implemented to identify potential microRNAs targets that bind to the 3'UTR region of the OGG1 mRNA gene. Those include miR-20b, miR-33, miR-let7, miR- 103, and miR-491. The binding between the potential miRNA candidates and OGG1 gene will be validated via immunoprecipitation studies.