

## **The Relationship Between DNA Damage Response and Accumulation of DNA Damage in LRRK2 G2019S Parkinson's Disease**

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Parkinson's disease (PD) is a neurodegenerative disease that affects 7-10 million people worldwide. Among PD patients, an accumulation of DNA damage has been noted, with one possible explanation for this accumulation being a dysregulated DNA damage response. Studying this DNA damage can open doors for new therapeutic targets of PD. The goal of the current study was to evaluate the role of ataxia telangiectasia mutated (ATM), a protein involved in DNA damage response, and leucine rich repeat kinase 2 (LRRK2), a kinase protein, in the accumulation of DNA damage in PD. I hypothesized that the implication of ATM and LRRK2 activation in LRRK2 G2019S PD indicates a relationship between a DNA damage response through ATM, LRRK2 kinase activity, and the accumulation of DNA damage. The results revealed increases in the phosphorylation of H2AX, a proxy for DNA double-strand breaks (DSBs), in LRRK2 G2019S cells. Increased baseline phosphorylation of ATM in LRRK2 G2019S cells and a decrease in H2AX phosphorylation following inhibition of ATM kinase activity suggested a relationship between a DNA damage response through ATM and the accumulation of DNA damage. Interestingly, the results also showed a reversal in DNA damage following inhibition of LRRK2 kinase activity, implicating LRRK2 kinase activity in the accumulation of DNA damage in PD. Ultimately, the results of this study indicate a relationship between the accumulation of DSBs in PD, the DNA damage response via ATM, and LRRK2 kinase activity, although the exact nature of this relationship is still unknown.