DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)

Antimony (Sb) is a highly toxic metalloid (half-metal) for all living organisms including humans. Recent studies have shown that prolonged exposure to Sb(III) causes several diseases including cancer. On the other hand, antimony-based compounds are one of the few effective drugs against leischmaniasis, a tropical disease affecting millions of people worldwide. Importantly, it has been recently demonstrated that compounds containing Sb(III) have strong antiproliferative properties which makes them good candidates for anticancer drugs, as it was the case for arsenic. However, precise mechanisms of antimony carcinogenesis remain elusive and are still a matter of debate. Because antimony pose a serious threat to human health and becomes more and more important for modern medicine, it is of high importance to understand the basis of its toxic activity in cells. In the frame of this project, we will determine what kind of DNA damage is induced by antimony and what is the mechanism of antimony genotoxicity. For this purpose, we will use budding yeast *Saccharomyces cerevisiae*, a unicellular organism, which serves as an excellent model organism to study DNA damage response. First, we will determine whether Sb(III) can generate DNA damage in any phase of cell cycle or only in replication-dependent manner. Next, we will determine which DNA repair pathways are essential for cell survival during exposure to Sb(III). We will also study the role of reactive oxygen species and oxidative stress in genotoxicity of antimony. Afterwards, we will determine if antimony is able to generate most dangerous DNA damage in the form of double-strand breaks or/and induce mutations in mitochondrial DNA. In addition, we will assess if antimony disturbs the structure of both actin and tubulin cytoskeleton that is crucial for maintaining genome integrity and accurate chromosome segregation during cell division. Finally, we will determine if antimony may increase genotoxicity of other DNA damaging agents, including anticancer drugs, or inhibit repair of DNA damage induced independently from Sb(III). The results of this project will greatly extend our knowledge about mechanisms of antimony genotoxicity and its negative impact on human health. In future, the outcomes of this proposal may also help to improve existing antiprotozoan and anticancer therapies or design completely new treatment strategies.

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