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“Structural and Biochemical Characterization of Mitochondrial DNA Repair and Cell Survival in Response to Anaesthetics: Role of DNA Pol Gamma and DNA2”

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Inhalational and intravenous anaesthetics are known to induce DNA damage in a broad variety of tissues. This is clinically associated with lung injury, endothelial cell death, impaired cardiac function and myocardial remodeling. We are studying the roles of two proteins involved in anaesthesia-induced DNA damage, repair and replication; DNA Polymerase γ and DNA2. We will be characterizing the interaction between the two proteins by solving the three-dimensional structure of the complex by X-ray crystallography. We will determine how these proteins affect cell survival and DNA repair in mammalian cell culture. The effect of anaesthetics on the ability of the cell to respond to oxidative stress, repair its genome, provide adequate cellular energy levels and avoid death will be assessed. This study can lead to the development of agents that may preserve cellular energy stores and thus cell survival, reducing adverse anaesthetic reactions and reducing post-operative recovery times.