

Wolfram Syndrome UK research grant funding of £15,000 has been awarded to Dr Sovan Sarkar at the University of Birmingham in UK. The project is related to the development of autophagy and NAD enhancers for the treatment of Wolfram syndrome (WS).

Brain diseases include common disorders such as dementia, and rare childhood-onset disorders like WS. In neurological disorders, a biological process that is commonly affected is called autophagy, which acts like a housekeeping process of a cell by removing undesirable cellular components such as protein aggregates and damaged organelles. When this process malfunctions, unwanted cell components build up and the cell can eventually die. Brain cells called neurons are particularly affected due to defective autophagy, leading to neuronal cell death by a process called neurodegeneration. On studying further as to why this happens, we found that autophagy promotes cell survival by maintaining the cellular level of a metabolite called nicotinamide adenine dinucleotide (NAD), whereas absence of autophagy causes brain cell death by NAD depletion.

Dr Sarkar's research team, involving Dr Malgorzata Zatyka and Ms Congxin Sun, has found defective autophagy along with NAD depletion in WS that contributes to the disease pathology pertaining to neurodegeneration. This forms the rationale to target the autophagy and NAD deficits in WS for developing a treatment strategy. To identify new therapy in a manner relevant for human biology, the research team will make neurons out of stem cells from patients' skin samples for testing medicines already in use for other conditions or as nutritional supplement. They will then determine the most effective drugs for enhancing autophagy and elevating NAD levels that will improve the survival of neurons generated from WS patients. The treatment strategy involving repurposing of drugs will be put forward in a future proposal for a clinical trial in children with WS. The ultimate goal of this research project is to improve the health of WS patients.

Dr Sarkar's primary research interest is related to the role of autophagy in neuronal survival and its biomedical implications in neurodegenerative diseases, utilising human pluripotent stem cell-derived neurons. He works on WS together with Professor Timothy Barrett at the University of Birmingham. This project is also in collaboration with Dr Laetitia Aubry at I-STEM in France for providing the control and patient-derived iPSC lines.