

Dear friends and colleagues,

I hope everyone is keeping OK and have managed to have some time relaxing over the Summer. I wanted to provide some updates from our research teams here in Birmingham.

Firstly, the TREATWOLFRAM trial is continuing in the follow-up phase. Some participants have completed their involvement, and the remaining people are being seen every 6 months for an eye test, and every 12 months for more detailed assessments including MRI scans. Our trials unit team, Amy Lamb and Lewis James, are working hard to check all the information that participants have kindly supplied, ready to be analysed when the trial closes in October 2024. I am pleased to say that we have secure drug supplies to the end of the trial, and over 80% completion rates for the tests that we need to look at to see if the intervention works to slow down the progress of the condition. I'll update further as we get nearer the end of the trial.

Secondly, our laboratory team, led by Dr Sovan Sarkar, has been very busy: Dr Malgosia Zatyka has been working on cell models of Wolfram, and her research has led to publication of a really interesting paper in the science journal "Stem Cell Reports". The report is titled: "Depletion of WFS1 compromised mitochondrial function in hiPSC-derived neuronal models of Wolfram syndrome". Essentially, mitochondria are the power houses of cells, generating the energy needed by cells to grow. Mitochondria operate closely with another part of the cell, the endoplasmic reticulum, to keep cells healthy. We've known for some time that the endoplasmic reticulum does not work properly in Wolfram syndrome. Malgosia has shown that in her Wolfram cell models, the mitochondria are also affected. This seems to relate to the way mitochondria interact with the endoplasmic reticulum. Her work implicates mitochondria in the disease processes that cause Wolfram, and suggests new targets for developing treatments for the condition.

Thirdly, my clinical consultant colleague Dr Renuka Dias has been investigating puberty and hormones in people affected by Wolfram syndrome. She has looked at a series of children and young people with Wolfram who have completed puberty. She and her team found that puberty was delayed or not completed in 40% of young men, and there were menstrual irregularities in 50% of young women. Testosterone supplements were effective in helping young men complete puberty, and there are treatments for young women to help make periods more regular. Dr Dias is presenting her findings at the European Society for Paediatric Endocrinology, so this study will reach a wide audience and help inform doctors to offer better treatments to people affected by Wolfram.

Finally, all our study team owes a big thank you to Wolfram syndrome UK as always for their generous support.

Sincerely