First ever multi-cellular model of Zellweger's syndrome developed

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Research groups worldwide have tried to develop a simple model of a rare, fatal disease called Zellweger's syndrome but none has succeeded, until researchers at the Faculty of Medicine & Dentistry at the University of Alberta did so in fruit flies.

Zellweger's syndrome is a form of peroxisome biogenesis disorder, a group of deadly genetic diseases that claim the lives of children usually before they reach their first birthday. Researchers have been stumped about how to make a multicellular model they can use to development treatments. The chair of the Department of Cell Biology, Richard Rachubinksi, and his Ph.D student Fred Mast, with the help of Drosophila [fruit fly] expert Andrew Simmonds, have been successful in developing a model of Zellweger's syndrome. This syndrome is the most common type of peroxisome biogenesis disorder.

"Mating two parents that have the mutated gene gave us a mutant fly that mimicked the human phenotype," said Rachubinski. The fruit fly is ideal for medical research because its development can be studied from fertilization through to adulthood, and the development is much more rapid than in mice or humans.

"The periods that you can allow for development are much shorter in flies so you can look at things much more quickly," said Rachubinski. "You get two generations per month."

It is also less expensive to use Drosophila. As the research group moves

forward testing compounds that could be used as pharmaceuticals to treat Zellweger's syndrome, they only have to use minute amounts compared to what would be needed for other laboratory models. And it helps that part of the study included a comprehensive gene analysis that will help them monitor the efficacy of compounds and point to new gene targets for pharmaceuticals.

This is a major step forward and it has clinicians at Johns Hopkins and McGill universities excited. They have paired up with the U of A basic scientists and hope to take what the researchers learn in flies right to patients.

"We have a plan all the way to the patient," said Rachubinski. "This really is what one calls translational research. It's going from basic molecular studies, to the hopeful development of compounds, to the application in patients."

"We hope it will be a cycle, in that we feed to the clinicians information which they will then use to generate more questions," said Simmonds. "We want them to then feed the questions right back for us to work it out."

For Rachubinski, this major advance, which is published in *Disease Models & Mechanisms*, is a great accomplishment. He has been working to understand peroxisome biogenesis disorders for almost 30 years.

"It's what I've worked for all my life and I hope to see in the next few years that we can actually move it on even farther and look towards the treatment of these patients," he said.

Provided by University of Alberta