

and the US Foundation for Prader-Willi Research will enable Associate Professor Marnie Blewitt to investigate whether awakening 'sleeping' genes could overcome some of the genetic errors underlying Prader-Willi [syndrome](#), and reduce the severity of some of its symptoms.

The researchers hope that in the long-term new drugs could be developed that keep these key genes awake, improving the quality of life of people with Prader-Willi syndrome.

Unusual inheritance

People with Prader-Willi syndrome have a range of severe and devastating symptoms including low muscle tone, an insatiable appetite and obesity, developmental delays and intellectual disability, scoliosis and short stature, and hormone dysfunction. Around one in 17,000 Australians are born with Prader-Willi syndrome, and require intensive care from families and health professionals to manage these symptoms.

Prader-Willi syndrome is caused by changes in certain genes—in this case, the relevant genes are located on a section of chromosome 15. Unlike most genetic changes Prader-Willi syndrome only occurs if the copy of these genes inherited from the father is affected, said Associate Professor Blewitt. "This is because it is only the copy from the father which is 'awake' and being used."

"People with Prader-Willi syndrome have another copy of chromosome 15—with the healthy form of the genes—that they have inherited from their mother. The problem is that these 'maternal' genes are inactive, or 'sleeping,' and can't compensate for the father's copy being absent or having an altered function," she said.

"If the maternal genes on chromosome 15 could be awakened, they could help to reduce the severity of some symptoms of Prader-Willi

syndrome. We think this could improve the lives of people with Prader-Willi syndrome and their carers. Our new funding from Prader-Willi Research Foundation of Australia and the Foundation for Prader-Willi Research will help us to explore a potential approach to awakening these genes."

Waking up genes

Associate Professor Blewitt and her research team study how genes shift between 'sleeping' to 'awake' states, and how this impacts a range of diseases.

"A protein called SMCHD1 keeps many genes in their sleeping state," Associate Professor Blewitt said. "We discovered that SMCHD1's targets include some of the maternal genes that are involved in Prader-Willi syndrome. We have already discovered that if the function of SMCHD1 is blocked, these genes will wake up and become functional."

The two research grants Associate Professor Blewitt has received will allow her to test the effect of removing SMCHD1 in cells provided by people with Prader-Willi syndrome: funding from the Prader-Willi Research Foundation of Australia will enable the team to develop the necessary tools for these experiments; while the experiments in these cells will be carried out with the support of Foundation for Prader Willi Research.

"If removing SMCHD1 does wake up the maternal [genes](#) in the cells of people with Prader-Willi syndrome, we would want to explore whether medicines that can block SMCHD1 could have the same effect," Associate Professor Blewitt said.

"Excitingly, we are already developing these medicines, and we hope they might help people with Prader-Willi syndrome by reducing some of

the serious symptoms and improving their quality of life."

Ms Kathlene Jones, CEO and founder of the Prader-Willi Research Foundation of Australia, said this research gives people with Prader-Willi syndrome and their families incredible hope for a life-changing treatment. "Prader-Willi syndrome is such a complex, multisystemic condition that the treatment of each symptom would involve an enormous research and development effort and require the person to take a multitude of medicines and interventions," she said.

Provided by Walter and Eliza Hall Institute of Medical Research

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