Australian team reveals world-first discovery in a 'floppy baby' syndrome

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In a world first, West Australian scientists have cured mice of a devastating muscle disease that causes a Floppy Baby Syndrome - a breakthrough that could ultimately help thousands of families across the globe.

The research, published online today in the Journal of Cell Biology, reveals how a team at the Western Australian Institute for Medical Research (WAIMR) has restored muscle function in mice with one type of Floppy Baby Syndrome - a congenital myopathy disorder that causes babies to be born without the ability to properly use their muscles.

The currently incurable genetic diseases render most of the affected children severely paralysed and take the lives of the majority of these children before the age of one.

Dr Kristen Nowak, lead author on the publication, said the team was extremely encouraged that it had been able to cure a group of mice born with the condition.

"The mice with Floppy Baby Syndrome were only expected to live for about nine days, but we managed to cure them so they were born with normal muscle function, allowing them to live naturally and very actively into old age," she said.

"This is an important step towards one day hopefully being able to better the lives of human patients - mice who were cured of the disease lived

more than two years, which is very old age for a mouse."

Dr Nowak said the team was able to cure the mice with the recessive form of the genetic condition by replacing missing skeletal muscle actin - a protein integral in allowing muscles to contract - with similar actin found in the heart.

"Earlier in our search to tackle these diseases, we discovered a number of children who, despite having no skeletal muscle actin in their skeletal muscle due to their genetic mutation, were not totally paralysed at birth," she said.

"On closer inspection, we found it was because heart actin - another form of the protein - was abnormally "switched on" in their skeletal muscles.

"We had already begun investigating whether we could use heart actin to treat skeletal muscle actin disease, so that discovery spurred us on, and we've now proved it can be done - we can use heart actin to overcome the absence of skeletal muscle actin in mice."

Heart actin is found in cardiac muscle and, during foetal development, it also works in skeletal muscles in the body, but by birth, heart actin has almost completely disappeared within skeletal muscle.

Using genetic techniques, the WAIMR research team has reactivated the heart actin after birth in place of skeletal muscle actin, reversing the effects of the congenital myopathy.

Head of the WAIMR research group Professor Nigel Laing said the team's next step was to apply their findings to human patients.

"We are now screening more than a thousand already-approved

medications looking for one that might increase heart actin in skeletal muscles, which could potentially offer a treatment for many patients," he said.

"Current therapies only target the effects of these conditions, not the condition itself - we hope our approach could lead to a much greater improvement for a range of muscle diseases."

This discovery is the latest for the team which has been investigating debilitating muscle diseases for more than 20 years.

The first major breakthrough for actin disease was in 1999, when the team identified that defects in the skeletal muscle actin gene, ACTA1 - responsible for producing skeletal muscle actin, cause multiple muscle diseases.

Since then, the team has classified and named a new muscle disease 'Laing Myopathy' - named after Professor Nigel Laing - and helped implement world-wide screening for families at risk of genetic muscle disease.

WAIMR Director Professor Peter Klinken said he was thrilled WAIMR was playing such an integral part in helping tackle devastating muscle diseases.

"The persistence and determination shown by Professor Laing and his team over many, many years is nothing short of inspiring," he said.

"They've asked some big questions in their quest to find a cure for this Floppy Baby Syndrome and have worked tirelessly to find the answers to those questions in the hope of helping families across the world.

"Research institutes like ours exist to help people live healthier lives and

I am delighted at the important discoveries we are making in this field."

This research has been funded by the National Health and Medical Research Council, WAIMR and a number of patient support groups including the Association Française contre les Myopathies (French Muscular Dystrophy Association) and the US Muscular Dystrophy Association.

The research project centred at the WAIMR laboratory was a collaborative effort with groups at the Medical Research Council and the University of Oxford in the United Kingdom, Cincinnati Children's Hospital Medical Center as well as the Centre for Microscopy, Characterisation and Analysis at the University of Western Australia and Perth-based Proteomics International which have also assisted the team's work.

Floppy Baby Syndrome

• The skeletal muscle actin mutations which cause congenital myopathies can be classified into five individual diseases which affect thousands of families worldwide.
• Children with recessive muscle actin diseases have no skeletal muscle actin because of mutations in the skeletal muscle actin gene which "knock out" the gene function.
• In Australia, dozens of families are affected by congenital myopathies which bring high emotional costs and personal suffering, as well as financial and community burdens.

Source: Research Australia (news : web)