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Babies born with no eyes: Scientists identify genetic cause

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Scientists at University College Dublin, Ireland, have identified a genetic alteration which causes a child to be born with no eyes – a condition called anophthalmia.

According to the findings published in the current issue (December 2011) of *Human Mutation*, a child's eyes will not develop fully in the womb if the child has alterations in both copies of its STRA6 gene which is responsible for transporting vitamin A into the cells.

This new discovery means that scientists can now develop a genetic test for couples who may be carrying the altered gene and planning to have children.

If identified, the couples can receive advice and counselling about the implications of carrying the gene alteration for their present and future children.

There is no clinical treatment for anophthalmia (the absence of one or both eyes), and children born with the condition must have prosthetic eyes fitted to help their face and skull to develop naturally.

Anophthalmia (absence of one or both eyes), and its sister conditions microphthalmia (small eye) and coloboma (malformed eye), arise during the development of the baby in the womb.

Although individually rare, these three major structural eye defects

account for 11% of all childhood visual impairments. They can also be associated with other birth defects such as malformations of the heart, lungs and diaphragm.

According to the Micro & Anophthalmic Children's Society UK, Anophthalmia occurs in around 1 in 100,000 births, and Microphthalmia and Coloboma occur in around 1 in 10,000 births.

"Our scientific study involved nine individuals from across several generations of an Irish ethnic minority family of nomadic descent who suffer with one or more of the three eye defects to varying degrees of severity," said Dr Sean Ennis from the UCD School of Medicine and Medical Science, University College Dublin, and the National Centre for Medical Genetics, who led the research.

"Using advanced gene sequencing technologies, we firstly scanned for regions of DNA shared by all patients before analysing a single common region for the disease gene. From this we pinpointed STRA6, a gene responsible for transporting vitamin A into cells."

Working with Dr Hui Sun and Dr Riki Kawaguchi of the University of California, the research team went on to show that the genetic mutation identified in these patients significantly impairs the ability of STRA6 to transport vitamin A into the cells. And consequently, the amount of vitamin A needed to support normal eye development in the embryo is lacking.

The research funded by the National Children's Research Centre at Our Lady's Children's Hospital in Dublin and the Health Research Board in Ireland has resulted in significant advances in the understanding of individual genes that can cause anophthalmia, microphthalmia, and coloboma, and it also adds important diagnostic criteria to the field of general eye malformations.

"Changes in the DNA sequence of STRA6 have previously been shown to give rise to Matthew-Wood syndrome, a severe developmental disorder that includes eye malformations," explained Jillian Casey, UCD Health Sciences, University College Dublin, the first author on the scientific paper which was part of her PhD.

"At present, only patients with Matthew-Wood Syndrome are considered for STRA6 genetic testing. Our findings show that alterations in the STRA6 gene can also give rise to isolated eye malformations and suggest that patients with eye defects of unknown cause should also be considered for STRA6 testing."

Having identified the novel genetic basis of these eye defects in the Irish population, the scientists now aim to translate the findings into clinical practice. This will involve developing and introducing a genetic test to the diagnostic laboratory at the National Centre for Medical Genetics (NCMG).

The molecular laboratory at NCMG offers carrier testing for genetic disorders common in the population and this condition can now be added to the testing panel.

"Accurate carrier testing and genetic counselling can be offered to those individuals planning to have children. And ultimately, this work may be used to develop preventive measures or possible treatments in the future," said UCD Professor Andrew Green, Consultant in Medical Genetics at Our Lady's Children's Hospital, Dublin, Ireland.

The scientific research team also included Dr Brendan Kennedy, UCD Conway Institute of Biomolecular & Biomedical Research, University College Dublin, Ireland.