# Novel genetic mutations may arise during early embryonic development

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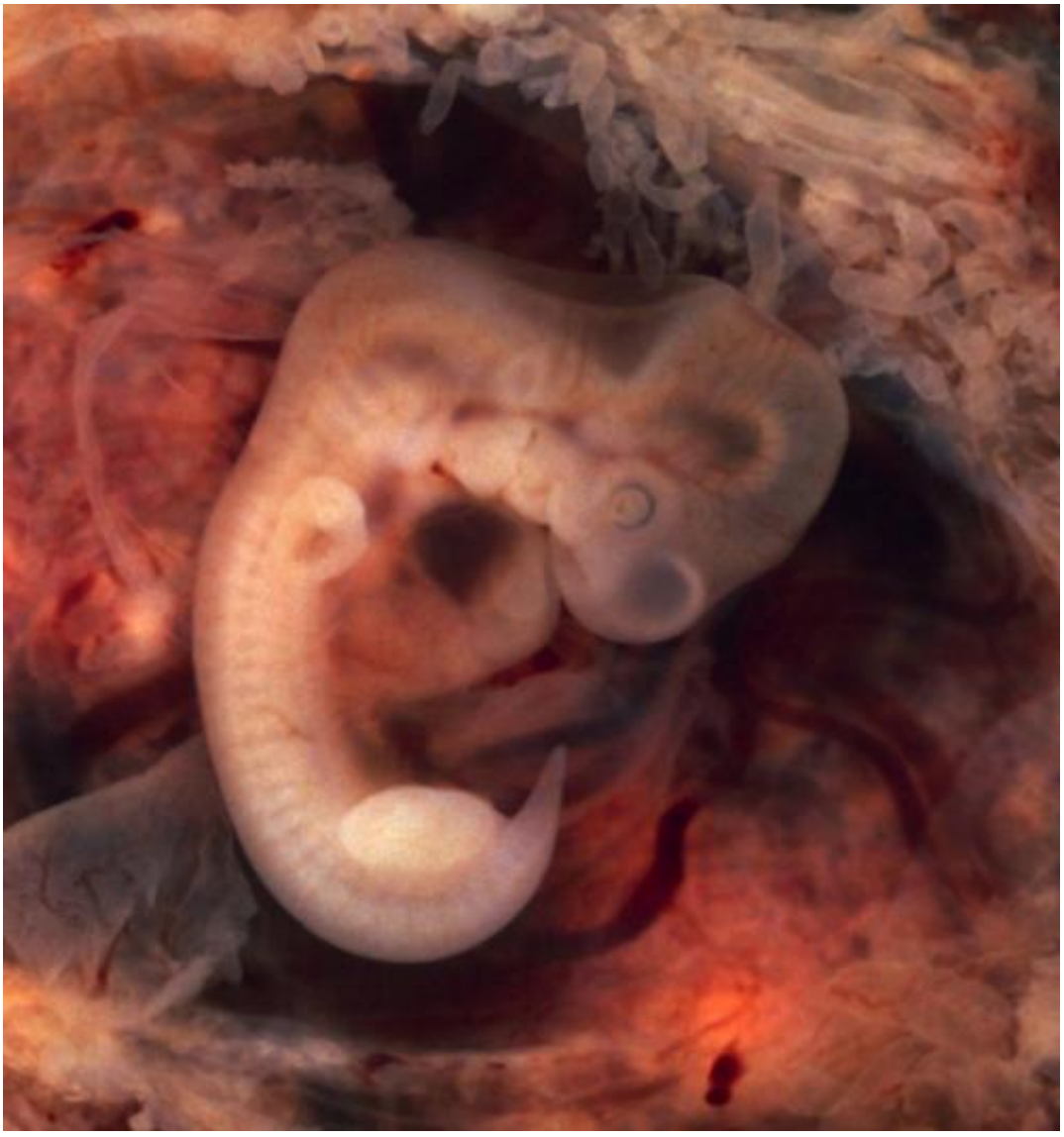

Human Embryo. Credit: Ed Uthman, MD/Wikipedia

Until now, de novo genetic mutations, alterations in a gene found for the first time in one family member, were believed to be mainly the result of new mutations in the sperm or eggs (germline) of one of the parents and passed on to their child.

Researchers from The Netherlands have now succeeded in determining that at least 6.5% of de novo mutations occur during the development of the child (post-zygotic) rather than from the germline of a parent. The research is published today in the *American Journal of Human Genetics*.

Christian Gilissen, PhD, Assistant Professor in Bioinformatics at Radboud University Medical Centre, Nijmegen, The Netherlands, will tell the conference that, due to the technical difficulties of identifying and validating post-zygotic events, until now there have been very few estimates as to how common they are. "Determining exactly how many mutations occur during the development of the child has been challenging because conventional genetic sequencing is not sensitive enough to reliably identify post-zygotic mutations," he will say.

Unlike germline mutations, the post-zygotic genetic changes are only present in a proportion of the cells of the individual. This is important because the proportion in which the de novo mutation is present in a patient, as well as the type of cells in which it occurs, may not only determine the clinical outcome of a disease for the patient, but also affect the risk of the parents having another child with the same disease in future pregnancies.

"Currently, patients with a child with a disease caused by a de novo mutation are counselled that the risk of recurrence due to the same mutation in another child is between 1 and 5 percent, but if the disease is the result of a post-zygotic change, the recurrence risk will be extremely low," says Dr Gilissen. Better information on the origin of de novo mutations will enable better information on recurrence risk, and will

enable parents to make more informed reproductive choices.

It is difficult at this stage to foresee the full impact of post-zygotic mutations in terms of treatment options for disease because the study was mainly focused on the technological aspects of these genetic changes , the researchers say. "The knowledge that our genomes may be much more dynamic and changeable than previously thought and the ability to detect such changes by using sophisticated sequencing techniques will certainly have clinical implications in the future. It may also be reasonable to assume that post-zygotic mutations restricted to specific types of cells, or organs, may also be involved in causing disease.

"We now also know that for us to be able to find post-zygotic mutations, our sequencing needs to be even more sensitive. We intend to follow up this work by trying to get yet more detail on the prevalence of such mutations as well as by testing for these events in other tissues; most genetic investigations are performed only in blood, so we may have missed some disease-causing mutations by not testing elsewhere," Dr Gilissen will conclude.

**More information:** *American Journal of Human Genetics*, www.cell.com/ajhg/abstract/S0002-9297(15)00194-9

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