

# New study sheds light on how deadly genetic diseases may be inherited

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Credit: University of Birmingham

A new study has shed light on how deadly genetic diseases may be inherited, according to research published today (27/06/2018) from a project led by the University of Birmingham, Imperial College London and European collaborators in the journal *Nature Communications*.

DNA in mitochondria, the powerhouses of the cell, is passed down from mother to child. But there are many mitochondria in each cell, and these mitochondria may have different genetic features. If a mother carries a mixture of mitochondrial DNA (mtDNA) types, this can make it hard to say which features their children will inherit. For mothers carrying a disease-causing mtDNA mutation, this makes family planning and clinical therapies challenging.

In particular, the role of a mother's age has long been a mystery. Is the probability of a child inheriting a particular mtDNA feature higher when mothers are younger or older? An answer to this question could help plan clinical strategies to improve fertility and prevent the inheritance of deadly mitochondrial disease.

To address this, the team used cutting-edge technology to reveal the mixtures of mtDNA in the egg cells of mother mice at a wide range of ages, and in the litters of offspring the mothers produced. In concert, they developed a mathematical model describing the changes to, and inheritance of, mtDNA from mother to offspring. In this study, they combined the model and data to learn how different biological processes affect mtDNA through and between generations.

The team found that the variability of mtDNA dramatically increased as mothers aged. This means that the probability of inheriting more extreme—both lower and higher—levels of a genetic feature increases for older mothers.

Dr. Iain Johnston from the University of Birmingham's School of Biosciences, who jointly led the study, said: "Moving forward, we're aiming to harness these powerful ways of using large datasets to describe and predict the dynamics of mtDNA inheritance in humans, and to learn what it is about these mtDNA types that predicts their evolution across generations."

Dr. Joerg Burgstaller at UVM Vienna said: "Older [mothers](#) have a higher chance of having some eggs with low levels of a given mtDNA type. This may improve their chance of selecting eggs with low mutation levels in IVF cycles."

The team also found that different mtDNA mixtures were inherited in different ways—with some mtDNA types favoured for inheritance and some disfavoured. They used their findings to create a way to predict how the risk that offspring would inherit disease-causing mtDNA [features](#) changes over time.

Dr. Nick Jones from Imperial College London, a co-lead author on the study, said: "It's this combination of a mathematical model with an unprecedented volume of experimental data that allowed us to reveal the subtle mechanisms affecting mtDNA [inheritance](#)."

**More information:** Joerg P. Burgstaller et al. Large-scale genetic analysis reveals mammalian mtDNA heteroplasmy dynamics and variance increase through lifetimes and generations, *Nature Communications* (2018). [DOI: 10.1038/s41467-018-04797-2](https://doi.org/10.1038/s41467-018-04797-2)

Provided by University of Birmingham

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