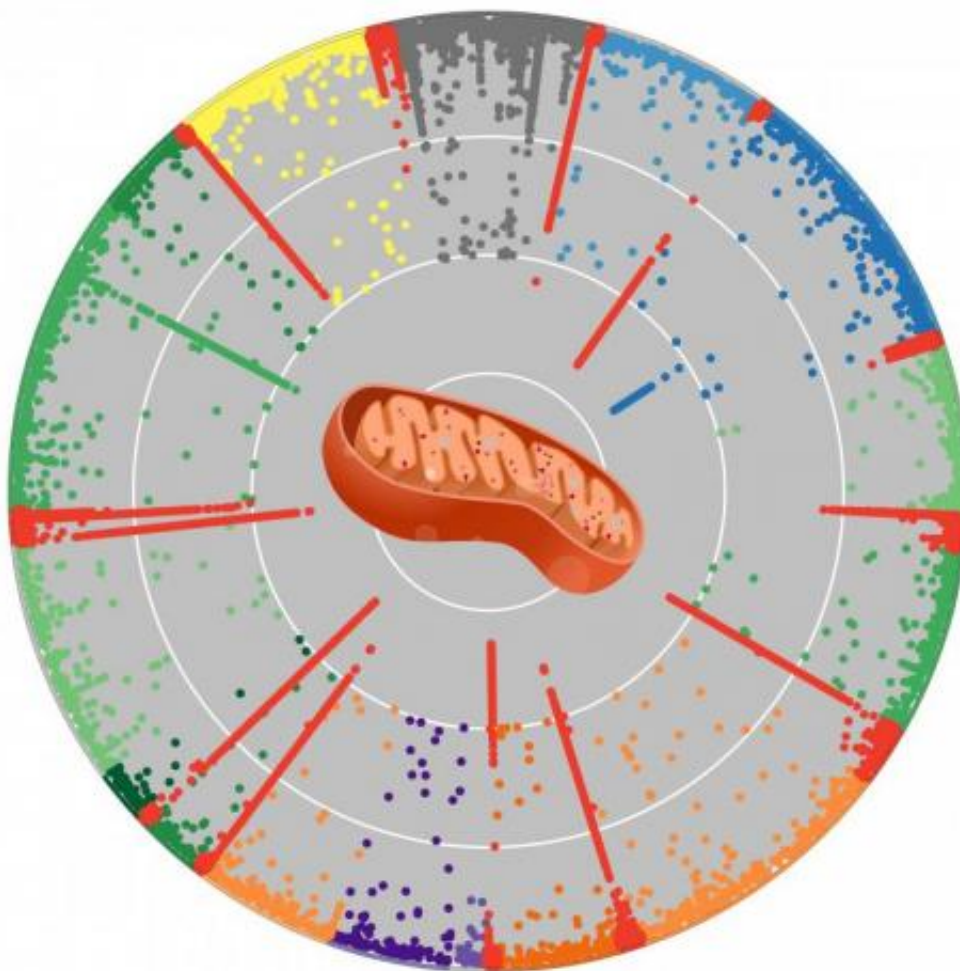


You may have billions and billions of good reasons for being unfit

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Mitochondrial RNA sequence variation across a large number of individuals.
Credit: Awadalla Lab

Although our chromosomes are relatively stable within our lifetimes, the genetic material found in our mitochondria is highly variable across individuals and may impact upon human health, say researchers at the University of Montreal and its affiliated CHU Sainte-Justine Hospital.

Genomes are changing, not just from generation to generation, but even and in fact within our [individual cells](#). The researchers are the first to identify the extent to which the editing processes of RNA code can vary across a large number of individuals. "Mitochondria are the [power stations](#) of our cells, and the more power a cell needs, such as a muscle cell, the more [mitochondria](#) it has. Mitochondria are organelles in our cells with their own [genetic code](#), separate from the DNA in our chromosomes, and the many mitochondria in the same individual can have different genetic mutations," explained Alan Hodgkinson, who is first author of the study. "The many mitochondria in the same cell can have different genetic mutations. Our research helps us to understand how variable mitochondrial RNA processing can be and what the possible consequences of that might be on health." By way of example, the researchers have found an association between the level of modification of RNA and our [basal metabolic rate](#) – the rate at which we are able to convert food into energy to power our bodies. The findings add extra layers of complexity to our understanding of how genetics influence our health.

The study was made possible thanks to the participation of nearly 40,000 Quebecers in the CARTaGENE initiative. CARTaGENE is one of the world's most comprehensive banks of genetic information: in addition to [genetic information](#), participants share their health history, residential information, ethnicity, languages spoken and their family history of disease. Philip Awadalla is Director of the CARTaGENE initiative and lead author of the study. "The people of Quebec want to take part in science," he said. "This program is unique in the world. Other initiatives are taking place, but they aren't as comprehensive. Elsewhere,

researchers are able to recruit 5% of the people they invite. Quebecers' collaboration rate is five times that." CARTaGENE's data and samples are available to the local and international research community.

The researchers looked specifically at mutations in the RNA of the mitochondria. If DNA is the printing press that determines the functions of a living organism, RNA is the print that it leaves behind. And just like with a printing press, sometimes the print (known as transcription) is slightly different from the press. "We looked at the variation within and across individuals in the mitochondrial RNA. This is the first survey of mitochondria-wide RNA variation at a population level," Hodgkinson explained. "We used the data of 1,000 participants in the CARTaGENE initiative, making this the largest RNA sequencing in the world to date. With this kind of depth of information, we've identified a vast array of fine-scaled differences not just between individuals but also within individuals – and that's the power of the data. But within that, we focused on one specific signature that we found really interesting – the signature in the sequencing data that represents the modification of RNA at important sites." "The other world first here is an unprecedented level of resolution – we're not only capturing change happening at the DNA level, now we're capturing "epiphenomena" happening at the RNA level. We can compare across individuals to see how variable different individuals are within themselves," Awadalla added.

Many other factors are at play in determining the variation in the transcription of mitochondrial RNA. "Your DNA is mostly found in the nucleus of each cell, and there is interaction between products from the genome of the nucleus and the genome of the mitochondria to create cellular energy – they're not completely separate," Hodgkinson explained. "We find an association between variation in a nuclear gene – the DNA that's from your chromosomes – with the level of modification in the mitochondrial RNA. The resulting modifications may impact cellular energy production, but there is much more work to be done to

confirm and fully understand these processes".

While the mechanisms at work in our body may offer couch potatoes a handy excuse, the actual outcomes in terms of our health may not be deterministic. "It makes sense that we would see an association between mitochondria and metabolism rates, because mitochondria are the power packs of each cell. We have determined that our genome's ability to modify itself is partly hard-wired – the open question is how does our genome react to exposures in the environment?" Awadalla said.

More information: "High-Resolution Genomic Analysis of Human Mitochondrial RNA Sequence Variation," by A. Hodgkinson et al. *Science*, 2014.

Provided by University of Montreal

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