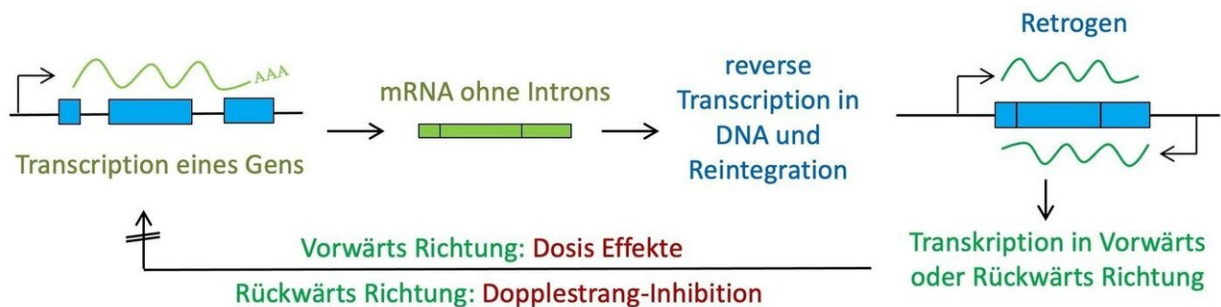


The underestimated mutation potential of retrogenes

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Retrogene function. Credit: MPI f. Evolutionary Biology

Genetic information is stored in DNA and transcribed as mRNA. The mRNA is usually translated into proteins. However, it has long been known that mRNA can also be reverse transcribed to DNA and integrated back into the genome. Such cases are referred to as retrogenes. In an article, a team from the Max Planck Institute for Evolutionary Biology in Plön and the Zoological Institute of the Chinese Academy of Sciences in Beijing now reports that this process was previously underestimated by at least a factor of one thousand and that it is an important new mutation mechanism.

There are two main reasons for this. On one hand, the common search algorithms used in genome sequence analysis do not usually take new insertions of retrogenes into account. These therefore remain hidden in

the mass of data. Only with an optimized algorithm like the one developed by the scientists can these insertions be systematically discovered. On the other [hand](#), the authors showed that most of the insertions are relatively short-lived. In previous genome comparisons between species, they appear to be comparatively rare.

Mutation by retrogenes is usually harmful

For this most recent study, it was therefore crucial to examine populations that have only recently developed. The authors found that mouse populations that have been separated for only about 3000 years carry different retrogenes (i.e. in each population, retrogenes emerge at a very high rate but are also lost again comparatively quickly). This is because retrogenes can be harmful—even if they are integrated into non-coding DNA. If retrogenes are transcribed back into mRNA (as is the case for most of them), this new mRNA can negatively influence the mRNA of the gene from which they originated. The retrogene thus acts as a regulatory mutation, which is usually harmful.

The scientists show that the genetic burden of this mechanism is higher than that of the [point mutations](#), which until now have been the primary focus of investigations. They therefore suggest that the search for disease-causing mutations also take the retrogene mechanism into account.

More information: Wenyu Zhang et al. The mutational load in natural populations is significantly affected by high primary rates of retroposition, *Proceedings of the National Academy of Sciences* (2021). [DOI: 10.1073/pnas.2013043118](https://doi.org/10.1073/pnas.2013043118)

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