PRESS RELEASE

Keeping the neighbours quiet: A lesson from *C. elegans* in using what you have to hand

(Mainz, 03 June 2019) *Researchers from the Institute of Molecular Biology (IMB) in Mainz have uncovered a new evolutionary origin for the anti-parasitic genome defence system, piRNAs, in worms. In their research paper published in* Genes and Development*, the group of Prof. René Ketting describe how the piRNA pathway developed out of a more ancient, evolutionarily conserved protein system that is needed for correct gene expression. This new finding highlights how evolution can build on existing structures to derive novel effective parasite-control systems.*

The genome of every organism is constantly under the threat of damage from parasitic genetic elements, which are often viral in origin. Such elements, called transposons, promote their own replication by 'jumping' into new locations within the genome. These reinsertions can occur in many locations, even within genes, potentially disrupting their function. Transposons are particularly active and problematic in germ cells, the cells responsible for reproduction, where their persistent activation can lead to sterility. As a consequence, virtually all organisms have developed countermeasures to inhibit transposon jumping in the germline. Interestingly, a common theme has developed across the majority of species, which is to use small pieces of RNA to identify transposons and subsequently disrupt their activity. In essence, these small RNA molecules, also named piRNAs, act as detectives within the cell and identify active transposons allowing for cellular countermeasures e.g. activating enzymes to degrade transposon RNA. Hence, the correct production of these piRNAs is crucial in the fight to keep an organisms' genome intact.

While studying the piRNA system in the small nematode *C. elegans*, the group of Prof. René Ketting at IMB in Mainz discovered a new protein complex essential for their production. Called PETISCO–tapas in Portuguese–, mutating any of its protein subunits eliminates the production of piRNAs. Interestingly, mutations in PETISCO are also lethal. This was a big surprise to the team as other piRNA mutants are sterile but otherwise viable. As Ricardo Rodrigues, the lead author on the paper, explains, "This told us there must be another, essential function of PETISCO besides that of piRNA production. We discovered that it sits at the interface between two different RNA pathways: one is involved in piRNA production, the other appears to be involved in a small nuclear RNA pathway responsible for correct gene expression in *C. elegans*." As Prof. Ketting then elaborates, "PETISCO members are quite well conserved across many species, even those that don't have a functioning piRNA system. Two different proteins, PID-1 and TOST-1, modulate the two flavours of PETISCO. PID-1, in evolutionary terms a relatively young protein, uses PETISCO to make piRNAs, while TOST-1, a genetically older protein, defines its gene expression function. While TOST-1's function still needs to be molecularly defined, it appears to be involved in producing small RNA molecules needed to join gene segments together. Our findings strongly suggest that this latter, essential PETISCO system has been coopted later during *C. elegans*' evolutionary history to produce piRNAs."

Across different species there is considerable variation in the proteins and strategies used to combat transposons. For example, in some nematodes the ability to produce piRNAs has evolved, been lost and evolved again. This makes a comparative analysis of piRNA systems in different species quite

challenging. This latest finding suggests a possible point of commonality that may act as a template for understanding the origin of piRNA pathways in other species.

Further details
The research paper used as the basis for this article can be found here.

Prof. René Ketting is a Scientific Director at IMB and a Professor in the Faculty of Biology at the Johannes Gutenberg University, Mainz. Further information about research in Prof. Ketting's lab can be found at www.imb.de/ketting

About the Institute of Molecular Biology gGmbH
The Institute of Molecular Biology gGmbH (IMB) is a centre of excellence in the life sciences that was established in 2011 on the campus of Johannes Gutenberg University Mainz (JGU). Research at IMB is focused on three cutting-edge areas: epigenetics, developmental biology, and genome stability. The Institute is a prime example of successful collaboration between a private foundation and government: The Boehringer Ingelheim Foundation has committed 154 million euros to be disbursed over between 2009 and 2027 to cover the operating costs of research at IMB. The State of Rhineland-Palatinate has provided approximately 50 million euros for the construction of a state-of-the-art building and a further 52 million in core funding until 2027. For more information about IMB, please visit: www.imb.de.

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