Research reveals unique solution to gene regulation

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Research on a unique vertebrate called the sea lamprey shows that more than a thousand genes are shed during its early development. These genes are paradoxically lost all throughout the developing embryo except in a specialized compartment called "primordial germ cells" or PGCs. The PGCs can be thought of as embryonic stem cells and are used, ultimately, for making the next generation of lampreys. Based on computational analysis, a significant number of genes that are lost in the embryo have signatures of "pluripotency," which suggests that they could also have undesirable effects if they were inadvertently turned on in the body. In effect, by undergoing programmed genome rearrangement and gene loss during embryogenesis, the sea lamprey "seals" the genes away in the small germline compartment so they cannot be misexpressed and thereby create untoward problems (such as development of cancer, for example).

The study was completed at the Benaroya Research Institute at Virginia Mason (BRI) and recently published as a featured article in Current Biology, along with an outside commentary highlighting its biological importance.

The article authors are Jeramiah Smith, PhD, former postdoctoral fellow at BRI and now Assistant Professor of Biology at the University of Kentucky; Chris Amemiya, PhD, Principal Investigator at BRI and Professor of Biology, University of Washington; Evan Eichler, PhD, University of Washington Genome Sciences Professor; and Carl Baker, Research Scientist, University of Washington.

The discovery builds on the group's previous work published in the Proceedings of the National Academy of Sciences in 2009. "Our new research confirms that lampreys experience rampant programmed genome rearrangement and losses during early development," says Dr. Amemiya. "The genes are restricted to the germline compartment suggesting a deeper biological strategy in order to regulate the genome for highly precise, normal functioning. The strategy removes the possibility that the genes will be expressed in deleterious ways. Humans, on the other hand, must contain these genes through other "epigenetic" mechanisms that are not fool-proof.

There are several implications of this work:

- By understanding how programmed genome arrangement occurs so pervasively in lampreys, scientists can gain insight into how vertebrate genomes can remain stable and what genetic factors contribute to this stability.
- Studies in distantly related species can provide unique insights into fundamental biological concepts and may be translatable to human health.
- Identifying the molecular and developmental mechanism of how lampreys regulate their genome may have implications for disease treatment.

Sea lampreys are "basal" vertebrates that lack jaws and have unique properties that are of interest to scientists. This includes a completely different genetic toolkit for their adaptive immune system, which was also discovered, in part, by Amemiya's group, as well as remarkable powers of regeneration that allow them to completely recover from a severed spinal cord.

High throughput genomic sequencing, computational analysis and other

state-of-the-art scientific advances made this research possible. Grant funding was provided by the National Science Foundation, National Institutes of Health and Howard Hughes Medical Institute.

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