How the modular structure of proteins permits evolution to move forward

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Changes in a short protein domain can alter a whole signaling network involved in organ development– this is the key result of a comparative study of the development of the egg laying organ in two species of nematodes. However, the outward appearance of the organ remains the same in both species. The study provides support for the theory of developmental systems drift – a theory maintaining that, over the course of evolution, analogous organs of different species can retain the same shape and function while the regulative mechanisms underlying their development can change considerably.

The new results, published July 26 in the online, open-access journal PLoS Biology, raise the question of whether the modular structure of proteins creates space for evolutionary development, even in otherwise highly conserved structures of organs and signaling pathways.

The nematode *Caenorhabditis elegans* (*C. elegans*) is a model organism of genetics. The worm is only about one millimeter long, and its genome has been completely sequenced, so scientists can trace the fate of every one of its 959 cells. In research lasting more than a decade, Ralf Sommer, Director of the Department for Evolutionary Biology at the Max Planck Institute for Developmental Biology in Tübingen, Germany, has established as a comparative model organism, a second nematode, Pristionchus pacificus (P. pacificus). At first sight, this species resembles *C. elegans*, but it belongs to another family. The last common ancestor of the two species lived 250 to 420 million years ago, well before the zenith of the dinosaurs.

"For [this sort of] comparison, the organisms should not be too closely related, since very small differences in the genome cannot be easily assigned to single events in the evolution," explains Xiaoyue Wang, first author of the study. "The two worms are ideal and a wide variety of genetic and molecular tools is available." The scientists studied the development of the worms' egg laying organ, the vulva, which looks identical in both species and is induced to develop from six precursor cells by signals emanating from surrounding tissues

To more thoroughly test the validity of the theory of developmental systems drift, Xiaoyue Wang analyzed the induction of vulva development from a signaling center in the posterior part of P. pacificus using genetic and molecular methods. The system was used because while similar signaling pathways are involved in vulva development of both species, they appear to exert their molecular activities in different ways: "I have found a single mutation in a stop element of the DNA, where in *C. elegans* the production of a protein ends, but in P. pacificus the protein is extended by 17 amino acids," Wang says. The protein, which functions as a receptor, obtains an additional binding site through the extension that enables it to interact with another signaling pathway.

Evolution seems to use the existing signaling pathways almost like a modular construction system: In P. pacificus, a novel binding site connects a different signaling pathway which is then used in a novel context. Wang continues, "I don't believe that what we have discovered in our study of nematodes is an unusual exception. Similar processes are known to lead to cancer development in humans. But likewise, they can initiate changes that can become subject to natural selection and eventually be propagated in the course of evolution."

The observation that changes in the regulatory mechanisms do not lead to changes in the organ could be due to redundancy. In the development of the vulva of the nematodes, for example, several mechanisms acting in parallel have already been described. The modular design of proteins makes it possible to conserve important parts of the molecule over the long time of evolution, while creating opportunities for short protein domains to change. The overall impact of these mechanisms in evolution remains to be investigated.

More information: Wang X, Sommer RJ (2011) Antagonism of LIN-17/Frizzled and LIN-18/Ryk in Nematode Vulva Induction Reveals Evolutionary Alterations in Core Developmental Pathways. *PLoS Biol* 9(7): e1001110. doi:10.1371/journal.pbio.1001110

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