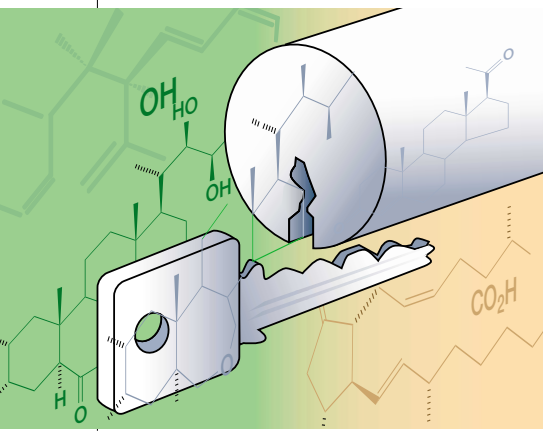
The key to signalling

Tetsuo Kushiro, Eiji Nambara and Peter McCourt

Cells of multicellular organisms need to communicate with each other to regulate their development and organize growth and cell division. Hormones contribute to these processes by acting as messengers between cells, telling them what's happening elsewhere and how they should respond. The manipulation of hormones can have profound effects on society — for example, the birth-control pill and the high-yielding crops that have fed the world since the 'green revolution' both rely on the manipulation of specific hormone functions. On the flip side, the use of performance-enhancing steroids is the bane of modern athletic competitions.

Among the many types of hormone, one particular class — the water-insoluble or hydrophobic hormones, which include mammalian steroids and many plant-growth regulators — is particularly interesting because the chemical structures of its members are often conserved between plants and animals. This similarity is surprising because it is generally thought that the plant and animal kingdoms separated from each other in evolutionary terms long before either group became multicellular. As a consequence, multicellular growth and development in these two kingdoms are very different. So why are similar keys (chemical structures) used to unlock fundamentally different developmental locks?

The conservation of biochemical molecules between say, mice and trees, could mean that common biosynthetic pathways existed before the plant and animal kingdoms separated, and that evolution has simply used these ancient pathways to create similar-looking signalling chemicals. This seems to be true for steroid-like hormone synthesis, as plants and animals have many biosynthetic steps in common. Other hormones are derived from common precursors found in plants, such as the animal retinoids and prostaglandins and the plant growth regulators abscisic acid and jasmonate. The use of common precursors certainly constrains the overall structure of hormones, but later synthetic steps are also often conserved to some degree, suggesting that the final structures have some inherent properties that make them good signalling molecules, regardless of the organism in which they function.



Part of the answer may lie with the origins of these structures. It has been speculated that the membranes of ancient, single-celled organisms were not the fatty-acid bilayers of today, but were more probably composed of terpenoid-based compounds. Perhaps steroids and retinoids, which are terpenoid derivatives, evolved from these early barrier membranes when organisms needed to know what was going on outside. If so, these hormones are some of the oldest types of signalling molecule. However, many of today's hydrophobic hormone structures require oxidation steps late in their biosynthesis. Molecular oxygen was not abundant in the atmosphere until after the development of photosynthetic organisms around 3.5 billion years ago, and so these final structures are unlikely to have evolved until after this time. Modern hydrophobic hormones may not therefore represent the original signalling hormones.

Every signal needs a receiver, and hormones in plants and animals are detected by protein receptors. In animals, steroid hormones interact with protein receptors within the cell that often bind directly to DNA to regulate gene expression. Despite the availability of completely sequenced genomes of both plants and animals, we cannot find anything that looks like an animal steroid or retinoid receptor in any plant genome. The one steroid receptor (brassinosteroid leucine-rich repeat receptor kinase) that has been identified in plants is completely unrelated to any of the known animal steroid receptors. So although hormone structures in plant and animals may have common origins, the receptors that recognize them probably evolved independently after the two kingdoms separated.

This raises some intriguing possibilities, because a signalling molecule needs something to signal to or else it would be discarded by evolution. Perhaps, then, hydrophobic hormones recognized some other ancient receptors. The recent reports of organic molecules binding directly to endogenous RNA sequences, turning them into 'riboswitches', indicates that RNA has the necessary specificity to be a receptor. This capacity could have predated the existence of complex proteins. The fact that several screens for genes involved in the response to abscisic acid have identified genes involved in RNA processing may hint at a link between this retinoid-like hormone and RNA in plants. If RNA hormone receptors did precede their modern protein counterparts, they would probably have regulated translation, whereas the first protein receptors probably bound directly to DNA, to regulate transcription. The regulatory DNA sequences or promoters that normally control transcription are usually a composite of binding sites for different proteins, thereby allowing a gene to respond to various inputs. Such input flexibility may have been more difficult to evolve at the level of translation.

Alternatively, if protein hormone receptors came into existence at the same time as the hormones they recognize, then coevolution of a receptor and its complementary hormone would be expected. Interestingly, although hydrophobic hormones are chemically diverse, their sizes are quite similar. Maybe the hormone-binding pocket of the first receptor constrained the overall size of any new chemical that could find use as a signalling molecule. This idea has been used to explain why one superfamily of related nuclear receptors seems to perceive all of the different hydrophobic hormones in animals. By analogy, perhaps the missing receptors for many of the plant hydrophobic hormones, such as abscisic acid and gibberellins, are encoded in the large family of genes that are related to the brassinosteroid leucine-rich-repeat receptor kinase.

Just as the filing of a hormone key may allow the opening of vastly different receptor locks, it may also be that a good lock can be used by many different keys. ■

Tetsuo Kushiro and Eiji Nambara are at the Laboratory for Reproductive Growth Regulation, Plant Science Centre, RIKEN 2-1 Hirosawa, Wako, Saitama, Japan.
Peter McCourt is in the Department of Botany, University of Toronto, Toronto M5S 3B2, Canada.

Hormone evolution

The similarity of hydrophobic hormones in plants and animals suggests that once you make a good key, with occasional filing it can be used in many different developmental locks.

FURTHER READING

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