

From one cell to many: how genetic flip helped in evolution

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NARWHALS AND newts, eagles and eagle rays — the diversity of animal forms never ceases to amaze. At the root of this spectacular diversity is the fact that all animals are made up of many cells — in our case, about 37 trillion of them. As an animal develops from a fertilized egg, its cells may diversify into a seemingly limitless range of types and tissues, from tusks to feathers to brains.

The transition from our single-celled ancestors to the first multicellular animals occurred about 800 million years ago, but scientists aren't sure how it happened. In a study published in the journal *eLife*, a team of researchers tackle this mystery in a new way.

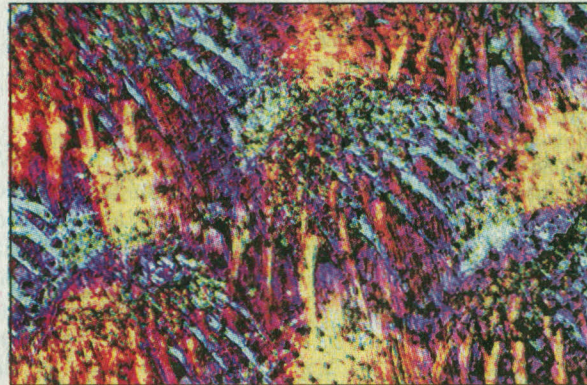
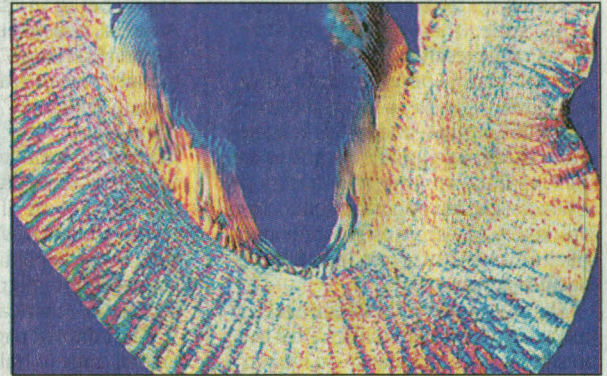
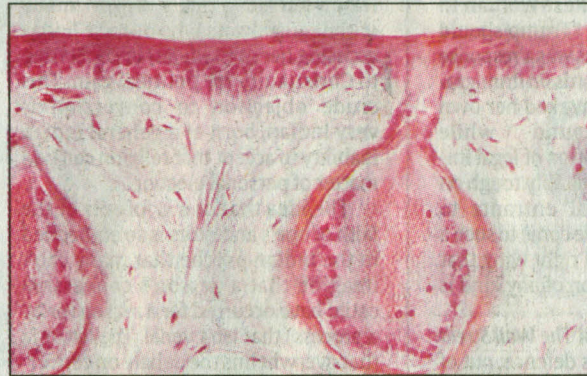
The researchers resurrected ancient molecules that once helped single-celled organisms thrive, then recreated the mutations that helped them build multicellular bodies.

The authors of the new study focused on a single molecule called GK-PID, which animals depend on for growing different kinds of tissues. Without GK-PID, cells don't develop into coherent structures, instead growing into a disorganised mess and sometimes even turning cancerous.

GK-PID's job, scientists have found, is to link proteins so cells can divide properly. "I think of it as a molecular carabiner," said Joseph W. Thornton, an evolutionary biologist and a co-author of the new study.

When a cell divides, it first has to make an extra copy of its chromosomes, and then each set of chromosomes must be moved into the two new cells. GK-PID latches onto proteins that drag the chromosomes, then attaches to anchor proteins on the inner wall of the cell membrane. Once those proteins are joined by GK-PID, the dragging proteins pull the chromosomes in the right directions.

Bad things happen if the chromosomes head the wrong way. Skin cells, for example, form a stack of horizontal layers. New cells need to grow in the same direction so skin can continue to act as a barrier. If GK-PID



(Clockwise from top left) Microscopic views of glands in frog skin, a sheep's hoof, a tamarin's skin and fish scales

how this important molecule might have evolved in the ancestors of animals. All animals (ourselves included) carry a gene sequence that's very similar to the one producing GK-PID. But that gene encodes a different molecule with a different job: an enzyme that helps build DNA. The enzyme can be found in other organisms like fungi too.

Thornton and his colleagues wondered whether that enzyme and its cousin GK-PID shared some kind of evolutionary history.

First, they made a careful study of the different forms of GK-PID and the DNA-building enzyme in about 200 species. Then they worked out how the genes for these mole-

single-celled ancestors of animals — a gene that hasn't been seen in hundreds of millions of years. Then Thornton and his colleagues did something even more amazing: They recreated those ancient molecules to see how they once functioned.

The ancestral version of GK-PID wasn't a carabiner, the scientists found. Instead, it behaved like a DNA-building enzyme. That finding suggests that in the ancestors of animals, the gene for the enzyme was accidentally duplicated. Later on, mutations in one copy of the gene turned it into a carabiner.

But how many mutations did it take to transform the molecule? That's the most re-

took a single mutation to flip GK-PID from an enzyme to a carabiner.

"Genetically, it was much easier than we thought possible," Thornton said. "You don't need some elaborate series of thousands of mutations in just the right order."

The evolution of a molecular carabiner did not by itself give rise to the animal kingdom, of course. Other adaptations were needed to grow multicellular bodies. Thornton said that it might be possible to resurrect other ancestral molecules to figure out how those adaptations evolved, as well.

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Bad things happen if the chromosomes head the wrong way. Skin cells, for example, form a stack of horizontal layers. New cells need to grow in the same direction so skin can continue to act as a barrier. If GK-PID doesn't ensure that the chromosomes move horizontally, the cells end up in a jumble, like bricks randomly set at different angles.

Previous studies have offered clues to

how this important molecule might have evolved in the ancestors of animals. All animals (ourselves included) carry a gene sequence that's very similar to the one producing GK-PID. But that gene encodes a different molecule with a different job: an enzyme that helps build DNA. The enzyme can be found in other organisms like fungi too.

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First, they made a careful study of the different forms of GK-PID and the DNA-building enzyme in about 200 species. Then they worked out how the genes for these molecules must have mutated over the years.

That analysis allowed the scientists to figure out the DNA sequence for GK-PID in the

single-celled ancestors of animals — a gene that hasn't been seen in hundreds of millions of years. Then Thornton and his colleagues did something even more amazing: They recreated those ancient molecules to see how they once functioned.

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But how many mutations did it take to transform the molecule? That's the most remarkable part. The scientists altered the gene for the ancestral enzyme with the earliest mutations that evolved in it. They found it

took a single mutation to flip GK-PID from an enzyme to a carabiner.

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And if GK-PID is any guide, Thornton said, their evolution may have been surprisingly simple. A single mutation might have been enough to switch a molecule from one job to another.

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