

LIFE SCIENCES: protein analysis

Evolution: a one way street

Mutations block the reversal of evolutionary changes

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WHAT is the difference between a fish without bones and a fish with bones? Biologists would say more than 40 million years of evolution and numerous mutations.

Scientists have been curious since the British naturalist Charles Darwin proposed the theory of evolution. They subsequently established that accumulation of mutations in the DNA over millions of years results in a new life form. But a question has intrigued many: is evolution reversible?

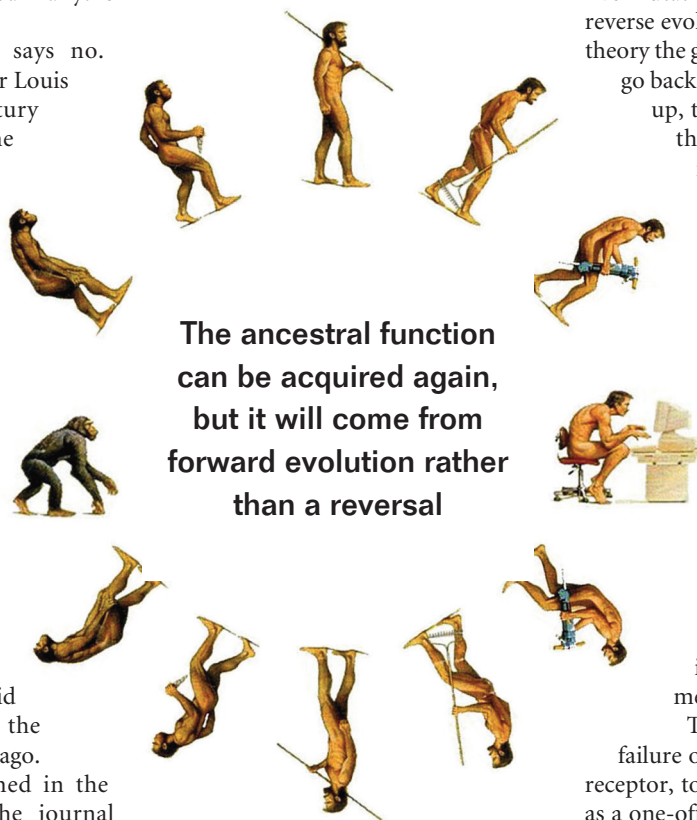
Conventional wisdom says no. Eminent dinosaur researcher Louis Dollo in the late 19th century said as evolution occurs, the changes are so intricate that it becomes nearly impossible for an organism to go back to its ancestral form. Dollo's theory has remained mostly unchallenged, barring a few instances.

In 2003, some researchers said a species of snail regained its ability to coil into a loop after having lost the trait in previous generations. "But their methods are notoriously unreliable and the merits of those claims are questionable," said Boris Igic, biologist at the University of Illinois at Chicago.

A recent study published in the September 24 issue of the journal *Nature* has confirmed Dollo's theory stating evolution is a one-way street. The group of scientists from University of Oregon and Emory University School of Medicine in the US studied for the first time the evolutionary process at the molecular level. The problem is the evolutionary process takes millions of years, which makes it difficult for scientists with their limited lifespan to make any

direct observation. Hence, Jamie Bridgham, Eric Ortlund and Joseph Thornton went around the problem by studying the evolution of a protein, glucocorticoid receptor. The receptor binds to the hormone cortisol and regulates stress response, immunity, metabolism and behaviour in humans and other vertebrates.

The scientists had earlier worked on this protein and recreated it the way it existed in boneless fish, the ancestor of all life forms on earth. They resurrected



the protein using computer and molecular biology techniques. The glucocorticoid receptor in the boneless fish was markedly different from its bony form; it could bind with hormones, aldosterone, deoxycorticosterone and, to some extent, cortisol.

During the 40 million years of its evolution into bony fish, the receptor

underwent 37 changes which made it specifically sensitive to cortisol.

The key differences between the two proteins lay in seven changes in their sequences. The team of scientists led by Bridgham, evolutionary biologist at Oregon university, made the changes to revert the receptor to its ancient state.

"To our surprise, we got a dead receptor," said Thornton, biologist at Oregon university. The scientists examined the protein at the genetic level and identified five mutations that conferred no genetic advantages, but acted as brakes and did not allow the reversal of evolution. Once the scientists fixed these five, manually, they found that the changes to seven key protein sequences worked and the new protein reverted to the ancient form.

Bridgham and his team called these five mutations ratchets; they prevented reverse evolution. This means even if in theory the glucocorticoid receptor could go back to the ancient genetic makeup, the ratchets would not allow the earlier function to be resumed. "This is not to say the ancestral function cannot be acquired again," said Igic. But the function will come from forward evolution rather than a reversal.

When whales evolved from a four-legged terrestrial ancestor, Igic said, they reacquired the ability to swim by independently gaining fins. It was a reversal in function towards its ancestor, but in biochemistry, it was a forward movement, he said.

Thornton did not see the failure of the protein, glucocorticoid receptor, to go back to its ancient form as a one-off case. However, many more studies with other proteins will have to follow before definitive conclusions can be drawn, he said.

"Everything that makes us who we are is stored in DNA. Changes at the macroscopic scale have to start at the molecular level. This is going to open up scope for further research," said Ortlund, professor of biochemistry at Emory university. ■