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Weizmann Institute Scientists Discover:

A "Risk Distribution Law" for Evolution

When are the genes adventuresome, and when are they conservative?

Prof. Naama Barkai will receive the Helen and Martin Kimmel Award for Innovative Investigation on Monday, Nov. 5 at the Weizmann Institute. The award is accompanied by a research grant of a million dollars over five years.

Taking a chance on an experiment – this is one of the impulses that drive evolution. Living cells are, from this angle, great subjects for experimentation: Changes in one molecule can have all sorts of interesting consequences for many other molecules in the cell. Such experiments on genes and proteins have led the cell, and indeed all life, on a long and fascinating evolutionary journey.

Prof. Naama Barkai of the Weizmann Institute's Molecular Genetics Department recently took a look at gene expression – the process in which the encoded instructions are translated into proteins – and the evolution of mechanisms in the cell for controlling that expression. Changes in genes, and thus in protein structure, are a double-edged sword: They can give cells new abilities or advantages for survival, but they can also spell disease or death for the organism. Not all genes evolve at the same rate. Indeed, some have been conserved through long stretches of evolution: Similar versions of some genes are found in yeast, plants, worms, flies and humans. When do cells hold on to specific gene sequences, and when do they allow evolution to experiment with them? Clearly, highly conserved genes fulfill some basic, universal function for all life, and changes in their sequences have drastic consequences, involving death or the inability to multiply. How does evolution "decide" which genes need to be conserved, and which it can change freely? What keeps these genes safe froom the ongoing experimentation that's constantly carried out on other genes?

Barkai and her team discovered a sort of "risk distribution law" for evolution. They found that a genetic "phrase" that regularly show up in the promoter region of genes (the bit of genetic code responsible for activating the gene) contains a key to gene conservation: The expression of gene that contains the sequence TATA in its promoter is more likely to have evolved than that of a gene that does not have TATA in its promoter. In other words, the level of risk appears to written in the gene code, in a way that's similar to financial risk analysis: When the cost of error is high, an investor's willingness to chance the risk is low, but if the cost of a mistake is negligible, even if the chance of making one is high, the possibility of gain may make the risk worthwhile. Evolution, it seems, discovered this principle millions of years before Wall Street.

In a different study, Barkai and her research team investigated the effects of a drastic evolutionary experiment that nature sometimes performs on living cells: the doubling of an entire genome. They looked at two related species of yeast, one of which (*S. cerevisiae*) had undergone genome doubling millions of years ago. After the duplication, *Cerevisiae* seem to have learned a new trick: They gained the ability to grow and multiply without oxygen.

To find if this difference is connected to changes in gene expression, the team tested 50 genes that play a role in processing oxygen in both species. They discovered one gene segment – a bit responsible for expression of these genes – that had changed in the course of the genome doubling in *cerevisiae*. The effects of this change were seen in over 50 genes and dramatically affected the oxygen requirements of the yeast.

The ability to live without oxygen might give *cerevisiae* a clear advantage over its sister yeast if there were a radical change in the make-up of the Earth's atmosphere. But it is exactly this combination of environmental change and genetic experimentation that has fueled evolution for millions of years and is still driving it today.

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