Abstractions

FIRST AUTHOR

Tropical cyclones go by many names — hurricanes, typhoons and tropical storms, as well as human names such as Katrina and Albert. Worldwide, there is an average of 86 such storms a year, more than half of which reach or exceed hurricane wind strength of 119 kilometres per hour. During the past 30 years, tropical cyclones over the Atlantic have strengthened, and some climate researchers have speculated that global warming may be to blame. Climatologist James Elsner of Florida State University in Tallahassee and his colleagues studied 26 years' worth of satellite data, and their findings may give more power to this argument (see page 92). Elsner tells *Nature* why stronger tropical cyclones need more than just hot air.

How was global warming implicated?

Kerry Emanuel discussed the possibility in a 2005 *Nature* paper (*Nature* **436,** 686–688; 2005), which made a lot of noise both in the scientific community and elsewhere. The standing theory on what drives a tropical cyclone is the 'heat engine' theory, whereby warm surface water evaporating from the ocean provides the 'fuel' that ignites the storm, which spirals similarly to a rotary motor. Kerry linked the increase in storm intensity to rising sea-surface temperatures — as waters warm, there is more energy available to convert to tropical cyclone wind.

What did your results show?

We speculated that if the theory is correct, you might not see a trend in the average intensity of tropical cyclones as oceans warm, but you should see a trend in the strongest storms. Our breakthrough came by thinking of the problem in terms of the subset of storms closest to their maximum potential intensity. We used satellite observations to create a consistent data set of storm intensity for all tropical cyclones around the globe. We looked at the maximum wind speeds in the strongest 30% of storms each year and showed that the strongest tropical cyclones are getting stronger, particularly in the North Atlantic. We also identified ocean temperature as an important factor in driving this trend by taking measurements in the tropics worldwide.

Is this an open and shut case, or are there other contributing factors?

Our results do not prove Kerry's theory. We've just shown that the data are consistent with his theory. We don't fully understand why some storms intensify and others don't. The heat engine theory is that you need a warm ocean — but you also need a cold upper atmosphere. We have an upcoming paper indicating that changes in solar activity that affect upper-air temperatures might also have an impact on tropical cyclone intensity. ■

MAKING THE PAPER

David Bartel & Nikolaus Rajewsky

RNA fragments tune the production of thousands of cellular proteins.

David Bartel (left) and Nikolaus Rajewsky.

When David Bartel and Nikolaus Rajewsky presented their work at a molecular biology symposium in Miami in February, the two scientists discovered that they were tackling the same issue. Each was addressing a vexing question: what effect tiny snippets of noncoding RNA called microRNAs (miRNAs) have on the production of a cell's many proteins, or 'proteome'. To answer this, the researchers needed to be able to look at changes in thousands of proteins at once; a feat that few labs in the world have the technology to do. By detecting differences in protein abundance, both Bartel and Rajewsky's teams were able to glean insight into how miRNAs act to fine tune the levels of thousands of proteins in a cell. And having realized that their studies complemented each other, the two groups decided to submit their papers for publication simultaneously.

Double action

MicroRNAs are tiny RNA fragments comprising 21 to 24 nucleotides that regulate gene expression in cells by pairing to specific regions of the messenger RNAs that carry the 'recipe' for a protein's synthesis. In some instances, this pairing reduces a protein's output by destabilizing the mRNA, causing its degradation. In addition, miRNAs can directly interfere with translation, the protein-building process. Previous studies had identified both of these means of repression and established that miRNAs have a widespread influence on mRNA levels through the first of these processes. But until now, researchers didn't have the technology to quantify the effect of the second process on protein levels — in theory, these could be changing even in the absence of a discernible change in mRNA levels. "Regulation of the translation level has been uncharted territory on a genome-wide scale," says Rajewsky, a systems biologist at the Max Delbrück Center for Molecular Medicine (MDC) in Berlin, Germany.

The two groups independently addressed the problem using a mass-spectrometry technique called SILAC, in which specific amino acids are labelled with isotopes that can then be used to flag proteins that have been manufactured by the cell. The researchers artificially increased the abundance of certain miRNAs in cultured human cells one at a time, and then detected the proteins that responded. Rajewsky's colleague, Matthias Selbach, also at MDC, took another step, creating a novel adaptation of the SILAC technique that allowed them to quantify dynamic changes in protein synthesis. In other words, this innovation could track how miRNAs affected the process of synthesis, not just the final output. The other group, co-led by Bartel, a molecular biologist at the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, and Steven Gygi, a mass spectrometrist at Harvard Medical School in Boston, Massachusetts, examined the effect of knocking out a certain miRNA from a type of mouse immune cell. By comparison with normal cells, they hoped to establish the normal interactions between a miRNA and its targets.

Both groups found that individual types of miRNA can repress the production of hundreds of proteins by inhibiting their translation, not just by destabilizing mRNA (see pages 58 and 64). The studies revealed that most proteins' levels dropped by less than 30% in response to a single type of miRNA — a relatively modest decrease and in many cases not much different from the numbers reported by previous work that measured changes in mRNA. "This tells us that if you only look at what happens to the messenger RNAs, you're missing some potentially important information, but not as much as people had feared," says Bartel.

Indirect route

Most changes exerted on protein expression by individual miRNAs are relatively mild, but a significant number of the effects are more profound, says Rajewsky. His team 'knocked down' — that is, reduced the expression of — a naturally occurring miRNA dubbed let-7b. This is a regulator of an enzyme known as Dicer, and let-7b knockdown decreased the enzyme's expression by as much as fourfold. Dicer regulates the biogenesis of all miRNAs, so let-7b has an indirect influence over thousands of gene products.

Rajewsky notes that new proteomics techniques will continue to reveal further details, such as shifts involved between the messenger RNA stage and the resulting proteins. Most of the regulation exerted by let-7b occurs at the translational level, not through reductions in mRNAs. Methods such as microarrays or RNA sequencing would not have captured these changes, Rajewsky says. "I think that it's just one example — and there are going to be many more — where you cannot explain what's going on without looking at the proteome." ■

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