IMBA Press Release

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NEW STRATEGY TO AVOID COLLATERAL DAMAGE IN CANCER

Scientists at IMBA have identified the final component that turns the RNA ligase into a fully viable enzyme in humans. That opens up perspectives for new treatment strategies for numerous types of breast cancer and leukemia.

Ligases are enzymes that aid the bonding of two molecules. For example, the RNA ligase ensures that copied parts of DNA are bonded into a viable tRNA, which in turn delivers the blueprint for producing proteins.

New starting point for cancer treatment

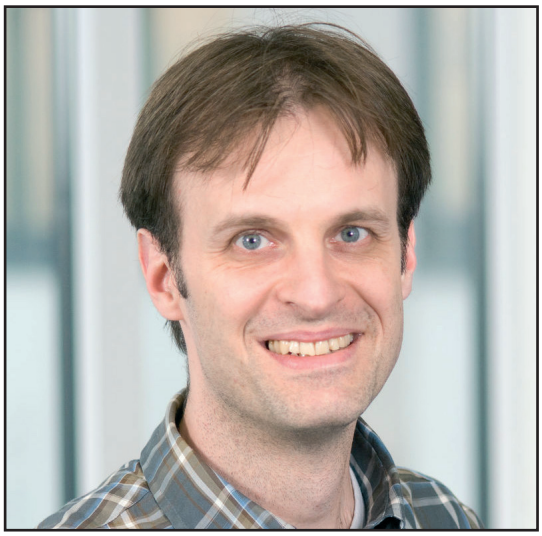
RNA ligases also have other functions that have not yet been researched in depth in humans because the composition of this important enzyme was not clear. "We already know from studies on yeasts that ligases are involved in defending cells from stress factors," said Javier Martinez, a group leader at IMBA. These functions are highly probable in mammal cells as well, and could be a new starting point for cancer therapies – especially for the treatment of various types of breast cancer and leukemia. Scientists already believe there is a close relationship between the function of the enzyme and the onset of these diseases.

"If we target and block one part of the ligase function, we will be able to approach cancer therapy in a much more specific manner than before. The impact of this enzyme is much farther down the cell's signal transduction cascade than conventional medicinal targets," said Martinez. This can be compared to a tree with one leaf affected by a disease. Of course it would be possible to cut off a thick limb to get rid of the diseased leaf. But it would be far less damaging to the tree to cut off just one thin branch.

This new approach is highly promising, and will certainly attract the interest of the pharmaceutical industry. But first Javier Martinez wants to test the function of ligases in mice.

Fundamental component of biology identified

This research into the function of ligases and their role in fighting cancer was made possible by the work of Martinez' team, in which the entire composition of ligase was resolved piece by piece. The researchers' initial success came in 2011, when they were first able to describe the most important basic components of the enzyme (Popow et al., Science 2011). Now Johannes Popow, a young, gifted scientist, has achieved a breakthrough, which the renowned scientific journal Nature has published in its current issue. He discovered that an important protein called archease is bonded to the ligase. Without this protein, the enzyme can catalyze only one single bonding process. Archease is what makes it possible for the enzyme to regenerate so it is ready for the next catalyzation process. Popow is very pleased "that we have identified this crucial component, and that by understanding the composition of ligase we will now be able to examine the function of this important enzyme more closely, and possibly apply the results for medical science."



Publication

J. Popow, J. Jurkin, A. Schleiffer, J. Martinez. Analysis of orthologous groups reveals Archease and DDX1 as tRNA splicing factors. Nature, 2014. DOI 10.1038/nature13284.