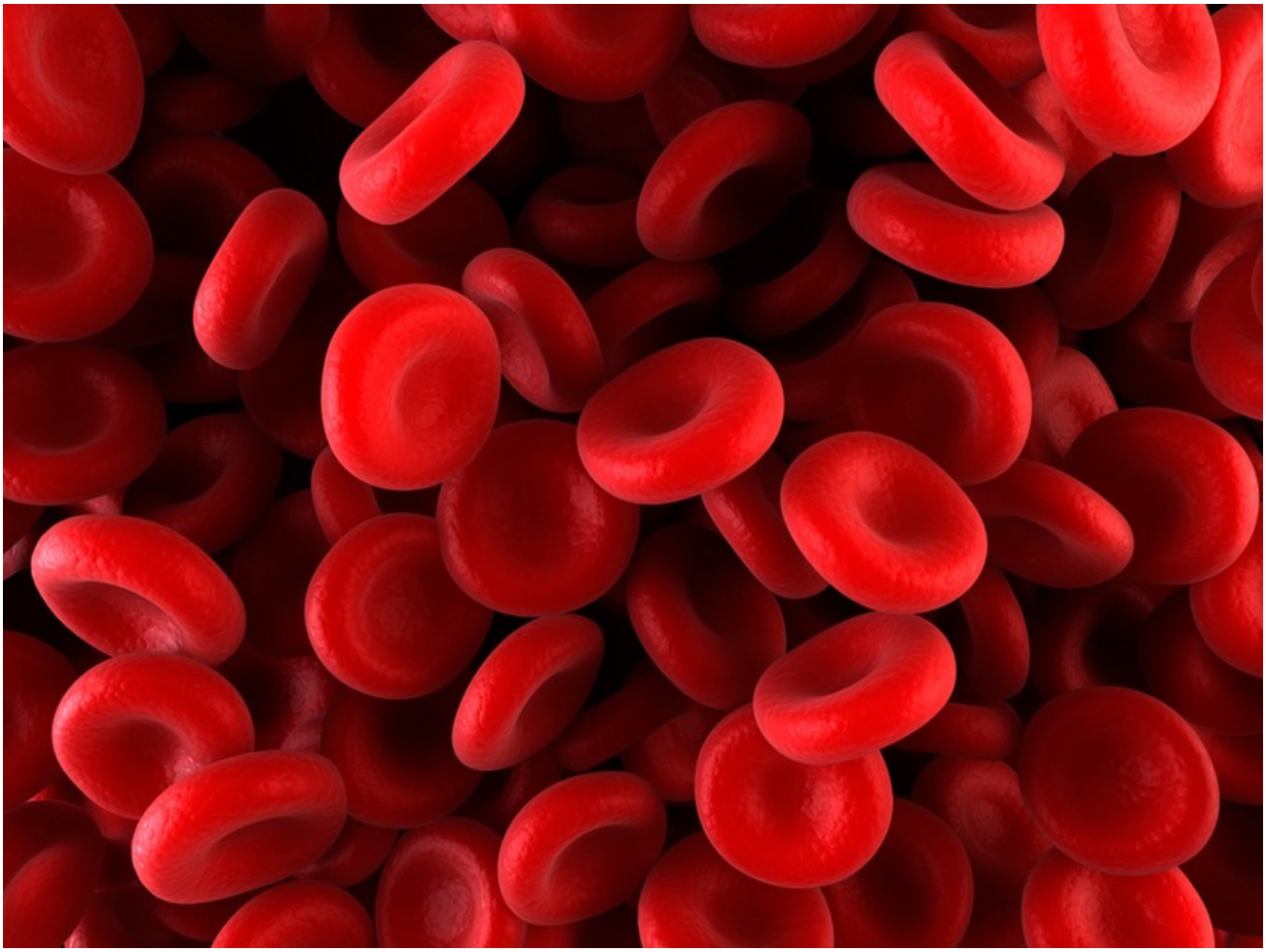
'Molecular prosthetic' replaces function of missing proteins

The molecule hinokitiol can move iron into cells when the body's own transport proteins are deficient, as occurs in conditions such as cystic fibrosis. Andrew Masterson reports.



Iron is vital to the function of red blood cells, which transport oxygen around the body.
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A molecule derived from a species of cypress tree native to Japan might hold the key to better treatment for diseases such as anemia and cystic fibrosis.

Researchers from the University of Illinois, Harvard Medical School and Northeastern University, all in the US, **report in <http://science.sciencemag.org/cgi/doi/10.1126/science.aah3862> *Science <http://science.sciencemag.org/cgi/doi/10.1126/science.aah3862>*** that the molecule – called hinokitiol – can restore iron levels to cells starved of the mineral by a shortage of proteins.

The lack of proteins to transport iron across cell membranes is a primary cause of anemia, cystic fibrosis and certain types of heart disease.

Currently there is no way to restore the missing function, reducing doctors and patients to simply managing the symptoms of the conditions.

The scientists, led by Martin Burke, discovered that hinokitiol acts as a "molecular prosthetic", transporting iron in the absence of the body's normal proteins.

Three hinokitiol molecules are needed to encase a single iron atom and make the delivery.

"If you've lost a hand, even a simple prosthetic device is really helpful," he says. "In the same way, we found that a small molecule that replicates the main job of a missing protein can be sufficient to restore functionality in cells and animals."

The cypress molecule has yet to be tested in living humans, but if animal test results scale up, administration is quite likely to be very simple.

Burke's team tested hinokitiol on mice, rats and zebrafish engineered to lack iron-transport proteins. The substance was orally administered to the rodents, and simply dropped into the fish's aquarium. In all cases iron levels in the cells were restored.

A second experiment tested the effects of the molecule on a culture comprising human gut cells. Once again, deficient iron levels were restored.

Hinokitiol has been a much-studied substance over the past few years. It is sometimes incorporated into cosmetics, although Japanese guidelines restrict it to low densities because of unanswered questions about possible toxicity.

In 2014 a team led by Lan-Hui Li from the National Taiwan University **reported in the journal <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0104203> *PLOS***

<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0104203> that the molecule showed "potent anticancer effects", inhibiting "proliferation and colony formation" in lung cancer cells.

Of the current research, which was supported by the US National Institutes of Health and Howard Hughes Medical Institute, Burke says it is hopefully a first step.

He and his team aim to search for other possible molecular prosthetic candidates, particularly in relation to cystic fibrosis.

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