Cells pumping iron to prevent anemia

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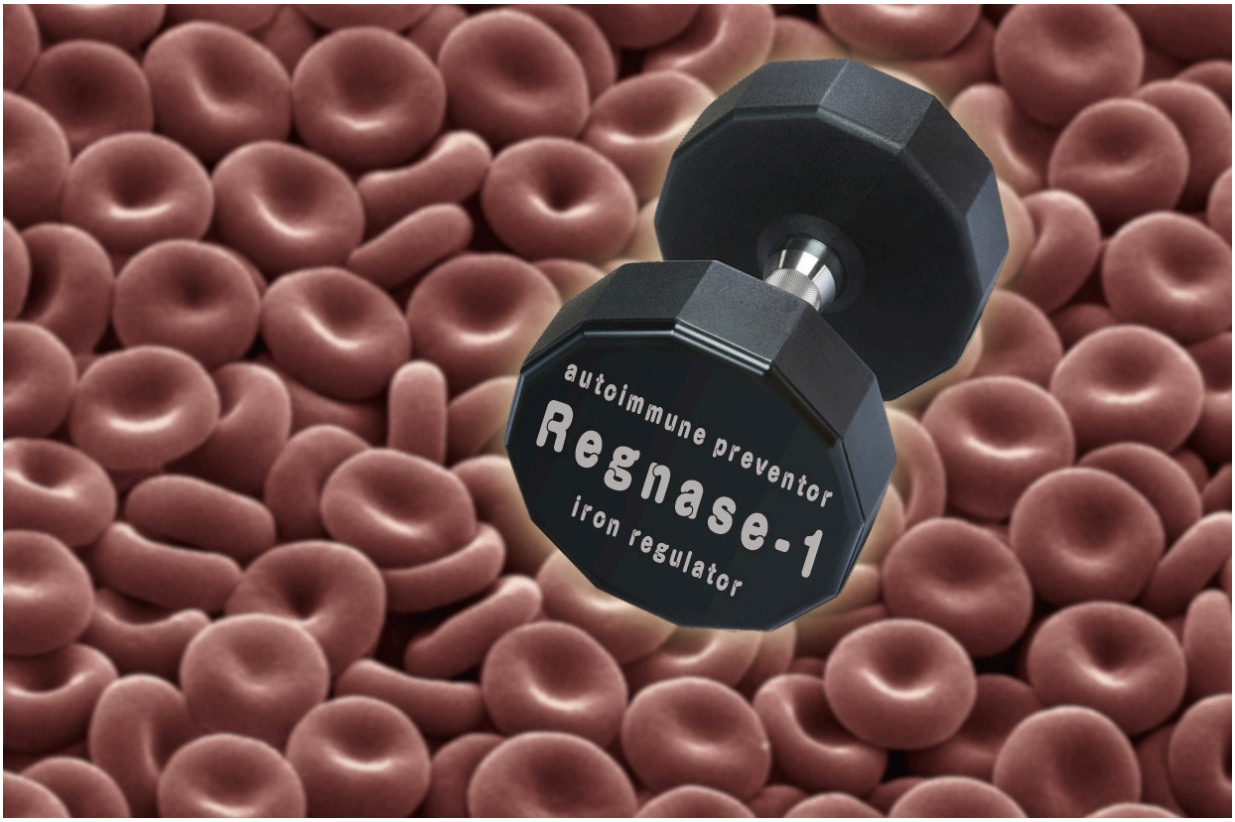

Kyoto University researchers identify Regnase-1, a gene previously thought to prevent autoimmune disease, as a key regulator in iron metabolism. Credit: Kyoto University

Maintaining a good balance of iron in the body is necessary for health: too little can lead to anemia, but too much can cause debilitating disorders such as *hemochromatosis*.

The uptake and metabolism of iron in the body is one of the most tightly-controlled systems in mammals. Iron 'regulation' occurs at multiple levels, from controlling gene expression to degrees of protein synthesis, but some key factors have yet to be uncovered.

As described recently in *Cell Reports*, Kyoto University researchers have now identified a specific gene—initially known to prevent autoimmune diseases—as a key regulator in iron uptake.

"We found previously that when mice lack the gene *Regnase-1* they suffer from severe autoimmune diseases and anemia," explains first author Masanori Yoshinaga.

"At first, we assumed that anemia was a secondary effect, but after detailed analysis we found that the two symptoms develop independently."

Continued study of mice with a Regnase-1 mutation revealed a functional defect in the principle site for iron absorption in the body, the *duodenum*, which is the first section of the small intestine, coming directly after the stomach.

"The next step was to find the role of Regnase-1 in iron-uptake maintenance. We started by looking at the most important iron-uptake gene, Transferrin Receptor 1, or *TfR1*," continues Yoshinaga.

"Our results showed that Regnase-1 degrades the mRNA of TfR1, thereby inhibiting the synthesis of the TfR1 protein, and additionally that it likely regulates other important iron-controlling genes."

"Further analysis of Regnase-1 in iron-related homeostasis," concludes team leader Osamu Takeuchi, "may provide insight into the mechanisms causing anemia and other iron-related disorders, perhaps eventually

leading to new methods of treatment."

More information: Masanori Yoshinaga et al, Regnase-1 Maintains Iron Homeostasis via the Degradation of Transferrin Receptor 1 and Prolyl-Hydroxylase-Domain-Containing Protein 3 mRNAs, *Cell Reports* (2017). DOI: 10.1016/j.celrep.2017.05.009

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