**New Hope For Sickle Cell Disease Treatment**

A new mouse study, published in this week's early online issue of the Proceedings of the National Academy of Sciences, appears to have discovered a way to trigger production of red blood cells, raising hope of a potential new treatment for preventing the painful episodes and organ damage often experienced by people with sickle cell disease. A team of experts in childhood blood disorders, pathologists and developmental biologists, both from the University of Michigan (U-M) Health System in the US and the University of Tsukuba in Japan. found that increasing expression in the proteins TR2 and TR4, more than doubled the level of fetal hemoglobin produced in sickle cell mice and reduced organ damage. They believe their "proof of concept study" is the first to target specific proteins to prevent a disease. Sickle cell disease or sickle cell anemia, is an inherited blood disorder where a mutation in the haemoglobin gene causes a change in the shape and effectiveness of red blood cells. Instead of being round and soft, the cells become rigid and crescent (sickle) shaped, so they can't pass through small blood vessels. The problem begins to develop in the first few weeks after birth, as fetal hemoglobin is replaced by adult hemoglobin.

The disease affects hundreds of thousands of people worldwide, who experience life-long debilitating pain episodes, chronic organ damage and significantly shorter lifespan.

A few patients, however, who are born with higher levels of fetal hemoglobin, show less severe complications and live longer, so boosting fetal hemoglobin is one way to treat the disease.

Lead author Dr Andrew D. Campbell, a pediatrician and director of the Pediatric Comprehensive Sickle Cell Program at the U-M Cancer Center, told the media:

"The vast majority of sickle cell disease patients are diagnosed early in childhood when adult hemoglobin normally replaces fetal hemoglobin, but the severity of the disease can differ markedly, correlating most strongly with the level of fetal hemoglobin present in red cells."

"Currently hydroxyurea is the only FDA approved drug known to increase the levels of fetal hemoglobin within sickle cell disease patients and a substantial number of patients do respond to it," he said, "But the long term consequences for hydroxyurea are unknown, especially in children."

In their study report, Campbell and colleagues describe how, using lab mice, they found a way to boost fetal hemoglobin levels by modulating TR2 and TR4 expression. Senior author Dr James Douglas Engel, professor and chair of the U-M's Cell and Development Biology Department, said:

"While the average fetal hemoglobin was 7.6% in the sickle cell mice, the TR2/TR4 treated sickle cell mice had an average fetal hemoglobin of 18.6%."

He explains that the both anemia and red blood cell turnover improved in the TR2/TR4 treated sickle cell disease mice. The authors write:

"In a "humanized" sickle cell model mouse, forced TR2/TR4 expression increased HbF abundance from 7.6% of total hemoglobin to 18.6%, accompanied by increased hematocrit from 23% to 34% and reticulocyte reduction from 61% to 18%, indicating a significant reduction in hemolysis."

They also describe how this lessened disease complications in the sickle cell disease (SCD) mice:

"Moreover, forced TR2/TR4 expression reduced hepatosplenomegaly and liver parenchymal necrosis and inflammation in SCD mice, indicating alleviation of usual pathophysiological characteristics. "

Engel says more studies should now be done, as should clinical trials, to determine whether the approach would work in humans. Funds from the American Heart Association, Cooley's Anemia Foundation, Robert Wood Johnson Foundation and the National Institutes of Health's National Heart Lung and Blood, helped pay for the research.

Written by Catharine Paddock PhD

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New Hope for Sickle Cell

Medical News today analyzes the possible findings of a new treatment for sickle cell anemia. Babies who are born with sickle cell are also born with fetal hemoglobin, which protects the babies from receiving the symptoms. This protection doesn’t last long however, as the fetal hemoglobin is replaced with adult hemoglobin a few weeks later. The fetal hemoglobin inside babies is what the online issue of *Proceedings of the National Academy of Science* says is a “way to trigger production of red blood cells, raising hope of a potential new treatment.” (Paddock, Catharine PhD) As of now the only FDA approved way of getting to fetal hemoglobin is through hydroxyurea however the long term affects are unknown. The difference between hydroxyurea and this experiment describe in the article is that there is an increased “expression in the proteins TR2 and TR4”(Paddock, Catherine PhD) which has increased the level of fetal hemoglobin found in lab mice with sickle cell.

The experiment conducted shows that there has been progression in the field of sickle cell, however they are still in the testing stage with lab mice. If proved successful for human use, this treatment would be a major discovery as it would decrease the amount and severity of sickle cell crises experienced by those with sickle cell. Also, when they do have the crisis, the amount of organ damage will be reduced, while at the same take reducing the severity of anemia by restoring oxygen in the blood cells to a healthy level. The number of positive affects this would have on the patient personally, physically, and mentally is priceless; therefore continued research to improve the state of the disease must tested and amended regularly.