Scientists have discovered that molecules called reactive oxygen species (ROS) produced by the energy factories, or mitochondria, in cells, may play a role in a rare inherited disorder in which uncontrolled inflammation damages the body's tissues. Their research in human and mouse cells suggests that blocking these molecules could reduce inflammation in TNF receptor-associated periodic syndrome (TRAPS) and possibly other inflammatory diseases.

In addition, working in collaboration with the laboratory of Dr. Michael Sack in the NIH's National Heart, Lung, and Blood Institute, Dr. Siegel and his team identified mitochondria as the source of ROS leading to inflammatory responses. Mitochondria provide energy for cells through a series of biochemical reactions that result in the generation of adenosine triphosphate (ATP), a key energy source; ROS are routinely generated as a byproduct of these reactions. In the cells of patients with TRAPS, however, the researchers found that mitochondria generate elevated levels of ROS. Blocking mitochondrial ROS in those cells reversed the inflammation.

Another crucial finding was that mitochondrial ROS play a role in inflammatory responses in normal cells, suggesting that this phenomenon also underlies normal inflammatory responses to some extent.

"Overall, I think the important idea is that there is a healthy balance of ROS in the cells," says Ariel Bulua, an M.D./Ph.D. student in the NIAMS Autoimmunity Branch and the study's lead author. "While there are some beneficial roles of ROS, when they are over produced, they can cause damage."

The researchers say blocking excessive ROS with...
antioxidants may be a way to reduce the inflammation in patients with TRAPS that is not controlled by TNF inhibitors alone. However, the efficacy of antioxidants in TRAPS will have to be studied in controlled clinical trials. "Although drugs that work in cells and mice do not always translate into humans, these studies provide a new avenue for future investigation," says Dr. Siegel.

Perhaps more importantly, he says this approach may lead to improved therapies for a wide range of inflammatory diseases - not just TRAPS. "This is like a test case on a very defined set of patients," he says. "If you get a big effect clinically, I think you could try other groups of patients."

For more information about autoinflammatory diseases, visit [http://www.niams.nih.gov/Health...flammatory/default.asp](http://www.niams.nih.gov/Health...flammatory/default.asp)

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