

Cancer drugs help the hardest cases of Pompe disease

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Kids with Pompe disease fail because of a missing enzyme, GAA, that leads to dangerous sugar build-up, which affects muscles and movement. An enzyme replacement treatment pioneered at Duke University has saved many lives, but some children with Pompe disease produce an immune reaction that blocks the benefits of the life-saving enzyme treatment.

To date there has been no success in eliminating or suppressing this [immune response](#).

Now research led by Duke University Medical Center, with collaborators at other centers, has resulted in successful [enzyme replacement therapy](#) for children who were predicted to have or who had the [immune reaction](#) blocking the effects of the enzyme therapy. In the past, children with this immune response died despite treatment.

In an article appearing in *Genetics in Medicine*, the researchers showed that a very low-dose combination of medicines typically used to treat [cancer](#) was successful in eliminating or preventing the immune response.

The drugs were rituximab, [methotrexate](#) and gammaglobulins - a mix of chemotherapeutic drugs and drugs to support the immune system. These drugs were the right mix for children who had Pompe, and who were most likely weren't going to benefit from the enzyme treatment because of their anti-GAA immune response.

"The goal is to get the new combination therapy to the child who is at risk of rejecting the enzyme, before or at the time the enzyme (recombinant human GAA (rhGAA), known as Myozyme) is infused," said senior author Priya Kishnani, M.D., professor of Pediatrics and Medical Genetics at Duke. "If you can get this combination to people early, before they are infused with the enzyme, they will likely have a very good response to the enzyme treatment. Once the body has been

exposed to the enzyme treatment, the babies at risk are likely to mount an immune response that blocks the effectiveness of the infused enzyme."

The group at Duke earlier showed the role of the immune response in children with [Pompe disease](#). Once this response occurred, children who were previously doing well failed to benefit from treatment and died.

The researchers in the current study, spread out in centers at Children's Hospitals & Clinics of Minnesota, Medical College of Wisconsin/Children's Hospital of Wisconsin, Sorka Medical Center in Israel and the Evelina Children's Hospital in London, worked together to treat the at-risk babies with the chemotherapy medicines at the time enzyme treatment started or shortly thereafter.

The team at Duke used [genetic](#) sequencing to identify the children at risk of enzyme-treatment failure. The experience of the Duke group allowed for identification of these cases early.

Senior author Kishnani said the stakes of failure are very high. "Until now, children with Pompe who make antibodies to the enzyme treatment die or are placed on invasive ventilation by age 27 months," she said. "It is very difficult for families, because some children who initially showed a benefit and were able to walk then started failing once the immune response occurred. It is heartbreaking to watch, not only for family members, but also for the team that cares for the children."

The study examined four children, two who had Pompe and had never been treated and two who were treated, but were failing.

"We have made a difference in the lives of four patients at medical centers around the world," Kishnani said. "All of them have achieved new motor abilities, in distinct contrast with the relentless downhill course of patients who were

unable to tolerate the enzyme therapy and would otherwise have died." Some of these [children](#) have now been doing well for a number of years, Kishnani said.

Provided by Duke University Medical Center

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