

Different genes are expressed at different stages during pregnancy, according to scientists

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We have a good understanding of how a woman's external features can change during pregnancy, but scientists know surprisingly little about

what biological changes occur internally.

A new Northwestern Medicine study, published June 5 in the journal *Frontiers in Immunology*, provides data about immune cells and [biological changes](#) ([gene expression](#)) in pregnant people at multiple timepoints before and during pregnancy. Using RNA sequencing and [computational methods](#) to estimate proportions of different activated types of immune cells in blood the team of scientists showed how pregnancy induces progressive changes in the maternal immune system each trimester, finding that neutrophil activation, one type of immune cell, changes dramatically.

"We estimated the proportions of different cell types in blood," said lead and corresponding study author Damini Jawaheer, research associate professor of rheumatology at Northwestern University Feinberg School of Medicine. "One cell type, called neutrophils, just shot up during pregnancy. We see it went up during the first and second trimesters and then went down a tiny bit by the third trimester and postpartum. This suggests to us that neutrophils probably are doing something important during pregnancy."

Few studies have looked at how immune cells behave during pregnancy and those that do do not include a pre-pregnancy baseline. This limited the information scientists could obtain from such studies because, in the absence of a pre-pregnancy reference, one cannot say exactly what changes happen during pregnancy. But a pre-pregnancy baseline involves identifying women who are going to be pregnant at some point in the future, which is difficult and therefore poses a barrier.

In the new study, the team identified healthy women who were planning to get pregnant and tracked them throughout their pregnancy. Only people with healthy pregnancies that were delivered at term were included in the results. The scientists looked at gene expression—rather

than genes themselves—to gain a global understanding of biological changes. Not all [genes](#) are expressed at the same time: For example, when you eat, your insulin gene turns on for a time to process food.

The scientists then collected [blood samples](#) and used those to examine how much RNA each gene was producing, indicating how highly a gene was being expressed, before pregnancy and in each trimester. One striking finding was a distinct change in one cell type called neutrophils.

The function of neutrophils in pregnancy is poorly understood, said Jawaheer. Scientists know they are one of the first [immune cells](#) to respond when a cell is attacked by bacteria and viruses. Neutrophils also are the most abundant type of immune cell in blood. Jawaheer said her research conflicts with some past studies that implied neutrophils may have a negative impact on pregnancy, and instead points to a potentially protective effect.

"We think they may have a beneficial role because otherwise we would not see such a huge increase in those cell numbers among healthy women in term pregnancies," Jawaheer said. "There needs to be more work done because we can't say much about the function of the neutrophils from what we studied.

Jawaheer seeks to use these results to develop a deeper understanding of why rheumatoid arthritis (RA) improves naturally during pregnancy. She said the study takes her one step closer to answering the question that's been her lab's main focus: How does an [incurable disease](#) like RA just go away during pregnancy?

Before, without a "normal" reference point to draw from to understand what may be abnormal in RA pregnancy, Jawaheer had to create her own "normal reference."

"This was just a first pass with very high-level findings," Jawaheer said. "We have also collected other samples at different time points, and we'll look at those next. Perhaps there's some cell types other than [neutrophils](#) that play an important role in pregnancy that we weren't able to see because we were looking at a mixture of all the cells in blood together.

"We also hope this normal reference can help people doing research on diseased pregnancies like preeclampsia because you need to know what 'normal' is to understand what's abnormal in a diseased pregnancy. And a 'normal' that includes a pre-pregnancy baseline was totally missing until now."

The study, "Pregnancy-associated systemic gene expression compared to a pre-[pregnancy](#) baseline, among healthy women with term pregnancies," is published in *Frontiers in Immunology*.

More information: Matthew L. Wright et al, Pregnancy-associated systemic gene expression compared to a pre-pregnancy baseline, among healthy women with term pregnancies, *Frontiers in Immunology* (2023). [DOI: 10.3389/fimmu.2023.1161084](https://doi.org/10.3389/fimmu.2023.1161084)

Provided by Northwestern University

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