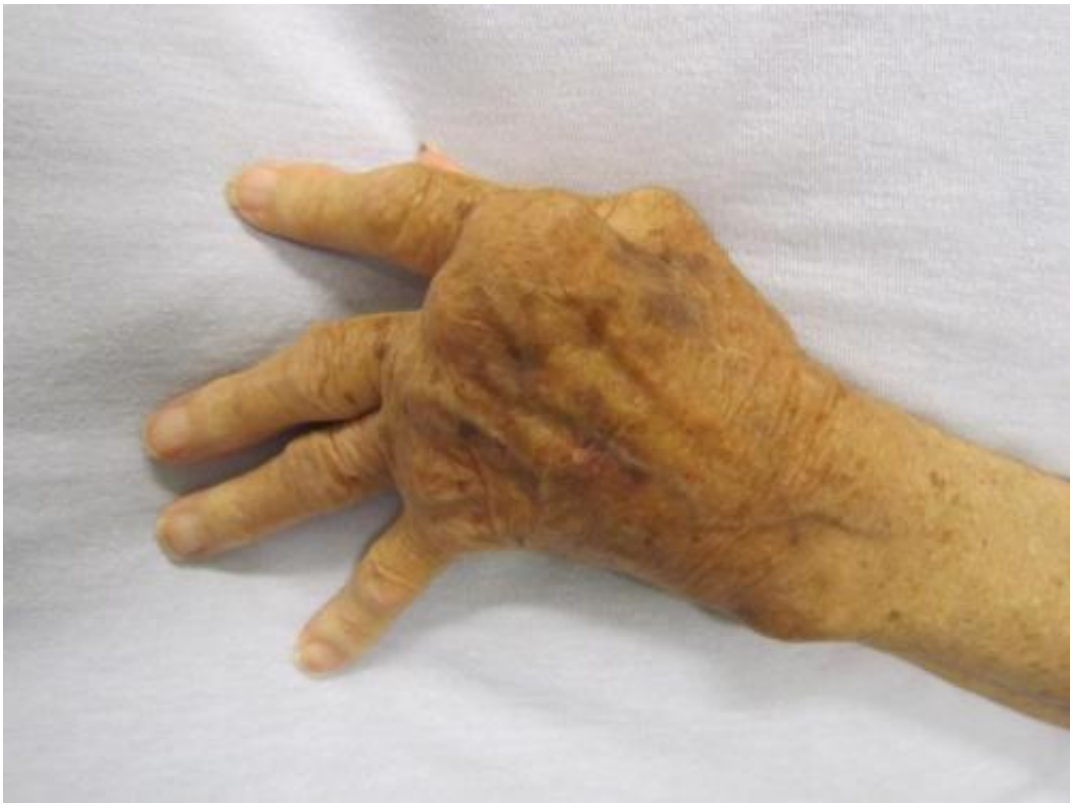
Rheumatoid arthritis meets precision medicine

March 19 2018



A hand affected by rheumatoid arthritis. Credit: James Heilman, MD/Wikipedia

Scientists are bringing precision medicine to rheumatoid arthritis for the first time by using genetic profiling of joint tissue to see which drugs will work for which patients, reports a new Northwestern Medicine multi-site study.

In the near future, patients won't have to waste time and be disappointed with months of ineffective therapy, scientists said.

"Now we can start to predict which drugs a patient will respond to," said co-senior author Harris Perlman, chief of rheumatology at Northwestern University Feinberg School of Medicine. "We can truly do precision medicine for rheumatoid arthritis. I believe this could be game changing. "

The paper was recently published as an uncorrected proof in *Arthritis & Rheumatology* and will be officially published in the journal in late May. Richard Pope and Deborah Winter also are lead Northwestern authors.

Treatment for rheumatoid arthritis now is trial and error.

"We have so many different biologic drugs and there's no rhyme or reason to give one drug versus the other," Perlman said. "We waste $2.5 billion a year in ineffective therapy. And patients go through 12 weeks of therapy, don't respond and get upset."

Scientists in the multi-site study were the first in the U.S. to use ultrasound-guided therapy to take a tissue biopsy in the affected joint. In the past, blood samples were used to try to determine the effectiveness of the therapy and disease progression.

"It's just like oncology, where you go to the tumor," Perlman said. "Why go anywhere else? In rheumatoid arthritis, we've never gone to the target organ."

Improved ultrasound guided techniques make the new technique possible, Perlman said, noting joint biopsies began in Europe about six years ago.

Scientists in the six-site study analyzed the tissue in 41 rheumatoid arthritis patients, separating out different immune cell populations. They focused on macrophages, essentially the garbage collectors of the immune system that are overactive in rheumatoid arthritis. These cells produce toxic, inflammatory proteins that destroy the joints. Biologic therapy removes the protein molecules being secreted by the macrophages.

The study included 30 patients from Northwestern and the remaining 11 from the University of Alabama at Birmingham; Washington University, Columbia University, Mayo Clinic and University of Michigan.

In the past, scientists have tried to determine therapeutic effectiveness by separating patients into groups based on their clinical parameters such as what antibodies they are producing against themselves, how swollen their joints are and medications they are taking. Then scientists tried to see if these parameters could predict therapeutic efficacy. But that hasn't worked, Perlman said.

Instead, Perlman and colleagues segregated patients based on the genes being produced by their macrophages. They identified two patient groups who shared aspects of the genetic profiles.

Next, the scientists identified which of these patient populations had joints that were getting better and what biologic therapies they were taking. They also identified a gene sequence associated in patients with early disease. The earlier the patient is treated, the more effective the therapy.

The next goal is to predict which patients will have the best response - based on their genetic signature - to a specific drug.

In a new study, researchers are taking joint biopsy tissue from patients at

the start of a new therapy and then six weeks later to see if they can find a predictor gene sequence that will clearly identify which patients respond to a particular therapy.

"The idea is to develop gene sequences to predict whether a patient will respond or not," Perlman said. "Our goal is that this procedure will become the standard of care of for all patients with rheumatoid arthritis ."

Provided by Northwestern University