Childhood arthritis: study identifies 14 new genes as potential treatment targets

A total of 14 new genes that could play an important role in developing treatments for childhood arthritis have been identified by scientists from the University of Manchester (Manchester, UK). The research, led by Wendy Thompson, working with scientists Anne Hinks and Joanna Cobb, was recently published in Nature Genetics.

DNA from blood and saliva samples of 2000 children with childhood arthritis was examined and compared with healthy people.

"...these 14 genetic risk factors ... will help us to understand what’s causing the condition, how it progresses and then to potentially develop new therapies."

Thompson, the principal investigator of the study, who also leads the Inflammatory Arthritis in Children theme at the NIH Research Manchester Musculoskeletal Biomedical Research Unit, said: "This study brought together an international group of scientists from around the world and is the largest investigation into the genetics of childhood arthritis to date".

Childhood arthritis, which is caused by a combination of genetic and environmental risk factors, affects one in 1000 people in the UK. Until recently, there was little data on the genes that are involved in the development of the disease, only three genes involved were previously known.

The results of the study present a significant advancement in the understanding of the biology of this disease and could help in the development of novel treatments. Hinks, joint lead author of the study, said, "Childhood arthritis, also known as juvenile idiopathic arthritis, is a specific type of arthritis quite separate from types found in adults and there’s been only a limited amount of research into this area in the past. This study set out to look for specific risk factors. To identify these 14 genetic risk factors is quite a big breakthrough. It will help us to understand what’s causing the condition, how it progresses and then to potentially develop new therapies".

At present, 30% of children with childhood arthritis continue to suffer from the disease in adulthood. These findings may allow a prediction of children that need early treatment for the disease and may result in better control of their pain management, quality of life and long-term outcome.

"There are lots of different forms of childhood arthritis so identifying the markers will help us understand a little more about the disease process. It will also help categorize children with juvenile idiopathic arthritis into subtypes dependent on which genes they have and allow us to determine the best course of treatment", said Cobb, joint lead author of the research.

As well as ultimately helping clinicians improve their management of children with this disease, the 2-year study provides potential avenues for the development of new treatments.

"Further work is now required ... to enable us to understand how they are involved in disease development and identify potential new therapeutic targets."

Alan Silman, medical director of Arthritis Research UK (Chesterfield, UK) who partly funded the research said, “We...
Risk of rheumatoid arthritis increases with years spent smoking and number of cigarettes

The risk of developing rheumatoid arthritis (RA) is influenced both by the number of cigarettes smoked per day and the number of years a person has smoked. Although this risk decreases upon giving up smoking, when compared with people who have never smoked, the risk in smokers is still elevated 15 years later.

Data from the Swedish Mammography Cohort was examined by researchers from the Karolinska Institutet and Karolinska University Hospital (Stockholm, Sweden). The cohort included 34,000 women aged between 54 and 89 years, of which 219 had RA. The study showed that there was an increased risk of RA even with light smoking. The risk was more than doubled by smoking one to seven cigarettes per day. Comparing people who had never smoked with women who had smoked for up to 25 years revealed that the risk also increased with the length of time a person had smoked.

A decrease in the chances of developing RA was seen upon stopping smoking and the risk continued to decrease over time. The risk of RA decreased by a third 15 years after giving up. However, the risk was still significantly higher at 15 years after giving up when compared with people who had never smoked.

Daniela Di Giuseppe, who led the study, said, “Stopping smoking is important for many health reasons, including the increased risk of RA for smokers. But the clearly increased risk of developing RA, even many years after giving up, is another reason to stop smoking as soon as possible, and highlights the importance of persuading women not to start at all.”


Zoledronic acid: is there a cloud around the silver lining?

A recent study of zoledronic acid has shown that although it slows bone loss in osteoporosis patients, the drug also increases levels of a biomarker that stops bone formation.

Osteoporosis patients are at a greater risk of suffering fractures as the disease weakens bones. The present study suggests that a more appropriate approach to treating this common condition may be combination therapy.

“The key to effectively treating osteoporosis lies in increasing bone mass,” said Antonio Catalano of the University of Messina (Messina, Italy) and lead author of the study. “Zoledronic acid halts bone loss, but it also signals to the body to stop forming new bone mass. The drug may need to be combined with other treatments to add bone mass.”

The treatment of 40 postmenopausal women at an ambulatory care center was followed by the researchers in this prospective intervention study. Of these women, half received zoledronic acid and...
the other half received placebo. The levels of a biomarker that inhibits bone formation, sclerostin, were seen to increase in those patients who were treated with zoledronic acid.

“The data points to an opportunity to increase bone mass by combining zoledronic acid with a drug that suppresses the resulting sclerostin’s effect”, Catalano said.

“An innovative combination therapy using zoledronic acid and selective antibodies to block the sclerostin could simultaneously stop bone loss and encourage new bone formation. This is an important avenue for researchers to explore as they develop new osteoporosis treatments.”


Atomic force microscopy: a force for good in the understanding of osteoarthritis

Additional mechanical properties of articular cartilage, which is a protective cartilage found on the end of bone that is worn down over time, have been discovered by a researcher at The Feinstein Institute for Medical Research (NY, USA).

Nadeen Chahine and collaborators at other institutions examined cells from articular cartilage using a technique known as atomic force microscopy. The mechanical properties of single cells were measured using this technology to reveal what gives them integrity and what causes them to wear down with aging. Studies in animal models showed that, in adult tissues, the mechanical properties of cells are higher than in young or old tissue. These findings are consistent with the fact that joints in adults have higher loads placed on them compared with joints in infants. It was also found that an intermediate filament protein, vimentin, is an important contributor to cell integrity.

“This research is exciting because we are using cutting-edge instrumentation to understand the mechanobiology of cells and cartilage, and what may cause or prevent osteoarthritis,” said Chahine, director of the Bioengineering–Biomechanics Laboratory at the Feinstein Institute. “Osteoarthritis is the most common form of arthritis, and patients who suffer from the disease experience joint pain, tenderness, stiffness and locking. It is my hope that this and additional research into articular cartilage will provide insight into how we may be able to alleviate these disruptive symptoms of osteoarthritis through innovative research at the interface of mechanics and biology.”