

Novel biologic Ab-IPL-IL-17 shows promise for rheumatoid arthritis and inflammatory bowel disease

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Researchers have shown that a novel antibody generated to target an 'essential amino acid sequence' of both interleukin-17A and F has

greater activity and potentially fewer side effects than existing biological therapies for conditions such as rheumatoid arthritis (RA), psoriasis, and inflammatory bowel disease (IBD).

The antibody, called Ab-IPL-IL-17, targets a specific section of signaling proteins IL-17A and IL-17F which play a central role in sustaining inflammation during onset and progression of autoimmune diseases.

Research published in the *Annals of Rheumatic Diseases* identifies the sequence, and reports the results of animal, cell and tissue studies that demonstrate the effectiveness of Ab-IPL-IL-17, and its potential clinical benefit for people with RA and IBD.

Authored by Dr. Asif Iqbal from the University of Birmingham and Professor Francesco Maione, Head of ImmunoPharma Lab from the University of Naples Federico II, the paper reports studies which showed:

- Ab-IPL-IL-17 displays potent anti-inflammatory activity in tissue and animal studies;
- Maintains this activity without triggering unwanted 'off target' effects seen with some currently available, less specific, antibody therapies;
- Reduces the pathological symptoms of arthritis and [inflammatory bowel disease](#) and is as effective as the current gold-standard treatment for RA at halting disease progression and triggering resolution.

A [patent application](#) has been filed covering the antibody and its therapeutic use. The researchers are seeking commercial partners who are willing to conduct a large-scale clinical evaluation of Ab-IPL-IL17 in patients with immune-mediated inflammatory diseases (IMIDs).

What is the essential part of IL-17?

IL-17A and IL-17F are known to stimulate a cascade of molecular signals that initiate inflammation and cause [tissue damage](#) and have been linked to numerous IMIDs.

The researchers designed a series of peptides based on IL-17A/F and tested their ability to mimic the actions of the full proteins in cell culture. They found a sequence that was only 20 [amino acids](#) long, and demonstrated for the first time that this sequence is responsible for IL-17's biological activity in both mice and humans. They called this sequence nIL-17.

They then determined the 3D structure of this amino acid sequence and conducted studies that showed, at an atomic level, how the sequence 'docks' onto receptors that are known to trigger an inflammatory response.

They demonstrated that this short sequence is a potent activator of the [inflammatory response](#), stimulating the release of cyto-chemokines (inflammatory molecules which generate and amplify inflammation), to the same extent as full-length IL-17 molecules, and driving immune cell migration to an even greater extent than the parent molecules.

The results from these cell culture experiments were confirmed in animal models, which showed the nIL-17 truly represents the most biologically active sequence of IL-17.

The researchers generated the novel antibody Ab-IPL-IL-17 to target this sequence. Further studies reported in the paper evaluated Ab-IPL-IL-17.

Results from antibody studies

In cell studies, Ab-IPL-IL-17 showed potent activity, significantly decreasing the production of cyto-chemokines and reducing white blood cell migration in tissues primed for inflammation.

Mouse studies evaluating the activity of Ab-IPL-IL-17 against existing anti-IL-17 therapies (secukinumab, ixekizumab and bimekizumab) showed Ab-IPL-IL-17 does not trigger unwanted immune responses, reduce the numbers of platelets, or increase the numbers of lymphocytes (white blood cells) in the blood. Further studies in mouse models of arthritis showed that therapeutic administration of Ab-IPL-IL-17 is as effective at halting disease progression and triggering resolution as the gold-standard current treatment for RA, infliximab.

Finally, the researchers conducted proof-of-concept studies that tested the response of tissues donated by patients with RA and IBD to Ab-IPL-IL-17. Here they found Ab-IPL-IL-17 was able to reduce the pathological symptoms of disease. In RA, where the researchers examined fibroblasts (connective tissue [cells](#)), the results strongly suggested that Ab-IPL-IL-17 specifically inhibits the pro-inflammatory actions of chronically inflamed fibroblasts within the rheumatoid joint.

In IBD, where the researchers demonstrated that Ab-IPL-IL-17 was able to deplete plasma IL-17A in samples obtained from treatment-naïve IBD patients, indicating its potential to alleviate pathological pro-inflammatory changes in this [disease](#).

More information: New biologic (Ab-IPL-IL17™) for IL-17-mediated diseases: Identification of the bioactive sequence (nIL-17™) for IL-17A/F function.

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