Bulletin Board

Protein fragment may offer new hope in treating systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is a chronic, inflammatory, autoimmune disorder. Currently, it is estimated that 50,000 people suffer from SLE in the UK; however, millions of people are affected worldwide. The disease is more prevalent in women than men and usually starts in the teens or 20s.

Many autoimmune conditions only affect a specific organ; however, lupus can affect several different regions of the body. Symptoms involve intense joint pain, skin lesions, fatigue, fever and renal impairment. Patients may also experience blood disorders (anemia, thrombocytopenia and leucopenia) and pulmonary or cardiac inflammation (pericarditis, myocarditis and endocarditis). Other symptoms include photosensitivity and gastrointestinal and eye problems. Cerebral impairment can also occur and may be quite severe. Although the list of symptoms is extensive, patients do not get all symptoms, meaning that the disease manifests itself differently in different patients.

The precise cause of SLE remains unknown, and as yet there is no cure for the disease. Several types of drugs exist that can be used to treat the complications of SLE; however, none are particularly specific to this condition. Therapy usually consists of administration of corticosteroids and in severe cases, immunosuppressant drugs. However, these may have serious side effects such as cardiovascular disorders, obesity, diabetes, impaired fertility and an increased susceptibility to infections. Therefore, there is a need for effective therapies to combat SLE.

In 2001, researchers at the CNRS Laboratoire d’Immunologie et chimie thérapeutiques (Strasbourg Cedex, France), led by Sylviane Muller at the Institut de biologie moléculaire et cellulaire (CNRS), discovered and patented a peptide that is able to restore the immune system to its normal mode. The effects of this peptide, named P140, were investigated in lupus-affected mice. Mice that were administered P140 displayed significantly reduced inflammatory and joint symptoms. Symptoms of renal disease had also considerably improved, and mice exhibited a lifespan comparable to unaffected control mice.

Promising data has led to Phase IIa and IIIb clinical studies. The Phase IIa clinical trial was an open-label, dose-escalation study undertaken in two centers in Bulgaria on 20 patients (two male, 18 female) with moderately active SLE. Patients received three subcutaneous injections of P140 peptide at 2-week intervals. Upon analysis, patients demonstrated a reduction in anti-DNA autoantibodies and immune globulin levels, which are both usually raised in SLE patients. Furthermore, the international disease activity score (SLEDAI) was considerably reduced in the group of patients who received the lowest dose of P140 peptide. No adverse events were reported apart from temporary minor redness at the injection site, making P140 safe and well-tolerated.

These results are certainly very encouraging, especially since this compound does not seem to affect the overall immune system and does not interfere with the animal’s ability to combat viral infection. It therefore appears that P140 may be a potential drug candidate for the treatment of SLE.

Currently, a Phase IIb clinical trial involving approximately 200 patients is being conducted in South America and Europe.

Short- and long-term use of oral osteoporosis drugs may be associated with osteonecrosis of the jaw, study reports

The study results are in contrast to drug makers’ prior assertions that bisphosphonate-related ONJ risk is only noticeable with intravenous use of the drugs, not oral usage, Sedghizadeh explained. “We’ve been told that the risk with oral bisphosphonates is negligible, but 4% is not negligible,” he commented.

The risk of developing ONJ is more for patients undergoing tooth extractions and other oral surgery, procedures that leave the jaw bone exposed.

The lead author hoped that other researchers will confirm their findings and as a result, encourage more doctors and dentists to talk to patients about the oral health risks associated with bisphosphonate use.

The results confirm the suspicions of many in the oral health field, Sedghizadeh stated. “Here at the School of Dentistry we’re getting two or three new patients a week that have bisphosphonate-related ONJ,” Sedghizadeh concluded, “and I know we’re not the only ones seeing it.”


About the Bulletin Board
The Bulletin Board highlights some of the most important events and research in the field of rheumatology.

If you have newsworthy information, please contact:
Shreya Nanda, Commissioning Editor,
International Journal of Clinical Rheumatology, Future Medicine Ltd,
Unitec House, 2 Albert Place, London N3 1QB, UK
Tel.: +44 (0)20 8371 6090;
Fax: +44 (0)20 8343 2313;
s.nanda@futuremedicine.com

In brief...
Time to treatment as an important factor for the response to methotrexate in juvenile idiopathic arthritis.


Individual response to methotrexate (MTX), a disease-modifying antirheumatic drug commonly prescribed for juvenile idiopathic arthritis varies and is difficult to predict. In order to tailor the treatment for individual patients, the identification of clinical and genetic factors that influence MTX response is very important. This retrospective study involved 128 juvenile idiopathic arthritis patients treated with MTX.

The researchers compared a variety of clinical parameters and genotypes of relevant genes between individuals who responded to the drug and those who didn’t. They found that the time from diagnosis to the start of MTX was one of the factors that had a significant correlation with response to MTX at 6 months following initiation of treatment. The authors concluded that their results indicated that starting MTX therapy at an earlier time could lead to an improved response to the drug.

The elaboration of the preliminary Rheumatoid Arthritis Impact of Disease (RAID) score: a EULAR initiative.


Response criteria in rheumatoid arthritis (RA) generally consist of only three patient-reported outcomes (PROs), namely pain, functional disability and patient global assessment. Factors such as fatigue, an important PRO, are currently not considered. The aim of the study was to establish a patient-derived composite response index, called the RA Impact of Disease (RAID) score, which could be used in RA clinical trials. Initially 17 areas of health were identified by 10 patients; these were then ranked in order of decreasing importance by 96 patients (10 per country in 10 European countries), and finally seven most important areas were chosen. Following further questioning of over 500 patients, the relative weight of each domain was determined. The domains that make up the preliminary RAID score include (in order of weighted importance): pain, functional disability, fatigue, emotional well-being, sleep, coping and physical well-being. The validity of the RAID score is being tested in an ongoing study, but it holds promise for the evaluation of the effect of RA.
Better management of available drugs may be more significant than new drugs in rheumatoid arthritis

In the past 10 years, there has been an improvement in disease activity in rheumatoid arthritis (RA) patients. It is thought that this is due to the increase in the number of new drugs and treatments, and also due to an improved assessment of the disease. However, a new study into the effectiveness of available drugs indicates that better management is the key.

The study in question involved the analysis of the treatment received by nearly 800 patients over a period of 4 years between 2000 and 2004.

“Our work shows that the treatment of rheumatoid arthritis at tertiary hospitals in Spain has improved from the year 2000. It is likely that better management of available drugs, mainly methotrexate, has been learned during the last decade – along with the clinical development of most biologic agents,” explained Isidoro González-Alvaro, lead author.

There has been a vast change in the management of RA over the past decade. During this period many biologic therapies have been developed, and a number of rigorous clinical trials have shown their efficacy – factors that have most likely contributed to the observed change. However, González-Alvaro commented, “In our study, we did not observe the amazing halt of radiological progression described in clinical trials.”

The researchers aimed to assess the real-life efficacy of new RA drugs, and to achieve this they analyzed RA patients with regard to disease activity, disability and radiological progression in the period following the introduction of leflunomide and anti-TNF drugs in Spain. “The most relevant finding of our work is that disease activity in RA has improved, independently of the availability of new therapies, in patients with severe and mild disease,” the authors stated.

“It is clear that we need specific markers of RA severity that allow us to select adequate patients for early biologic treatment in order to improve their therapeutic response, as well as their functional outcome. These tools may also help to improve cost–effectiveness of these drugs, avoiding unnecessary prescriptions,” the authors concluded.


Research reveals potential of CT colonography in screening for osteoporosis

Results of a new study presented at the Radiological Society of North America (RSNA) 94th Annual Meeting suggest that computed tomography (CT) colonography, a technique also known as virtual colonoscopy, can be useful in screening patients for osteoporosis.

“With CT colonography, in addition to screening for colorectal cancer, we were able to identify patients with osteoporosis,” commented Rizwan Aslam, lead author of the study.

CT colonography is a noninvasive imaging technique used for the detection of precancerous polyps in the colon and it involves an abdominal CT scan, in which cross-sectional images of all the structures in the abdomen, including the spine, are generated. Subsequently, a computer program is used to collate the CT images to generate an internal view of the large intestine.

In this study, the researchers utilized a different computer software to generate three-dimensional images of the spine from the same CT images. As a result, they were able to measure the bone mineral density (BMD), the assessment of which is critical to the diagnosis of osteoporosis.

“With CT colonography, in addition to screening for colorectal cancer, we were able to identify patients with osteoporosis.”

A total of 35 patients (30 men and five women) aged 54–79 years were involved in the study, which took place at the San Francisco Veterans Administration Hospital, CA, USA. They all underwent CT colonography and BMD testing with dual-energy x-ray absorptiometry (DXA), which is the standard diagnostic test used to determine bone density. A good correlation was observed between the DXA BMD results and the data obtained from the CT colonography.

“The bone density measurements obtained from CT colonography were comparable to the DEXA results,” Aslam stated. “Both tests identified osteoporotic bones.”

“CT colonography isn’t a replacement for DEXA testing, but it could be a way to screen more people for osteoporosis,” concluded Aslam. “When an individual undergoes CT colonography, we can also obtain a bone density measurement with no additional radiation and at minimal cost.”