

## **ARTHRITIS & RHEUMATIC DISEASES RESEARCH FACT SHEET**

### **Arthritis & Allied Disease**

More than 46 million Americans suffer from arthritis and other chronic joint diseases. Arthritis and rheumatic diseases encompass over 100 different conditions. They are characterized by chronic pain and progressive physical impairment of the joints and soft tissues, but can sometimes affect any internal organ. These diseases include osteoarthritis, rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, systemic lupus erythematosus, scleroderma, vasculitis and gout. These diseases are among the most prevalent chronic conditions in the U.S. and a leading cause of disability, with potentially severe economic, psychological and social impact. Several of these diseases, including rheumatoid arthritis, are autoimmune diseases in which the body's immune system, designed to protect against infection, attacks the body's own tissues instead.

### **BRI Research**

Currently, no true cures exist for any of these conditions, although recent advances in some fields have significantly improved the effectiveness of available therapies, and have furthered understanding of the underlying mechanism(s) which promote the diseases. At BRI, research programs study the cells which regulate these diseases in an effort to understand why these diseases begin and progress. We then translate these findings into better laboratory tests for the disease and new therapies. Recently, using cutting-edge tetramer technology developed at BRI, scientists here found the T cells that drive rheumatoid arthritis (RA). This technology now allows scientists to study how RA starts, how current therapies may impact how and if a patient's immune systems will attack joints and how to create therapies that target these cells therapeutically. BRI also conducts clinical trials to evaluate novel therapies in these diseases. Following are the areas that BRI is investigating:

### **Rheumatic Disease Registry**

The rheumatic diseases encompass many very different diseases, each of which is caused by the immune system attacking healthy tissue, be it the joints in rheumatoid arthritis, the cartilage in relapsing polychondritis, the skin in scleroderma or the entire body in systemic lupus. BRI leaders in rheumatic disease research include VM rheumatologists, Jane Buckner, MD, BRI Director of the Translational Research Program; Jeffrey Carlin, MD, Kori Dewing, DPN, ARNP; Elizabeth Jernberg, MD; Vivian Stone, MD; and Eyal Kedar, MD. The rheumatic disease registry is procuring samples from individuals with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), relapsing polychondritis (RP), early arthritis and scleroderma. These samples are being used for research at BRI but also by researchers across the U.S. who are collaborating with BRI to understand these diseases.

### **Rheumatoid Arthritis**

RA is a chronic disease that can begin at any age. An estimated 1.3 million people in the United States have RA – almost 1 percent of the nation's adult population. There are nearly three times as many women as men with the disease. In women, rheumatoid arthritis most commonly begins between the ages of 30 and 60. As many as 300,000 children are diagnosed with a distinct but related form of inflammatory arthritis called juvenile arthritis.

We know that the disease is in part hereditary but must be triggered by the environment. BRI was an early leader in understanding the genetic component of RA and continues to study how the genes linked to RA lead to disease.

In the last 10 years, a series of discoveries have begun to show an interaction between the environment and those genes. Scientists at BRI are collaborating with scientists at University of Colorado Denver, Stanford University and The Karolinska Institute in Sweden to begin to understand these interactions. These studies have used tetramers – a biomarker tool developed at BRI – to successfully identify the T cells that attack the joint tissues. This discovery helps researchers address the underlying cause of RA and thus develop more targeted therapies.

Another area of great interest for BRI researchers is the initiation of the disease. Dr. Buckner is involved with the Studies of the Etiology of Rheumatoid Arthritis (SERA) that is identifying established and new important blood and genetic markers. SERA is looking for the presence of various autoantibodies in the blood of healthy people. (An autoantibody is manufactured by the immune system and is directed against the individual's own body.) These

autoantibodies may be present before physical symptoms of the disease are evident. SERA is also looking at possible environmental factors that could contribute to RA. SERA's findings may lead to earlier diagnosis and possible prevention of RA in the future.

## **Systemic Lupus Erythematosus**

Lupus is a chronic, autoimmune disease that can damage any part of the body (skin, joints, and/or organs inside the body). At least 1.5 million Americans have lupus. The disease strikes mostly women of childbearing age (15-44). However, men, children, and teenagers develop lupus, too. In 2008, BRI teamed up with the University of Washington to develop a systemic lupus erythematosus (SLE) registry. This project has been supported by the Life Sciences Discovery Fund and is now well underway with over 300 SLE patients enrolled. Samples from participants in this study are being used in the laboratory to understand how the immune cells respond differently from those of healthy individuals. In particular, scientists at BRI are trying to understand how one gene known to be altered in SLE may lead to the production of anti-nuclear antigens (ANA) by B cells. Understanding how B cells function in SLE will allow us to target them more specifically. Clinical research studies are often conducted at BRI to find new, more effective and better-tolerated therapies for lupus.

## **Relapsing Polychondritis**

Relapsing polychondritis (RP) is a rare disease which results in immune system attacks on cartilage. This includes pain and deformity of cartilage within the ear, nose, trachea and joints. Dr. Buckner has a longstanding interest in the immune mechanisms that cause this disease because of the need for better treatments. RP is also of interest because it is a true tissue-specific autoimmune disease which could enlighten our understanding of other autoimmune diseases such as RA. Currently, the RP registry is among the largest in the world with Over 300 participants, generously giving blood samples and clinical information sometimes from great distances. These samples are being used to understand the genes that may be linked to RP, how immune cell function is altered in RP and most importantly to understand if RP shares common factors with other autoimmune diseases. Each study had the potential to better inform Rheumatologists how best to treat RP patients.

## **Scleroderma**

Scleroderma is an autoimmune disease of the connective tissue which causes skin thickening, spontaneous scarring, blood vessel disease and varying degrees of inflammation. Although scleroderma is a rare disease, it can be devastating and finding new treatments is vital. The Rheumatology Section at Virginia Mason Medical Center has had a long history of caring for patients with scleroderma and was the impetus for the development of the Scleroderma Registry. Currently, the registry includes over 200 patients.

Ongoing research in scleroderma at BRI includes studies to identify the immune cells that cause disease. In addition, studies of the genetic signature in scleroderma are being used to understand how the immune system contributes to this disease. Importantly at BRI, scientists are also asking what different diseases of the immune system share with each other.

The scleroderma registry has been central to these studies. Clinical research studies are often being conducted to find better treatments for scleroderma.

## **Other Studies**

BRI has studied and/or has plans to study other causes of arthritis and rheumatic diseases, such as ankylosing spondylitis, psoriatic arthritis, or connective tissue diseases like Sjogren's syndrome.

To join the fight against autoimmune diseases and help advance medical knowledge, consider participating in a Biorepository by contacting [Biorepository@BenaroyaResearch.org](mailto:Biorepository@BenaroyaResearch.org) or volunteering for a clinical trial by contacting [CRP@BenaroyaResearch.org](mailto:CRP@BenaroyaResearch.org).

## **Community Support**

BRI needs community support to continue its crucial work of finding the causes and cures to eliminate these autoimmune diseases. For more information about supporting BRI call (206) 583-6083 or visit [BenaroyaResearch.org/donate-now](http://BenaroyaResearch.org/donate-now).