ARTHRITIS AUSTRALIA NATIONAL RESEARCH PROGRAM
2016 RECIPIENTS

Fellowships

The ARA Victorian Fellowship - $ 19,000 *(funded by Australian Rheumatology Association Victoria)*
Dr Louisa Chou
Department of Epidemiology and Preventative Medicine, Monash University
Project: ***Identifying and predicting hip osteoarthritis***

Hip osteoarthritis (OA) is a major cause of pain and disability with no cure. Symptomatic hip OA is a leading public health problem with one in four people developing this condition in their lifetime. Prevention is important to reduce the burden of disease. Nevertheless, most efforts have concentrated on understanding end-stage disease, with outcomes focusing on plain x-rays and joint replacement surgery. There is a lack of data examining structural change of the hip prior to clinical disease, as well as the risk factors for progression of structural disease. Magnetic resonance imaging (MRI) offers the ability to improve understanding of the early changes of hip OA and identify new targets for preventive strategies. This research program builds on an existing cross-sectional study in a cohort of community-based adults without hip OA at baseline, thus providing a cost-effective approach to address this issue. This study aims to determine whether early structural changes, such as cartilage defects and bone marrow lesions, predate deleterious joint changes and symptom development. Moreover, the program aims to identify whether modifiable risk factors for end-stage disease, such as obesity and occupational activity, can modify early joint changes and development of clinical disease.

The ARA Victorian Fellowship - $30,000 *(funded by Australian Rheumatology Association Victoria)*
Dr Claire Owen
Department of Rheumatology, Austin Hospital
Project: ***Predictors of relapse in polymyalgia rheumatica patients treated with low-dose glucocorticoid therapy***

Despite the fact that Polymyalgia Rheumatica (PMR) is the most common inflammatory rheumatic disease of the elderly, it is under-researched and poorly understood. With no diagnostic tests available, diagnosis is dependent upon a history of muscle pain and stiffness in the shoulder and hip regions, combined with raised inflammation levels in the blood. Treatment consists of prednisolone (commonly referred to as "cortisone") prescribed in a "one size fits all" approach. However, the way in which PMR patients' symptoms respond is very variable; some improve almost overnight, whilst other individuals require higher doses for much longer periods of time. Unfortunately, such long-term prednisolone use can result in many complications including osteoporosis, weight gain, high blood pressure and diabetes. This project aims to identify the characteristics of patients that fail to respond adequately to treatment with prednisolone, be it following a recent diagnosis or years of established disease. It is hypothesized that this information will delineate a distinct subset of "refractory" PMR patients, thereby permitting further study of alternate therapy in this group and minimizing the side effects of prednisolone use long-term.

The Ken Muirden Overseas Training Fellowship - $100,000 *(funded jointly by an educational research grant by Australian Rheumatology Association, Celgene Pty Ltd and Roche Products Pty Limited)*

Dr Clare Owens

Department of Rheumatology, Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds and Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust

Project: ***The role of bisphosphonates in hip osteoarthritis: can this therapy reduce pain and slow structural deterioration?***

This trial seeks to establish the clinical efficacy of the intravenous bisphosphonate ZA in reducing the symptoms of painful hip Osteoarthritis (OA). The study builds on a cutting edge theme in OA research that looks to establish if treating the subchondral bone with pharmacological interventions may provide symptomatic relief for OA patients selected for the presence of subchondral bone abnormalities (visualised on MRI as BMLs) and present in > 60% of symptomatic hip OA patients. In this study, we intend to translate this data into the hip joint, for which new therapies are desperately needed and where no previous studies have examined the potential use of bisphosphonates as a therapeutic agent.

The study aims are:

- To provide mechanistic evidence of the role of the subchondral bone in OA pain
- To establish preliminary evidence of therapeutic efficacy of bisphosphonates in hip OA (with implications for other anatomical disease sites)
- To assess the responsiveness of 3D shape biomarkers in hip OA
- To provide data to support a large RCT

In addition to the trial, there are other studies Dr Owens will have the chance to be involved with, such as two ongoing phase II knee OA trials using novel treatments which are not yet licensed; there are also ongoing imaging-based studies on shoulder pain which will provide her with a thorough grounding in conducting clinical research studies for common musculoskeletal problems. In addition to research Dr Owens will also have the opportunity to interact with and learn from their team of experienced clinical statisticians and work with a group that is world-leading in the development of imaging biomarkers.

Leanne Stafford Award - $50,000 *(funded by Australian Rheumatology Association)*

Dr Rebecca James

Department of Rheumatology, Great Ormond Street Hospital, UK

Project: ***To observe the incorporation of clinical and laboratory-based research into day-to-day clinical practice in a major quaternary Paediatric Rheumatology centre, over a 12 month period, with a view to developing the current under-represented contribution of Australia and the Asia-Pacific region to international paediatric rheumatology clinical trials and research, and thus to improve the care of children with rheumatic disease in this region***

Paediatric rheumatology remains in its infancy in the Asia-Pacific region, despite some childhood rheumatic diseases disproportionately affecting children of Asian/Indigenous/Pacific Islander ethnicity. Despite current standards of care dictating that children with rheumatic disease should be cared for by a specialist paediatric rheumatology service, such services are lacking in our region. Even in developed nations such as Australia and New Zealand, the number of practicing Paediatric Rheumatologists remains vastly out of keeping with more established paediatric subspecialties, and there is substantial workforce need. This is likely to compound the already well recognised delays in the diagnosis of rheumatic disease in childhood and thereby lead to poorer disease outcomes.

Furthermore, the contribution of Australasia in international research in Paediatric Rheumatology is currently lacking. This, despite many centres in other developing parts of the world such as Africa and South America, making substantial contributions to international research collaborations such as

PRINTO (Paediatric Rheumatology International Trials Organisation), or PRSCG (Pediatric Rheumatology Collaborative Studies Group). It is vital that children in Australasia and their unique disease phenotypes and genetics, begin to be represented in international biobanks clinical trials and other research. This will allow advancement of the specialty as a whole, as well as greater relevance of international research to our own population base.

During the fellowship Dr James will observe how research in Paediatric Rheumatology is incorporated into clinical practice at a major international Paediatric Rheumatology research centre (Great Ormond Street Hospital), with a particular focus on gaining experience in the use of clinical outcome measures. Dr James will use her training in Paediatric Rheumatology and pre-existing commitment to Asia-Pacific studies to develop Paediatric Rheumatology in this region and to enhance the contribution of our region to international research.

Project Grants

ARA Project Grant- $13,000 *(funded by Australian Rheumatology Association)*
Dr Mandana Nikpour
Department of Rheumatology and Medicine, The University of Melbourne at St. Vincent's Hospital
Project: ***A Disease Damage Index in Scleroderma***

'Scleroderma' is an immunologic disease that can cause irreversible multi-organ damage. As a result, patients have a reduced life expectancy that is 20 years less than healthy Australians. We are proposing to develop the first tool to measure organ damage in scleroderma. This tool is intended to be firstly a marker of prognosis, and secondly a measure of response to the treatment of this disease. The Damage Index (DI) tool is intended to capture the most meaningful outcome, namely the accrual of irreversible organ damage in scleroderma. By serving as a useful treatment target in the disease, the DI will allow us to optimise treatment with the ultimate goal of improving outcomes for patients.

ARA Project Grant- $40,000 *(funded by Australian Rheumatology Association)*
Dr Linda Rehaume
The University of Queensland Diamantina Institute, Queensland
Project: ***Modification of the microbiome to protect against spondyloarthropathy in SKG mice***

Spondyloarthropathy (SpA) describes a group of common, rheumatic disorders that cause inflammation of the spine, joints, skin, eyes, intestine (ileum and colon) and site of tendon/ligament insertion into bone (enthesis). Depending on which clinical feature(s) dominates, patients are diagnosed with ankylosing spondylitis (spine inflammation and bone fusion), reactive arthritis (arthritis following infection), or arthritis associated with inflammatory bowel disease (IBD) or psoriasis. These conditions share overlapping symptoms and gene mutations, but the genetic risk factors do not absolutely predict development of disease. Environmental factors may also contribute to disease but their identity and involvement are not well understood. In particular, there is evidence that commensal bacteria (microbiota) of our skin and gastrointestinal tract play a role. We hypothesize that genetic risk factors influence gut microbiota, and the relationship of the microbiota to inflammation in different organs. We have described the SKG mutant mouse as a novel model of SpA that recapitulates human disease. Our published data show that the intestinal microbiota is different in SKG and wild type BALB/c mice, and that SKG mice lacking microbiota (germ-free) have reduced arthritis frequency and absent intestinal (ileum) inflammation. Expression of inflammatory markers within the ileum was dependent on the presence of the microbiota. When mutant SKG and wild type BALB/c mice were housed together SKG mice had reduced ileum inflammation, which we propose is through transfer of protective microbiota. Key aspects of this research is determining which bacteria protect against SpA, and how genetic

mutation(s) affects the host microbiota relationship. This project aims to address these questions to determine the bacterial and host factors that protect against disease in order to design a novel therapeutic such as a probiotic (good bacteria) supplement.

ARA Project Grant- $15,000 *(funded by Australian Rheumatology Association)*
Mr Tom Walsh
Department of Rheumatology, School of Medicine, Flinders University
Project: ***Is a change in body composition and adipokines associated with foot pain?***

Foot pain is a common ailment in adults, with one in four aged ≥45 years complaining of frequent pain. Obesity has been associated with both current and developing future pain. Whilst the assumption that increasing *body* mass (and therefore pressure on the feet) would cause foot pain seems credible, a number of studies have found it is in fact *fat* mass that is more important. This study hopes to determine if a reduction in body/fat mass via bariatric surgery in a morbidly obese cohort is associated with a reduction in foot pain and if the reduction in pain may correlate with a change in the chemicals released into the blood by fat tissue.

Arthritis Australia and State & Territory Affiliate Grant - $25,000 *(funded by Arthritis South Australia)*
Dr Anak Dharmapatni
Discipline of Anatomy and Pathology, School of Medical Sciences, University of Adelaide
Project: ***Autophagy in rheumatoid arthritis***

Rheumatoid arthritis (RA) is chronic inflammation of the joint resulting in destruction of cartilage, bone damage and disability. It has been reported to affect up to 0.5-1% of the population and RA results in a considerable burden to the health system due to its chronic nature, and the increased risk of RA patients developing other diseases such as cardiovascular disease, infections and some cancers. Our work over the past decade has discovered that type of cell death or cell 'self killing', called apoptosis, is inhibited in RA causing longer survival of the inflammatory cells within RA joint consequently damage the joint. The cell 'self killing' is regulated, non-inflammatory cell death that our body naturally uses to regulate cell numbers. This natural cell death is impaired in RA leading to excess cell numbers particularly in the inflamed synovial tissues. This project investigates ways of allowing 'self killing' to ensue thus reducing numbers of damaging inflammatory cells. A related cell process known as the cell's "self eating" process, can inhibit the cell's"self killing" indicating a mutual inhibition between the cell's self killing and cell's self eating. Interestingly, one of the oldest medications for Rheumatoid Arthritis, hydroxychloroquine (HCQ), acts by inhibiting the cell's self eating process indicating that the inhibition of cell's self eating process may be a potential new pathway in treating RA. We have reported the beneficial effects of HCQ, which inhibits the cell self eating process in living bone cells (presented at ARA SA branch meeting 2014, Invited talk ARA national scientific meeting 2015). Interestingly, HCQ ultimately induced cell self killing similar to the Embelin, a compound that induced cell's self killing. We have observed some proteins along the cell self eating and cell self killing pathway that are targeted by these medications. This study proposes to extend the findings using a mouse model of inflammatory arthritis. The use of mouse model is an important step of preclinical investigation. Overall this proposed project is expected to demonstrate that treatments regulating cell 'self killing' and 'self eating', could be used to suppress the inflammation as well as to prevent bone damage in RA.

Arthritis Australia and State & Territory Affiliate Translational Grant - $40,000
(funded by Arthritis South Australia)
Dr Elizabeth Hoon
School of Population Health, University of Adelaide
Project: ***Customising pathways to self-management support for people with osteoarthritis***

People who suffer from osteoarthritis (OA) generally don't know about or don't access local self-management resources. At the same time many general practitioners report feeling overburdened with

managing this condition, and unaware of locally accessible self-management resources. This study will assess the feasibility of a program designed to improve connections to self-management resources using a GP consultation as the point of intervention. Through the use of computer software which connects patient record and appointment booking systems this program will identify patients with a diagnosis of OA as they arrive for an appointment. At this point the software will generate a personalised flier which will encourage the patient to discuss their self-management needs with their general practitioner or practice nurse and this flier will also provide customised information about a range of locally available community based courses and resources. The study's feasibility will be examined in terms of: willingness of patients, general practitioners, practice nurses and practice staff to be involved; whether the initiative is acceptable and workable; and appropriate ways to measure whether the program increases people's access to self-management resources. The study's findings will indicate whether this approach is a useful model for patients to increase their engagement with their general practice and self-management resources. If the outcomes of the pilot are positive, the program will be refined and scaled up to in order to assess the effect of this approach on patient health outcomes.

Arthritis Australia and State & Territory Affiliate Grant - $20,000 *(funded by Arthritis Tasmania)*
Prof Graeme Jones
Musculoskeletal Unit, Menzies Institute of Medical Research
Project: *Bone shape predicts Femoroacetabular Impingement*

In Australia, approximately 2 million people were reported suffering from Osteoarthritis (OA) in 2012. It is projected that by 2034, OA would be one of the four most common and fastest growing musculoskeletal diseases. The hip is the second most affected joint by OA. Hip OA is an unpredictable and progressive musculoskeletal disease which causes chronic pain, immobility, lower quality of life and permanent joint deformity. One of the most common causes of hip OA in the young and in older adults is femoroacetabular impingement (FAI) [when the ball shaped femoral head rubs abnormally]. Interestingly even though FAI is a surgically modifiable risk factor of hip OA there are limited studies examining this concept. Also, as no known treatment can control OA progression, in comparison to surgery, prevention of OA can be a good option. In this study of 1099 (2198 hips) participants, we will be using a computerized method to estimate the proportion of FAI. Furthermore we also would explore its link with pain, cartilage damage and other bone structure changes relevant to OA. Assuming there is a link between FAI and all these factors, this study would be the largest and the first to define the proportion of FAI in Southern Australia and will also help in identifying people who are at higher risk of hip OA.

Arthritis Australia and State & Territory Affiliate Grant - $25,000 *(funded by Arthritis Western Australia)*
Dr Johannes Nossent
Rheumatology, The University of Western Australia
Project: *Epidemiology of RA in Western Australia*

The objective of this research is to describe the epidemiology, burden of disease and health care needs of West Australian (WA) patients with rheumatoid arthritis (RA). Based on evidence from abroad there is an expectation that RA patients in WA will have increased rates for comorbidity, mortality and health care resource utilization, but there is no data to support this. To achieve these aims, the project will use data from the WA Data Linkage System to analyse the longitudinal trends of hospital-based disease presentations for comorbid conditions (e.g. severe infection requiring hospital admission, the need for prosthetic surgery, the frequency of osteoporotic fractures etc.) as well as the risk for cancer development and early mortality in Western Australia (WA) for RA patients over the last thirty years. In addition, the rate and reasons for emergency care utilization by RA patients in WA over the last ten years will be examined. These findings will then be compared with data from matched non-RA controls in the community to allow quantification of the risks for comorbidity as well as the economic burden to society that RA represents. The outcomes of this research will delineate important epidemiology features and

state-wide demand for rheumatology services in WA, particularly for patients with RA but with potential ramifications for other groups of rheumatic diseases. Ultimately, it is anticipated that the findings of this research will generate recommendations for the provision of rheumatology services and guide investment into health care resources for this large group of patients in WA.

Eventide Homes Grant - $25,000 *(funded by Eventide Homes NSW)*
Dr Elizabeth Clarke
Kolling Institute of Medical Research, University of Sydney
Project: ***Is mild joint injury an osteoarthritis risk?***

Osteoarthritis (OA), a painful joint disease in humans, is a common long-term outcome after severe joint injury (e.g. tearing the ligaments or meniscus in the knee). Approximately half of all severe joint injuries lead to symptomatic (painful) OA within 15 years, and the risk of developing the disease is more than 5 times higher in these individuals than in the general population. The risk of developing OA following a milder (non-catastrophic) joint injury is completely unknown. These injuries are not routinely tracked or managed, making it difficult to study their effect on long-term OA outcomes in humans. In addition, a previous injury may increase the risk of having another injury. If joint injury reduces joint stability or strength at any time after injury, a previously injured joint may be more vulnerable to severe injury, which in turn is a known risk for developing OA. This study investigates the effects of mild joint injuries on OA risk and severity, and the effects of mild joint injury on risk of severe re-injury.

SA LSS Support Group Grant - $25,000 *(funded by Arthritis South Australia)*
Dr Joanne Reed
Immunology, Garvan Institute of Medical Research
Project: ***Self reactive immunoglobulin repertoires in Sjögren's syndrome and Lupus***

One of the ways our immune system protects us is through the production of antibodies, which attack viruses and bacteria. However, 5% of Australians suffer from autoimmune diseases, where their immune system produces antibodies that attack their own organs (termed autoantibodies). This research will focus on two debilitating autoimmune diseases, Sjögren's syndrome and lupus. The presence of autoantibodies in the blood of these patients is associated with joint pain, dry eyes and mouth, kidney failure, cancer and giving birth to a child with heart defects. This research project will isolate immune cells from patients with Sjögren's syndrome and Lupus to identify the cells from which autoantibodies originate. Cutting-edge technology in genetics will then be used to characterise the genes used to produce autoantibodies associated with clinical symptoms. This information will improve our knowledge of how autoantibodies develop, which is essential for targeted therapies and improved diagnostic testing.

Marion A Simpson Grant - $25,000 *(funded by The Estate of the Late Marion Alice Simpson)*
Prof Christopher Jackson
Sutton Arthritis Research Laboratory, Rheumatology, University of Sydney
Project: ***A novel broad-acting therapy for inflammatory arthritis***

Rheumatoid arthritis (RA) is the second most common type of arthritis and one of the most destructive forms. Despite the ability of current biological treatments to suppress disease activity, they are only effective for 60% of patients and RA symptoms re-emerge following discontinuation of the biological therapy in the majority of patients. Furthermore, the long term effects of biological therapies include increased infection rates and possibly the incidence of some cancers. This project examines the potential of a novel combination therapy to treat RA. We will test the effect of this therapy on two major destructive RA features by investigating blood vessel damage and synovial tissue invasion, using in vitro models. This project will provide novel data that will create a competitive basis for larger grant applications.

Scleroderma Australia Grant - $20,000 *(funded by Scleroderma Australia)*
Assoc Prof Peter Youssef
Department of Rheumatology Royal Prince Alfred Hospital
Project: ***The utility of biomarkers of interstitial lung disease in systemic sclerosis***

Systemic sclerosis is associated with significant lung inflammation and damage (interstitial lung disease) resulting in significant loss of function and early death. The current treatment for interstitial lung disease is very toxic and may cause significant side effects and the current way of monitoring therapy with CT scans is associated with high radiation exposure and an increased risk of developing cancer. At present, it is not possible to predict those patients who will develop this condition or in whom the condition will progress and therefore not possible to determine with accuracy those patients who should be treated. This study measures several markers in the blood which may allow the prediction of patients who will develop this problem and result in early treatment. At present, some patients are treated with toxic therapy who do not require this treatment as their disease will not get worse. These markers may help predict those patients who will not develop disease progression and therefore avoid toxic therapy.

UCB Australia Project Grant- $30,000 *(funded by UCB Australia Pty Ltd)*
Dr Julia Kuliwaba
Discipline of Orthopaedics and Trauma, University of Adelaide
Project: ***Molecular profiling of bone marrow lesions in osteoarthritis***

Osteoarthritis is a painful degenerative disease of the joints that significantly reduces an individual's quality of life. It is the predominant condition leading to joint replacement surgery in Australia. Currently, there are no treatments available that prevent the progression of the disease. Osteoarthritis is characterised by progressive degenerative damage to the cartilage of the joint, but actually the whole joint is affected. Bone marrow lesions are common magnetic resonance imaging abnormalities seen in the bone beneath the cartilage in osteoarthritis. There is growing evidence that bone marrow lesions may offer diagnostic and predictive value in osteoarthritis, and potentially represent a therapeutic target for this disease. Despite this, the nature of bone marrow lesions is not yet understood and nothing is known about what is happening to the cells, and the molecules that regulate them, in these regions of bone. The proposed project will use a new proteomics technology that spatially localises and identifies hundreds of molecules in a single tissue imaging experiment. We will use this powerful technology to image bone marrow lesions in tibial tissue from patients with knee osteoarthritis, with the aim to discover the molecular signature(s) characteristic of bone marrow lesions. This project will provide insight into how these lesions arise, and thus how they may be a treatment target for osteoarthritis.

Zimmer Australia Grant - $40,000 *(funded by Zimmer Australia)*
Dr Claudia Di Bella
Department of Surgery, University of Melbourne
Project: ***The 'Biopen'. Innovative 3D printing for treatment of arthritis***

The "Biopen" is a novel hand-held 3D-printer (that the surgeon holds like a pen). This novel technology can change the way how tissue engineering will be used for clinical applications in the treatment of early osteoarthritis. The Biopen will be used to improve cartilage formation in the joint surface of a live animal by printing scaffold ("Bio-ink") and cells directly into the injured area. In this proposal we will evaluate the characteristic of the new cartilage made with the Biopen compared to the currently treatment modalities available to the surgeons. If this approach results in successful generation of healthy joint cartilage, the use of the Biopen can potentially change the fate of young patients with cartilage injuries and prevent the development of early arthritis, which is a progressive disease with no known cure and one of the leading causes of disability and health-related costs in Australia.

Grant-in-aid

UCB Australia Grant in aid & Zimmer Australia Grant - $15,000
(funded jointly by UCB Australia Pty Ltd and Zimmer Australia)
Dr Daniel Harvie
CONROD Injury Research Centre, Griffith University
Project: ***Sensory training for persistent pain***

People with arthritis, like others affected by persistent pain, show reduced tactile acuity, which is the ability to precisely feel the location and quality of touch on the body. These impairments appear to be localized to the area of pain. Training a person in locating tactile stimuli leads to better tactile acuity, and more importantly, reduces pain. However, such training protocols require many hours of training and are thus burdensome to deliver, and not widely used clinically or in research. This project will deliver and test a tactile training device for clinical use for people with persistent pain, including those with arthritis. The device will be designed for use by the patient, with no need for a therapist to be present. This would not only increase the clinical utility of this treatment tool, but would also enable further research into this promising area.

UCB Australia Grant in aid - $15,000 *(funded by UCB Australia Pty Ltd)*
Dr Jodie McClelland
School of Allied Health, La Trobe University
Project: ***Long-term outcomes from knee replacement***

Total knee replacement is the most common and effective treatment for disabling knee osteoarthritis. Knee replacements can improve pain and quality of life for people with arthritis. However, it is not known whether these improvements are maintained beyond 2 years after surgery, and why there is a decline in outcomes. This study will assess the change in pain, function, quality of life and biomechanics from prior to surgery, to one year and at least 7 years following knee replacement. This information will help us to identify the best ways to develop and modify intervention so that initial improvements from knee replacement are maintained as long as possible after surgery.