ARTHRITIS AUSTRALIA NATIONAL RESEARCH PROGRAM
2015 RECIPIENTS

Fellowships

AFA-ARA Heald Fellowship - $50,000
(funded jointly by Australian Rheumatology Association and Vincent Fairfax Family Foundation)
Dr Sultana Hussain
Department of Epidemiology and Preventive Medicine, Monash University
Project: ***Towards a better understanding of low back pain***

A recent Global Burden of Disease study ranked low back pain second only to cancer as the leading cause of disability in Australasia. Moreover, musculoskeletal disease, of which low back pain is the most prevalent and costly, is the seventh National Health Priority Area in Australia. Low back pain causes true functional disability, not just pain and is poorly treated. There is increasing evidence that obesity, which is in epidemic proportions, is a risk factor for low back pain. However, it is unclear how obesity and low back pain are linked. While it is clear there is an urgent need for innovative and cost-effective treatments for low back pain, these are currently limited. Radiological investigations are being used excessively with associated high costs for investigating low back pain. Likewise there is widespread concern on the increasing use of narcotics to manage low back pain, since this is associated with significant side effects, including deaths. This project will examine the relationship between obesity and low back pain, and the determinants of health service utilistion in those with low back pain in terms of radiological investigation and narcotics (such as oxycontin).

The ARA Victorian Fellowship - $12,500
(funded by Australian Rheumatology Association – Victoria)
Dr Lucy Croyle
Centre for Inflammatory Diseases, Monash University
Project: ***Optimising treatment in systemic lupus erythematosus***

Treatment algorithms are glaringly absent in systemic lupus erythematosus (SLE), possibly due to the multisystem nature of the disease and imprecise treatment targets. There are however tools that can be applied to improve current treatment strategies. Three of the widely used medications in SLE, utilised for all manifestations of the disease, have quantifiable whole drug levels. Research over the past fifteen years has provided good evidence that attaining certain levels of these drugs correlates with attaining and sustaining remission, flare prevention and avoidance of serious toxicity. Additionally, these measurable drug levels can give reliable indications of patient compliance, which is well evidenced to be poorly intimated by physicians as a whole. Further, these three medications show large interpatient variability, and current weight based dosing regimens do not appropriately incorporate this variability. Dosing algorithms based on measurable levels have potential to be a cost effective strategy, through use of single time appropriate measurements to achieve therapeutic targets and decrease morbidity associated with ongoing disease activity. Current available evidence is scant in lupus and this project would seek to add to this in order to employ a dosing algorithm based on metabolites or whole blood levels. The project will seek to determine whole drug or metabolite levels in our unselected Lupus cohort. It aims to provide further, reliable evidence of their utility as a treatment tool to optimize treatment outcomes.

The ARA Victorian Fellowship - $25,000
(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 Polymyalgia Rheumatica (PMR) being the most common inflammatory rheumatic disease of the elderly, it is poorly understood. With no diagnostic tests available, diagnosis is dependent upon a history of muscle pain and stiffness in the hip and shoulder 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 highly variable; some improve almost overnight, while 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. Similarly, uncontrolled PMR is associated with increased risk of heart attacks and stroke. This project aims to identify the characteristics of patients that fail to respond adequately to Prednisolone treatment. It is hypothesised that this information will delineate a distinct subset of 'refractory' PMR patients, thereby permitting further study of alternate therapy in this group and minimising the side effects of Prednisolone use long-term.

Arthritis Australia and State & Territory Affiliate Grant - $50,000
(funded by Arthritis South Australia)
Dr Benny Eathakkattu Antony
Menzies Research Institute Tasmania, University of Tasmania
Project: *Vitamin D effects on osteoarthritis: A randomised control trial*

This project will take advantage of a National Health and Medical Research Council (NHMRC) funded clinical trial - Vitamin D Effects in Osteoarthritis (VIDEO) - which has recently completed a 24 month follow-up of 410 participants. Vitamin D deficiency affects up to 80% of older adults and is associated with knee pain and knee cartilage loss. The aim of this study is to compare, over a 2- year period, the effects of vitamin D supplementation versus placebo on knee pain and knee structural change (assessed by Magnetic Resonance Imaging, MRI) in patients with symptomatic knee osteoarthritis. Identifying the significance of vitamin D is an important step towards disease prevention and it may be possible to slow disease worsening and delay or prevent subsequent joint replacement.

The Arthritis Queensland Fellowship - $50,000
(funded by Arthritis Queensland)
Dr Karsten Schrobback
Institute of Health and Biomedical Innovation, Queensland University of Technology
Project: *Biomarkers of mechanical stress and harmful loading on osteoarthritic knee cartilage*

Osteoarthritis (OA) is an age-associated disease affecting 1.6 million Australians but there is no cure, due in large part to our lack of understanding of the disease. Abnormal biomechanical loading of cartilage tissue in the joint plays a major role in the development of knee osteoarthritis and is linked to important osteoarthritis risk factors, such as obesity, joint injury, malalignment and occupational overuse. This project will identify novel stress marker molecules released from knee cartilage in response to harmful tissue loading. These biomarkers will be validated in human body fluids taken from a cohort of older adults with and without knee osteoarthritis before and after controlled physical activity. The biomarkers will allow early detection of knee osteoarthritis and could be used to guide the

design of patient-specific, physical exercises to increase joint health and defer costly knee replacement surgery. The project will also improve our holistic understanding of the impacts of mechanical load on cartilage.

The Ken Muirden Overseas Training Fellowship - $100,000
(funded jointly by an educational research grant by Australian Rheumatology Association and Roche Products Pty Limited)
Dr Ju Ann Tan
Department of Experimental Medicine, University of British Columbia, Vancouver, Canada
Project: *Overall and cause-specific mortality in patients with systemic vasculitis*

The purpose in undertaking this graduate program is to gain training in research, specifically to:

1. acquire knowledge and skills on research methodology;
2. obtain the ability to read and criticize scientific literature;
3. apply critical thinking in clinical practice;
4. mentor trainees by defining problems for potential research;
5. conduct research on an independent basis; and
6. effectively communicate the results of research to peers in my field of practice.

Formal teaching for this program includes two required and two elective courses from the School of Population and Public Health.
The required courses are:

1. A basic science-focused series of lectures followed by a written final exam.
2. A research rotation (two rotations of 20-40 hours each) with training in oral presentation and mock grant write-ups.

The focus of the proposed research for this program will be on systemic vasculitis.

Aims:

1. To determine overall mortality risks in patients with AAV (MPA, GPA and EGPA), PAN and GCA.
2. To determine cause-specific mortality risks (including cardiovascular disease, infections, malignancy and renal disease) in patients with AAV (MPA, GPA and EGPA), PAN and GCA.

Leanne Stafford Award - $50,000
(funded by Australian Rheumatology Association)
Dr Richard John Holland
Department of Rheumatology, Royal National Hospital for Rheumatic Diseases, UK
Project: *Evaluation of the PsAID Questionnaire*

Psoriatic Arthritis (PsA) is a chronic inflammatory arthropathy affecting up to 40% of patients with skin or nail psoriasis[1]. Disease activity and damage contribute to reduced physical and psychosocial health-related quality of life, with significant social and economic impact[2]. Psoriasis is a complex disease, and has a multitude of clinical manifestations including dactylitis, enthesitis, peripheral joint disease, and axial disease. This complexity has resulted in the development of a number of disease activity indices, all of which perform similarly and use a 'biomedical model' for determining disease activity[3].

Patient reported outcomes (PROs) have been found to be a reliable indicator of baseline status, change during treatment and are predictive of long-term outcome[4,5,6]. There is a therefore a need to measure PROs as part of routine clinical practice and current treatment recommendations for Psoriatic arthritis suggest measuring the patient global assessment (PGA) to assess overall disease burden, the health assessment questionnaire (HAQ) for physical function as well the short-form 36, SF-36)[7] as a measure of health status.

A recent literature review[8] indicated that pain, PGA and HAQ were frequently measured in clinical trials, however other measures of how the patient feels or functions, such as fatigue and sleep, were rarely reported. The SF-36, whilst a recognised measure of the economic impact of disease, is long and the interpretation of the score is complex. The HAQ has also been shown to change with disease duration, and with longer disease duration less reliably reflects active disease[9].

A EULAR taskforce developed a questionnaire to calculate a score reflecting the impact of psoriatic arthritis from the patients' perspective, termed the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire[10]. Development of this questionnaire involved 12 patient research parties and determined 12 domains important to health and well-being, including fatigue, functional capacity, sleep and coping. The PsAID questionnaire was validated with more than 470 patients, and had good face validity and good generalizability and also correlated strongly with patient global assessment. The authors noted that further validation of the PsAID score was needed, in particular regarding sensitivity to change in comparison with other outcome measures.

A similar score has been developed for rheumatoid arthritis[11], and has been shown to correlate strongly with other global measures of health (patient global score, Rheumatoid Arthritis Disease Activity Index)[12], can be used to define an acceptable disease status, and is also sensitive to change[13]. The PsAID could be similarly useful in clinical trials as well as in standard clinical practice to comprehensively measure the patient-reported burden of disease.

The RNHRD is ideally suited to undertake research in PsA as it has the largest individual database of patients with psoriatic arthritis in the UK. It has clinical, demographic and radiographic data from a cohort of over 700 patients with PsA. Statistical support will be available from the department of Pharmacoepidemiology at the University of Bath, which has extensive experience on the analysis of large epidemiological data sets, and a strong track record of high impact publications.

UCB Australia Fellowship - $50,000
(funded by UCB Australia Pty Ltd)
Dr Helen Benham
Autoimmunity Division, Diamantina Institute,University of Queensland
Project: *Pre-clinical rheumatoid arthritis - prediction and prevention*

Rheumatoid arthritis (RA) is a common and incurable chronic inflammatory joint disease affecting 1- 2% of the population. It is a disease associated with significant disability and reduced life expectancy leading to enormous social and economic burden. In this project Dr Benham will investigate at-risk first-degree relatives (FDR) of patients with RA. She will establish a prospective cohort of FDR to identify genetic, environmental and immunological factors contributing to the development of RA in order to find predictive risk biomarkers prior to the onset of disease. These biomarkers will be used in future trials of preventative strategies including lifestyle interventions and novel immune therapies. Dr Benham will also initiate in the FDR cohort a trial of a disease-modifying agent currently used in early RA patients, to attempt to delay or prevent the onset of RA.

Scholarships

Marion A Simpson Grant - $25,000
(funded by The Estate of the Late Marion Alice Simpson)
Mr Raul Chavez Valencia
Department of Paediatrics, University of Melbourne
Project: *Investigating the epigenetic profiles of children with Juvenile Idiopathic Arthritis (JIA)*

Epigenetics is touted as the exciting link between nature and nurture, as it is a mechanism for regulating gene expression and is responsive to environmental stimuli. In complex diseases like juvenile idiopathic arthritis (JIA), where the interaction of genes and environment contributes to disease risk, epigenetic disturbances are highly likely to form part of the disease risk profile. Whilst the epigenome of adult rheumatoid arthritis has been repeatedly examined, the JIA epigenome is largely unexplored. Mr Chavez Valencia is undertaking this research project to unveil the epigenetic profile of JIA CD4+ T cells, an immune cell type highly relevant to the JIA disease process. Specifically, he is looking at a critical epigenetic mark, DNA methylation, one essential for immune cell development.

This project will be comparing CD4+ T cell DNA methylation across the genome between children with active JIA, and healthy children. With the support of a 2014 Arthritis Australia scholarship, he has now successfully selected 60 pairs of children from the CLARITY JIA biobank, extracted CD4+ T cells from their blood, and measured T cell DNA methylation at over 480,000 sites across the genome. By studying the relevance of epigenetics to JIA, this project is highly likely to produce data of considerable impact. In doing so, they can begin to piece together the links between nature and nurture in JIA whilst providing significant potential for translation to improved clinical outcomes.

SA LSS Support Group Grant & Arthritis Australia and State & Territory Affiliate Grant - $30,000
(funded by Arthritis South Australia)
Dr Premarani Sinnathurai
Rheumatology Department, Royal North Shore Hospital
Project: *Psoriatic arthritis in Australia*

Psoriatic arthritis (PsA) is an inflammatory arthritis which occurs in association with psoriasis. PsA can present in a variety of ways in patients, affecting different patterns of joints. It can also vary greatly in its severity, causing significant deformity and disability in some patients. The aim of this study is to investigate factors, which predict which patients may develop particular variants of psoriatic arthritis and the severity of the disease. This research will involve analysis of data from the Australian Rheumatology Association Database. A cohort of patients with psoriatic arthritis will be recruited and followed over time. Their disease will be assessed clinically, in addition to the measurement of laboratory markers of inflammation in blood and also the measurement of other factors, which may be associated with disease presentation and severity.

Grant-in-aid

ARA Project Grant- $10,000
(funded by Australian Rheumatology Association)
Dr Elizabeth Hoon
School of Population Health, The University of Adelaide
Project: *Developing a patient reported outcome measure in polymyalgia rheumatica*

Polymyalgia rheumatica (PMR) is a common inflammatory disease effecting older people. While new treatment options have emerged for many inflammatory diseases, treatment for PMR continues to rely on corticosteroids. These steroids are known to cause adverse effects with long term use, and the dilemma for people with PMR is that they are commonly unable to cease steroids because their symptoms cannot be adequately controlled without them. Although common steroid side effects in inflammatory diseases are somewhat understood, less is known about how these effects impact on people with PMR, as well as the impact of other adverse events (e.g. mood and sleep disturbance, skin fragility and body image). It is also recognised that current tools used by researchers and clinicians to measure side effects may not be relevant or sensitive enough to capture PMR patient experiences. This project forms the first important stage in the development of more appropriate patient outcome measures: It focuses on prioritizing patient experiences using an explorative research approach. The findings of this current project will inform the development of specific and accurate measures of adverse events for the PMR population, which in turn, may inform evaluations of the effectiveness of changes to treatment for PMR.

ARA Project Grant- $10,000
(funded by Australian Rheumatology Association)
Dr Bernadette Fitzgibbon
Monash Alfred Psychiatry Research Centre, Monash University
Project: *Interventional repetitive transcranial magnetic stimulation treatment for fibromyalgia*

In 2012 alone, musculoskeletal conditions including fibromyalgia were estimated to affect 6.1 million Australians and to cost Australia a total of $55.1 billion in health care and lost productivity costs. There are no reliably effective treatments for fibromyalgia, which is likely due to the fact that there is an absence of etiologically-driven treatment options. One promising new treatment option is repetitive Transcranial Magnetic Stimulation (rTMS); a non-invasive technique that can change the activity of neurons in the brain. The use of this technique in fibromyalgia is strongly supported by extensive evidence of central nervous system changes in sufferers. The majority of these studies have targeted the motor cortex, however, whereas the dorsolateral prefrontal cortex (DLPFC) may offer a more relevant target site for diffuse pain syndromes like fibromyalgia due to its critical role in pain modulation as well as related symptoms including mood. The proposed study aims to carry out a randomised, double-blind, sham-controlled clinical trial of a course of DLPFC rTMS treatment in patients who suffer from fibromyalgia. It is anticipated that this study will successfully demonstrate a 4 week DLPFC rTMS treatment course as a new treatment option for people with fibromyalgia. In which case, the findings from this study will provide support for a revolutionary new pain management option for sufferers of fibromyalgia that is also likely to be applicable to other pain syndromes.

ARA Project Grant- $15,000
(funded by Australian Rheumatology Association)
Mr Jason Rogers
Menzies Research Institute Tasmania, University of Tasmania
Project: *Clinical and metabolic factors and imaging abnormalities in chronic plantar heel pain*

Longstanding pain on the underside of the heel is known as chronic plantar heel pain (CPHP) and affects 10% of the population. The most common diagnosis is plantar fasciitis although bone, nerve and other soft tissues can be a source of pain. The cause of CPHP is currently unknown, as are the factors that predict a good or bad outcome. As a consequence, interventions are not well targeted and the most comprehensive review to date identifies that current treatments "bring only marginal gains over no treatment" at all. Therefore, as part of a larger study, this project will compare 30 participants with CPHP and 30 age- and sex-matched controls, and look for specific clinical, imaging, psychological and blood based markers that are associated with the condition. The project will compare the two groups for imaging abnormalities on Ultrasound, MRI and a new, novel bone imaging tool, high resolution quantitative CT. It will also assess a range of clinical factors including fat levels, foot alignment, ankle strength and mobility, lower limb nerve sensitivity to stretch, and measure physical activity in real time in both groups with 'accelerometers' (pedometer like devices). As pain is an essential feature of the condition, the project will also assess for known psychological drivers of pain such as depression and anxiety. Many of these factors of interest are novel for study in CPHP, and will provide important insight into the factors that contribute to the disease.

ARA Project Grant- $15,000
(funded by Australian Rheumatology Association)
Dr Linda Rehaume
Diamantina Institute, The University of Queensland
Project: *Immunogenetic background and microbiota interaction promotes ileitis in the SKG mouse model of spondyloarthropathy*

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 (AS) reactive arthritis (arthritis following infection), 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. Current therapies target the inflammation associated with SpA but do not treat the underlying cause(s) of disease.

A key aspect of this research is determining which bacteria promote ileum inflammation, how these bacteria mediate disease, and how genetic mutation(s) affects the hostmicrobiota relationship. This project aims to address these questions to determine the bacterial and host factors predictive of disease to design novel therapeutics targeting synergistic host-microbiota disease-promoting mechanisms.

Arthritis Australia and State & Territory Affiliate Grant - $13,000
(funded jointly by Arthritis South Australia)
Dr Kade Paterson
Department of Physiotherapy The University of Melbourne
Project: *A multi-faceted podiatry intervention for the management of foot osteoarthritis: a pilot randomised controlled trial*

Osteoarthritis (OA) is a common and debilitating condition that adversely affects health, daily activities and quality of life. Although the hand, knee and hip have traditionally been considered the most commonly affected joints, recent population statistics show that the prevalence of foot OA is as high as knee OA. In contrast to hip and knee OA however, there are few studies investigating treatment options for foot OA and there are no randomised clinical trials to help guide clinical practice. The aim of this *'proof of concept'* study is to investigate a multi-faceted podiatry intervention in people with symptomatic foot OA. It is expected that this intervention will have superior benefits on pain and function compared to the usual care of analgesia advice.

Eventide Homes Grant and Arthritis Australia and State & Territory Affiliate Grant - $15,000
(funded jointly by Eventide Homes NSW and Arthritis Australia)
Mr Adam Culvenor
School of Allied Health, College of Science, Health and Engineering, La Trobe University
Project: *Identification of phenotypes in early post-traumatic knee osteoarthritis: an exploratory study*

Rupture of the largest knee ligament, the anterior cruciate ligament (ACL), increases a person's risk for early-onset knee osteoarthritis (OA) development, irrespective of conservative such as exercise therapy or surgical ACL reconstruction management. Since most ACL injuries occur in adolescents and young adults, these individuals are prone to develop OA before they reach 40 years of age. But not everybody progresses to OA after ACL injury.

The objective of this study is to identify phenotypes at risk of articular cartilage deterioration on MRI over the first five years following ACLR.

Are there specific groups of people following ACL injury who are at greater risk of OA progression? In a recent study using magnetic resonance imaging (MRI) scans, we identified knee cartilage loss (a central process of OA disease) already in the first year following ACL reconstruction in 75 of 111 participants (68%). These 75 individuals will be re-recruited five years following ACL reconstruction in this study and identical MRI scans obtained. The change in cartilage structure will be investigated and potential baseline factors that predict cartilage deterioration (eg. age, body mass, activity level/sports participation, physical performance, knee range of movement, strength and flexibility, knee symptoms, concomitant injury and/or surgery to meniscus) will be explored. We will therefore identify specific groups of people who are at particular risk of accelerated disease progression. The knowledge obtained from this study will create opportunities for improved, targeted application of therapeutic strategies to help reduce the morbidity associated with ACL reconstruction.

Eventide Homes Grant - $15,000
(funded jointly by Eventide Homes NSW)
Dr Brigitte Tampin
Physiotherapy Neurosurgery, Sir Charles Gairdner Hospital
Project: *Assessment of neuropathic pain and altered sensory nerve function in patients with lumbar radicular pain*

Low back pain affects 80 – 85% of people over their life time; it is the world's leading cause of years lived with disability and associated disability continues to rise. Health costs due to back problems in Australia were estimated to be $4.79 million in 2012. Low back-related leg pain or sciatica is a common variation of low back pain with a prevalence ranging from 1.2% to 43% in the general population.

Although the prognosis for sciatica is good in most patients, up to 30% of patients continue to have pain for 1 year or longer. People with sciatica may or may not present with signs of nerve damage and associated nerve-related pain. It is important to determine the presence of altered nerve function associated with pain as this may (i) contribute to people having persistent pain and/or disability, both of which are associated with greater health costs and poorer patient outcomes; (ii) help direct more targeted treatment for the underlying condition with the aim of improving patient outcomes and reducing health costs.

This study will investigate responses to various sensory stimuli (to heat and cold, to light touch and pressure, to pin-prick and vibration) that can be used to assess nerve fiber dysfunction. Should the bedside examination findings match the laboratory findings, then bedside examination may potentially replace time-consuming laboratory testing in the future. We will also investigate if sensory examination findings may be associated with the persistence of pain in patients with sciatica. The outcome of the study will inform clinical pathways to optimise time and cost efficient health outcomes for this patient cohort.

UCB Australia Grant in aid - $15,000
(funded jointly by UCB Australia Pty Ltd)
Assoc Prof Helen Keen
School of Medicine and Pharmacology, University of Western Australia
Project: ***The prevalence of subclinical synovitis and urate deposition in a pyperuriceamic cohort of the Fremantle Diabetes Study***

Australia has the second highest rate of gout in the world (estimated at 16% of elderly males), and the prevalence is rising as our population ages. Gout is a form of arthritis caused by high levels of uric acid in the blood (hyperuricaemia) but is also associated with heart attacks and death. Gout is easily treated with drugs that lower the uric acid level, and these drugs have been shown to reduce heart attack rates. The only risk factor for gout is hyperuricaemia, but 90% of people with hyperuricameia do not get gout (asymptomatic hyperuricaemia), and as yet it is not possible to accurately predict which patients with hyperuricaemia will get gout.
Current recommendations are not to treat hyperuricaemia; most of these people will not develop gout, and the association with heart attacks remains controversial, allopurinol is associated with significant side effects and, in population studies low uric acid levels are also associated with an increased risk of death. If it was possible to identify which patients with hyperuricaemia were likely to get gout, or to diagnose people with gout in the very early stages, then it might be possible to treat patients earlier and improve outcomes for people with gout.

The Fremantle Diabetes Study Phase II provides the opportunity to study a well characterised group of subjects with hyperuricaemia for subclinical signs of gout (as demonstrated by US), and determine the prevalence of subclinical gout, determine is subclinical inflammation is associated with serial uric acid levels in the preceding 6 years, and determine if joint inflammation predicts the risk of clinical gout in the future.

The aim of this study is to establish a sub cohort within the Fremantle diabetes Study Phase II to document the prevalence of synovial inflammation and uric acid deposition in joints of people with asymptomatic hyperuricaemia. The study will also determine if synovial inflammation and uric acid deposition in the joints of people with asymptomatic hyperuricaemia reflects historical serum acid levels.

Zimmer Australia Grant - $15,000
(funded by Zimmer Australia)
Ms Carina Blaker
Kolling Institute of Medical Research, University of Sydney
Project: *Investigating osteoarthritis following different injury mechanisms*

Arthritis affects nearly a 5th of the entire Australian population making it the most widespread musculoskeletal disease in Australia. Half of these cases are attributed to osteoarthritis (OA), for which there are currently no therapies available to reverse or even halt disease onset and progression. Post-traumatic OA (ptOA) is the form of the disease that occurs after a known joint injury and accounts for approximately 25% of all knee OA. Recent evidence has suggested that the trauma severity and ensuing inflammatory response may not only be important for causing the initial pain and disability but also have a direct effect on the likelihood of progression to ptOA. To develop more effective treatments, a better understanding of the driving cell and molecular events is needed. Determining whether these differ with time and the triggering event (e.g. injury mechanism) may also be vital for individualised treatments.

Zimmer Australia Grant - $15,000
(funded by Zimmer Australia)
Ms Charlotte Ganderton
Physiotherapy Department, La Trobe University
Project: *Hormone replacement therapy and exercise in post-menopausal women with greater trochanteric pain syndrome*

Greater trochanteric pain syndrome (GTPS) causes severely debilitating pain on the outside of the hip, resulting in limited activity, employment and decreased capacity to exercise. The pain of GTPS has been shown to be as severe and debilitating as osteoarthritis of the hip in those waiting for hip replacement. It most commonly affects post-menopausal women and limits capacity for physical activity that is critical for older women to achieve healthy ageing. In addition to tendon injury, ageing women suffer a myriad of conditions and diseases that burden both the individual and society, all of which can be ameliorated by physical activity (cardiovascular disease, obesity and osteoporosis). Conservative management is the first line treatment, although evidence is limited and the condition can be resistant to treatment. This study aims to investigate the effect of female sex hormone therapy and exercise on pain and function in post-menopausal women with GTPS. Eighty women will be recruited and randomised to one of four groups; female sex hormone supplementation (FSHS) or placebo, and strengthening exercise or sham exercise. Interventions will be 12 weeks in duration and outcomes (VISA-G questionnaire, ultrasound tissue characterisation imaging, clinical tests and quality of life) will be examined at baseline, 3 months, 6 months and 12 months

Zimmer Australia Grant & Arthritis Australia & State and Territory Affiliate Grant - $10,000
(funded by Zimmer Australia & Arthritis South Australia)
Assoc Prof Leslie Nicholson
Biomedical Sciences, Physiotherapy, The University of Sydney
Project: *Clinical characteristics of children with generalized joint hypermobility – 3 year follow up*

Generalised joint hypermobility (GJH) is recognized within the general population as the state of being at the end of the normal spectrum of joint range, and often believed to be an advantage for sporting pursuits such as ballet, dancing and gymnastics. However, many children with GJH report a broad range of musculoskeletal and systemic complaints that include, but are not limited to, chronic joint pain, recurrent episodes of joint instability, poor wound healing, gastrointestinal dysfunction, delayed gross motor development and fatigue. This form of symptomatic GJH is defined as Joint Hypermobility Syndrome (JHS). The signs and symptoms associated with JHS are often not outwardly visible to others, and perhaps as a result, JHS is a poorly recognised condition by both health professionals and the greater community Despite growing interest and evidence regarding the presentation and functional disability associated with this condition in the adult population, the presentation and impact of this condition on children and adolescents remains less well-understood. No study has followed a group of children with JHS to determine the prognosis of the condition in childhood.

The project aims to describe the physical characteristics, physical skills and social and psychological problems of children with GJH and JHS, and how they change over time. One hundred and twenty children have been recruited for this study, with follow-up data already collected on 70 out of the 100 who have reached 18 months since their initial recruitment. We would like to continue the 18month follow-up of the remaining 30 children, and commence the 3 year follow-up of the baseline 100. The ongoing follow-up at aims to understand how GJH and JHS affect children and adolescents as they grow and mature. Do they become less hypermobile as is commonly believed but never proven in a longitudinal study?

Which children become more or less symptomatic and how do they differ? How does their condition impact their quality of life? Do children move between the different sub-types of JHS that were identified from the baseline data collection?

Zimmer Australia Grant - $15,000
(funded by Zimmer Australia)
Mr Tom Ranger
Department of Epidemiology and Preventive Medicine, Monash University
Project: *Does the structure of the spine matter in low back pain?*

Low back pain is a major public health problem and obesity is in epidemic proportions. It has been hypothesised that the additional body weight associated with obesity may accelerate degeneration of the spine. However, no study has compared the structure of the spine between obese and non-obese individuals. This project will undertake a 2 year longitudinal cohort study to examine the relationship between structures of the spine (eg discs, joints, fascia) and low back pain, and whether this differs between obese and non-obese individuals. Structural features of the spine, including the lumbar discs, facet joints, muscles and fascia, will be measured from MRI images of 75 participants from the Monash University Obesity study and their relationships with obesity, pain and disability examined. Understanding the role of structures of the spine in low back pain has the potential to provide novel approaches to the management and prevention of this debilitating condition.

Project Grants

The Allan and Beryl Stephens Grant - $30,000
(funded by The Estate of the Late Beryl Stephens)
Dr Gethin Thomas
Diamantina Institute, University of Queensland

Project: ***An oasis in the desert: A novel non-coding RNA underlies the genetic association with ankylosing spondylitis at the 21q22 gene desert locus***

Ankylosing Spondylitis (AS) is a common inflammatory arthritis, affecting more than 22,000 Australians and costs up to AU$500M annually. Current treatments only slow disease progress thus new therapeutic approaches are urgently needed for AS. There is a strong genetic component in the risk of developing AS however it is not clear exactly what genes are responsible for driving the disease. Genetic studies have shown that particular sections of the genome, containing no known genes, contribute towards heritability in AS. Variants in these 'intergenic regions' do not directly alter any proteins but likely contribute to disease by altering a genetic control mechanism called transcription. Transcription is the production of "working blueprints" called transcripts from the genome which act as the template for production of proteins or regulate that production. Preliminary studies have identified a novel transcript being produced from the 21q22 region of the genome, a region associated with AS. The transcript is specifically produced in monocytes, an immune cell-type which may play a key role in the auto inflammatory aspect of AS. In this project they will further characterise the product of the 21q22 locus and elucidate how it contributes to AS. By identifying novel regulators in AS and investigating the role they play in disease.

ARA Project Grant - $25,000
(funded by Australian Rheumatology Association)
Prof Matthew Brown
Human Genetics Group, Diamantina Institute, University of Queensland
Project: ***VCAM1 as a therapeutic target in scleroderma***

Scleroderma treatments are limited, with no treatments available which change the natural history of the disease or induce remission. Treatments that are available are supportive or reduce symptoms, but have not been shown to increase life expectancy. Genetic variants in the gene VCAM1 which codes for a protein (called VCAM-1) have been identified and are found on the lining 'endothelial' cells of blood vessels. When there is inflammation of those blood vessels, more VCAM-1 is produced. VCAM-1 catches passing white cells by interacting with a protein on those white cells called VLA-4. By catching the white cells and moving them into the inflamed tissue surrounding the blood vessel, VCAM-1 increases local inflammation. VCAM-1 is therefore a potential target for new therapies in scleroderma. This project will test whether VCAM-1 function is increased in scleroderma, as our preliminary data suggests. If this is proven to be the case, then blocking
VCAM-1 would be likely to be of benefit to scleroderma patients.

H J & G J McKenzie Grant - $30,000
(funded by The Estate of the Late Heather Joy McKenzie)
Dr Nagaraja Haleagrahara
Physiology and Pharmacology, James Cook University
Project: ***Molecular mechanisms and therapeutic potentials of anti-inflammatory bioflavonoids in collagen-induced arthritis***

Rheumatoid arthritis (RA) is an autoimmune disease characterised by synovial inflammation and erosion of bone and cartilage, which lead to the destruction of joints. It is currently treated with anti-rheumatic drugs that exhibit numerous side effects which can be quite adverse. There is an urgent need to find new and safe anti-inflammatory compounds to treat chronic inflammatory arthritis. Anti-inflammatory agents are capable of suppressing the actions of cytokines that play a key role in the pathogenesis of rheumatoid arthritis. Bioflavonoids belong to a group of natural substances occurring normally in the diet and exhibit a variety of beneficial effects on health. Flavonoids are known to possess significant anti-inflammatory properties. Recent studies have demonstrated that some flavonoids modulate the expression of inflammatory gene expression, thus leading to the attenuation of the inflammatory responses. Although

flavonoids have the potential to inhibit inflammatory cytokines, their effects on RA have not been investigated at the cellular levels. This study aims to look into the molecular mechanisms involved in the anti-inflammatory activity of flavonoids and determine the protective effects on inflammatory arthritis.

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Dr Tania Crotti
Discipline of Anatomy and Pathology, School of Medical Sciences, The University of Adelaide
Project: *Abrogating inflammation and bone loss in a mouse model of inflammatory arthritis*

Local bone loss is a serious complication of chronic inflammatory diseases such as Rheumatoid Arthritis (RA) and there appears to be an intimate relationship between the inflammation and bone lysis. As RA is a systemic disorder, it is now appreciated that changes occur within organs outside of the joint including the gastrointestinal tract. This may result from the disease process but more commonly as a side-effect of treatments. Since the implementation of methotrexate as a first line therapy the disease activity of RA has been dramatically reduced, however 50% of patients are non-responsive. Anti-TNF treatments have been revolutionary in reducing the inflammation and bone loss in patients non-responsive to methotrexate, however not all patients achieve remission, they require regular visits to their doctor for injections and there can also be various adverse side effects. In addition by the time patients are started on anti-TNF the erosion may have already occurred.

There are few effective therapies that specifically target both inflammation and bone loss. It is, therefore, not surprising that in RA most bone erosion occurs in the first 2 years after diagnosis. Targeting inflammation alone achieves limited benefits in regard to bone erosion. This means that inflammation is often only controlled in order to restore function and reduce pain but it is not eliminated thus allowing chronic bone erosion to progress.

It takes time it to establish the correct therapy and in this time there is continuing bone destruction. Caffeic Acid Phenethyl Ester (CAPE), an antioxidant derived from the propolis of honeybee hives, has been shown to have immunomodulatory and anti-inflammatory properties and inhibit cancer at high doses. At a low dose it has been demonstrated that CAPE has the ability to reduce bone loss in a model of implant wear particle induced bone loss. This project will now use a model of inflammatory arthritis to test whether CAPE is able to inhibit the local bone loss, inflammation and systemic bone resorption. Additionally they will assess the systemic effects of the inflammatory arthritis and CAPE treatment on the gastrointestinal tract. This treatment could provide add on treatment to conventional disease modifying anti-rheumatic drugs (DMARDs).