PARLIAMENTARY INQUIRY QUESTION ON NOTICE

Department of Health and Aged Care

Standing Committee on Health, Aged Care and Sport

Inquiry into Childhood Rheumatic Diseases

17 February 2022

PDR Number: IQ22-000025

Research projects through the MRFF

Spoken

Hansard page number: 2

Member: Trent Zimmerman

Question:

CHAIR: Thank you. My next question was about the research. You mention in your submission some of the research work that is happening through the Medical Research Future Fund, although I note that your submission indicates that none of the funding available for that has specifically gone to juvenile manifestation of rheumatic disease. But you also highlight the $12 million that has been spent through the NHMRC. Have those research projects been completed or are they ongoing? It might be one you want to take on notice. I'm interested in, of that $12 million, how many have been completed and how many are ongoing and whether there is a snapshot of the outcomes of that research that we might be able to get. And I am happy for you to take that on notice.

Ms Wallbank: That would be wonderful. Someone gave me a list of the names of the research projects, but I don't have that detail with me, unfortunately. But we can get that to you, I'd say, in the next day or two.

Answer:

Childhood rheumatic disease research is in scope under the $20 million grant opportunity targeted at chronic musculoskeletal conditions in children and adolescents, funded through the MRFF's Emerging Priorities and Consumer Driven Research Initiative.

The grant opportunity will fund projects in three streams of research:

- Stream 1: Chronic autoimmune diseases that affect the musculoskeletal system, and
- Stream 2: Chronic musculoskeletal pain; and Stream 3: Congenital musculoskeletal diseases.

Applications focusing on childhood rheumatic diseases could be funded under Stream 1 or Stream 2.

The exact amount of funding that could be awarded to childhood rheumatic diseases cannot be determined at this time. However once applications are assessed, and funding decisions made the amount of funding towards on childhood rheumatic diseases related research will be known.

The attached spreadsheet (Attachment A) provides details of all the grants that we were able to identify as being relevant to childhood rheumatic disease, that add up to the $12 million in total research funding. Applications have closed and assessment of applications is anticipated in April-May 2022 with announcement of outcomes currently expected in June 2022.

NHMRC Funding for research relevant to childhood rheumatic diseases

Grant ID	Application Year	CIA Name	Funding Type	Funding Subtype	Grant Title	Administering Institution	State	Sector	Grant Start Date	Grant End Date	Total Grant Budget	Broad Research Area	Field of Research	Keywords	Media Summary	Final Report Achievements	Final Report Expected Future Benefits
GNT0229312	2002	Shona Bass	Project Grants	Standard Project Grant	How does exercise increase bone strength during different stages of growth?	Deakin University	VIC	University	1/01/2003	31/12/2005	$180,000.00	Clinical Medicine and Science	Endocrinology	loading and the attainment of peak bone mass | the effect of loading on bone strength | exercise, bone strength, males, females and stage maturation | attainment of peak bone density | bone geometry and bone strength | osteoporosis |	Osteoporosis is a condition in which the skeleton becomes fragile and susceptible to fractures. It is a public health problem that affects both men and women over the age of sixty. Although osteoporosis affects the elderly, the most opportune time to prevent osteoporosis may be during childhood. Physical activity is a lifestyle factor known to affect the strength of the skeleton. Bone density is commonly used as a measure of bone strength because it is easily measured and is related to the breaking strength of bones. However changes in the shape of bones can also affect bone strength with or without an increase in bone density. Changes in bone shape in response to exercise in children or adults have rarely been investigated, and little is known about the effects of exercise on bone shape during different stages of growth. This study is the first to investigate how exercise during childhood may affect bone strength by changing bone shape. 45 elite female tennis players aged between 6 to 18 years have completed two years of this study. 90 novice and competitive male tennis players aged between 6 to 20 years and 60 healthy age matched controls will be asked to participate in this study. Measurements will be made annually for three years. The bone shape and density of the dominant and non-dominant arms of the players will be compared with the children who don't play tennis - comparisons will also	The objective of this project was to investigate the effects of tennis playing (as a model of repetitive loading) on bone strength in boys and girls during different stages of growth. The unique feature of the study was to use magnetic resonance imaging to obtain cross sections of the bone in order to describe how the growing bones respond to repetitive mechanical stimuli. Measuring the effects of exercise was obtained by comparing the dominant and nondominant arms of young tennis players. The preliminary results show that loading the skeleton before puberty leads to a significant improvement in bone strength in boys and girls. The prepubertal skeleton has the capacity to respond to loading by adding more mineral on the external surface of the bone, leading to a marked increase in bone size and bone strength. Interestingly, boys seem to have a larger window of opportunity than girls to optimize their bone strength through exercise: the benefits obtained before puberty in boys was further enhanced in peri-puberty if training was maintained whereas it was not the case in	The three-year data will provide valuable information on how much bone strength increases during growth, what benefits can be obtained by participating in high-impact exercise and to what extent these benefits may differ between boys and girls in terms of magnitude and timing. Exercise prescription for bone health could then be re-designed according to maturity status and gender.
GNT0229903	2002	Prof Thomas Gordon	Project Grants	Standard Project Grant	Autoantibodies in neonatal lupus	Flinders University	SA	University	1/01/2003	31/12/2005	$428,250.00	Clinical Medicine and Science	Autoimmunity	autoantibodies | rheumatology | systemic lupus erythematosus | sjogren's syndrome | autoimmunity | rheumatology | systemic lupus erythematosus |	Autoimmune diseases represent the third greatest clinical burden to the community after heart disease and cancer. Management of the diseases remains primitive because of our poor understanding of the disease mechanisms. Autoantibodies are one of the key markers of diseases such as lupus and Sj gren's syndrome, but their role in producing tissue damage is largely unresolved. However in the neonatal lupus syndrome, autoantibodies from the mothers cross the placenta and appear to cause inflammation of particular target organs such as the heart and skin in the babies. Neonatal lupus offers a unique opportunity to investigate the pathological role of autoantibodies and other factors (e.g. infection) in autoimmune diseases, and is likely to offer vital clues to lupus in adults. For example, the skin disease in babies with lupus mimics the cutaneous lesions in adult lupus patients. Recent work from our group using an animal model has shown that certain autoantibodies cross the placenta and bind to cells undergoing physiological death in the fetus, in the same organ distribution as human neonatal lupus. Using sophisticated imaging techniqes we can now trace the fate of maternal autoantibodies in the babies for the first time and understand how the target proteins in heart and skin become exposed to the damaging effects of these autoantibodies. We also believe that certain types of autoantibodies can	This research has focussed on the role of circulating autoantibodies in systemic autoimmune diseases such as lupus and Sjogren's syndrome. These autoantibodies can rarely cross the placenta and cause a neonatal lupus syndrome in babies of mothers with lupus and Sjogren's syndrome. Two types of autoantibodies were studied, termed anti-Ro/La and anti-muscarinic. In experimental models, the deleterious effects of both autoantibodies were able to be blocked by a therapeutic agent termed intravenous immunoglobulin (IVIG), and a pilot study showed a beneficial effect of IVIG in patients with circulating anti-muscarinic autoantibodies. In a newly developed implant model, anti-Ro/La were shown to bind to apoptotic (dying) human cells in vivo, overcoming problems with an earlier animal model. The anti-Ro/La have the potential to cause inflammation and tissue damage in neonatal lupus and adult lupus. It was possible to identify the precise anti-La autoantibodies mediating this effect. These antibodies may be used to more accurately predict which mothers are more	International trials using IVIG to prevent neonatal lupus and its complication of congenital heart block are being contemplated. Better diagnostic tests to identify "pathogenic" anti-Ro/La (causing neonatal lupus) and anti-muscarinic (causing bladder and sleep disturbance) autoantibodies are likely to be developed. Approaches to increase the removal of dying cells in lupus may be developed.
GNT0249400	2002	Prof David Little	Project Grants	Standard Project Grant	Bisphosphonates in Perthes disease	Children's Hospital at Westmead	NSW	Health	1/01/2003	31/12/2005	$199,750.00	Clinical Medicine and Science	Orthopaedics	drug action | osteoarthritis | osteonecrosis | osteoporosis | prophylaxis | legg-perthes disease | osteoarthritis | osteonecrosis |	Perthes Disease (Legg-Perthes Disease) is a common childhood disorder, which leads to collapse and deformity of the growing hip joint. This can lead to arthritis in adult life, as well as a short leg on the affected side. The cause is as yet unknown. A class of drugs called bisphosphonates has been shown to help children with osteogenesis imperfecta (brittle bone disease). We believe, based on our extensive studies of the effect of these drugs on bone healing, that they could also help children with Perthes disease. Although proving to be safe and effective in children with osteogenesis imperfecta, before exposing children with Perthes disease to the risk of any side effects, animal studies are needed. A certain type of rat called the spontaneously hypertensive rat gets a condition almost exactly the same as Perthes disease. This study will treat a large number of these rats and perform detailed study into whether it has a positive effect on preserving the shape of the hip joint, as well as looking into how this actually occurs. A successful outcome would pave the way for trials in children with Perthes disease, and could result in the avoidance of surgery and improved health outcomes for the children.	Perthes disease is a childhood disorder where the head of the femur loses its blood supply (osteonecrosis). These series of experiments have shown for the first time that a class of commonly used drugs, bisphosphonates, can change outcome in a model of spontaneous osteonecrosis. We used the bisphosphonate zoledronic acid (ZA) in an animal model called the spontaneously hypertensive rat (SHR). 50% of male rats sustain a Perthes-like onset of osteonecrosis during growth. We had previously shown that ZA was effective in improving outcome in a model where we induced osteonecrosis in the femoral head of Wistar rats. This is useful information,direct applicability to Perthes disease could be questioned as the osteonecrosis was induced and did not occur spontaneously.In the SHR model we have definitively shown:1. Early treatment with ZA is effective in preserving the architecture of the femoral head2. Cssification of the femoral head is advanced by ZA treatment3. Late treatment is ineffective4. Ossification of the femoral head can also be accomplished in normal rats	This study represents an important component of an emerging body of work both from our lab and from overseas. It documents that bisphosphonate drugs, by slowing resorption of necrotic bone, can improve the structural retention of shape in a femoral head recovering from osteonecrosis. These concepts are now being clinically translated, highlighting the extremely high impact of these studies.
GNT0302203	2003	Prof Graeme Jones	Project Grants	Standard Project Grant	A sixteen year study of bone development in children	University of Tasmania	TAS	University	1/01/2004	31/12/2005	$144,750.00	Clinical Medicine and Science	Paediatrics	foetal origins | osteoporosis | peak bone mass | bone density | children | fracture | osteoporosis |	Osteoporosis is a major public health problem resulting in 50-75,000 fractures each year in Australia costing the community about 800 million dollars per annum. Bone strength is a risk factor for fractures in both childhood and in later life. Relatively little is known about bone development with the exception of calcium intake and physical activity. This study will follow 500 children from birth in 1988 to 2004 with the aim of understanding the contribution of lifestyle factors to bone development in this time period.	This study followed 415 children from birth to age 16 years observing the development of healthy bones in children. At age 8, we found that breastfeeding, smoking during pregnancy, diet during pregnancy, birthweight, physical activity, sun exposure, asthma medication and fruit and vegetables were all associated with bone mass. By age 16, smoking during pregnancy was no longer associated but both breastfeeding and birthweight were suggesting an effect on peak bone mass. Diet is still being analysed. Vitamin D deficiency was common (40%) and was associated with bone mass. Fractures were common in these children (179/415) and were predicted by bone mass (heel ultrasound and DXA), breastfeeding, asthma medication and physical fitness at age 8. Bone density also tracks from age 8 to age 16. This study has provided novel data on the role of lifestyle factors in bone development in children which should lead to the development of programs to prevent fractures in both younger and later life.	This work is likely to lead to prgrams which increase peak bone mass and decrease fracture risk in both early and later life
GNT0323200	2004	Prof Leon Straker	Project Grants	Standard Project Grant	Development of adolescent spinal pain	Curtin University	WA	University	1/01/2005	31/12/2008	$682,800.00	Public Health	Clinical Sciences NEC	epidemiology | inactivity related disorders | multivariate risk modelling | musculoskeletal system capacity | physiotherapy | low back pain | neck pain | spinal pain | thoracic pain |	This project aims to understand the development of back and neck pain in adolescence. By the age of 16 around half of all adolescents have suffered back pain and one third have suffered neck pain. For many adolescents this pain is disabling and over a third of sufferers miss school, miss recreation and seek medical help. The current understanding of back and neck pain in adolescence is quite limited - restricting the effectiveness of initiatives to prevent adolescents having to suffer spinal pain and of treatment of those adolescents unlucky enough to have an episode. Better understanding and interventions for adolescent spinal pain will also have longer term implications by reducing adult spinal pain. Four out of 5 adults will experience spinal pain. In the USA treating adult back pain is the 4th largest health care cost. Many adults with chronic back pain had their first episode during adolescence. A better understanding of spinal pain in adolescence may help prevent it developing into a lifelong disability. We will collect information from 2,000 adolescents on their experience of back and neck pain and on potential physical, lifestyle and psychosocial risk factors. We believe factors such as their posture, muscle capacity, TV and computer use, mental health and social situation all combine to influence whether a person develops back or neck pain. The project is unique as it will not only collect a broad range of	The project funded the collection and partial analysis of information about back and neck pain in adolescents at 14 and 17 years in the Raine pregnancy cohort study. Spinal pain was found to be already common at 14 years of age and to already be associated with disability at 17 years of age. Information on a wide range of physical, lifestyle and psychosocial risk factors was also collected. Posture, fitness, obesity, motor competence, physical activity, computer use, school bag carriage, diet, smoking and alcohol use, depression, externalising behaviours, self worth, parental pain experience, socioeconomic status, family functioning and life stress events were all related to spinal pain. Subgroups of individuals with spinal pain were also identified suggesting interventions could be targetted. The findings refuted a common misperception that adolescent spinal pain is trivial. They also suggested windows for interventions to reduce spinal pain risk (early life and adolescence) and arrest a trajectory to chronic, disabling adult spinal pain. Grant applications have been submitted to follow	The publiction of the results of this project will correct a misperception about the importance of adolescent spinal pain. We have identified several opportunities to reduce risks and will apply for funding to assess the efficay of targetting specific interventions.
GNT0403035	2005	Prof Tania Winzenberg	Early Career Fellowships	General Practice ECF	Chronic disease prevention: investigating how to improve bone mass, fracture risk and obesity at different life-stages.	Menzies Research Institute	TAS	Research Institutes	1/01/2006	31/12/2009	$305,500.00	Public Health	Preventive Medicine	children | nutrition | obesity | osteoporosis | physical activity |	Media Summary not available	With the award of this GP Training Fellowship, Dr Winzenberg has undertaken a range of projects investigating chronic disease prevention in both adults and children, focussing work initially on prevention of osteoporosis and other musculoskeletal conditions. With the recognition of the range of issues shared across prevention other chronic diseases, this work expanded to also consider prevention of cardiovascular diseases. Key outcomes of her work include: *demonstrating that informing women of their fracture risk could lead to them making lifestyle changes to improve not only their own bone health, but potentially that of their children as well; * providing definitive evidence that calcium supplements in healthy children have only minor effects on bone mineral density and do not affect body weight, thus clarifying that calcium supplements have only a limited place as a public health intervention; *developing an easy-to-take dosage regimen to treat vitamin D deficiency in adolescents; *identifying the previously unrecognised issue of poor accessibility of the	Dr Winzenberg is investigating further ways to improve children's bone health including determining if vitamin D supplementation is effective in either healthy children or children who have sustained a broken bone. She is also studying whether informing people of their risk of cardiovascular disease might cause them to improve their lifestyle, as seen with fracture risk feedback.
GNT0435700	2006	Prof Graeme Jones	Practitioner Fellowships	Practitioner Fellowship	Practitioner Fellowship	University of Tasmania	TAS	University	1/01/2007	31/12/2011	$360,312.91	Clinical Medicine and Science	Rheumatology and Arthritis	epidemiology, clinical trials | osteoarthritis | osteoporosis | osteoporosis in children | quantitative mri |	I am a rheumatologist and epidemiologist who concentrates on epidemiological studies understanding the causes and treatment of osteoarthritis and osteoporosis.	This fellowship allowed the publication of over 100 papers, 10 international talks and new grants worth over 4 million dollars. During the 5 years, much new data was gleaned from epidemiological studies on causes and time course of structural changes in osteoarthritis. In the latter period, trials of fish oil, zoledronate and 4jointz for osteoarthritis were completed, all of which had positive outcomes. Also during this time a key trial in rheumatoid arthritis was completed with the CI appointed principal investigator. This medication (tocilizumab) was then listed on the PBS and useage in Australia has been substantially influenced by this trial. Work on fracture protocols and more appropriate sun guidelines also happened during this time frame. Creation of NHMRC GRPs for musculoskeletal conditions was also initiated successfully by the CI to attempt to address underfunding of this national health priority.	This fellowship has been renewed for a further 5 years. There will be a nmber of trials demonstrating the efficacy or otherwise of new treatments for osteoarthritis in this time which will ease the suffering from this very common disease.
GNT0490006	2007	Prof Changhai Ding	Project Grants	Standard Project Grant	Can childhood physical activity and fatness affect the potential to develop knee osteoarthritis?	Menzies Research Institute	TAS	Research Institutes	1/01/2008	31/12/2009	$301,977.40	Clinical Medicine and Science	Rheumatology and Arthritis	bone | osteoarthritis | childhood obesity | childhood physical activity | knee cartilage | bone | childhood obesity | childhood physical activity | knee cartilage | osteoarthritis |	Interventions to increase participation of physical activity (PA) and to reduce obesity in childhood are advocated to reduce the risks of cardiovascular and other diseases in adulthood, but the associations of childhood PA and obesity with knee osteoarthritic changes in adulthood are unknown. This study, with follow-up of a large cohort of Australian children over 20 years, will be the first to determine these associations using the powerful technique of magnetic resonance imaging.	The aim of this study is to determine the associations between physical activity and fatness in childhood, and knee cartilage defects, tibial bone area and cartilage volume in young adults 25 years later. In addition, the associations between physical activity and fatness in childhood, and adult knee pain will be determined. We have recruited 298 young subjects (aged 31-41 years, 48.7% female) from the Childhood Determinants of Adult Health study. They underwent T1-weighted fat- supressed magnetic resonance imaging of their dominant knee and knee structures including cartilage volume and tibial bone area were measured. Currently we have looked the associations between childhood physical measures (physical work capacity at 170 beats per minute (PWC170), leg and hand muscle strength, sit-ups, long-run, and short-run) and knee structures in adulthood. We found that there were consistent and significant associations of all childhood measures with adult total tibial (medial plus lateral) bone area in multivariable linear regression. Similarly,	We will look at the associations betweenchildhood obesity measures (BMI, waist & hip girths, sum of skinfolds) and knee structures in adulthood, and expect that childhood obesity measures are associated positively with knee cartilage defects, tibial bone area, and negatively with cartilage volume. These will be independent of current body composition.
GNT0502612	2007	Prof Louise Purton	Project Grants	Standard Project Grant	Understanding how TNFalpha affects bone and blood cell production	St Vincents Institute of Medical Research	VIC	Research Institutes	1/01/2008	31/12/2010	$589,425.35	Basic Science	Haematology	bone | haemopoiesis | haemopoietic stem cells | retinoic acid receptors | tnf alpha | ageing | bone marrow transplantation | genetic diseases of the blood | leukaemia | osteoporosis |	Recent studies have identified that bone plays an important role in blood cell production. We have discovered that elevated levels of TNF alpha (which increases with ageing and can negatively impact on health) contributes to a blood cell disorder that can progress to leukaemia. There are also reduced numbers of blood stem cells and bone in this mouse model. In these studies we will determine how TNFalpha contributes to blood and bone defects, which may lead to better treatment of such diseases.	We have a mouse model that develops a blood cell disease called a myeloproliferative syndrome (MPS). This type of blood cell disease is very difficult to treat as we do not understand why it occurs. Our research has demonstrated that non-blood cells within the bone cavity that help to regulate blood cells can cause the MPS. One complication has been that this mouse model has high levels of a substance involved in inflammation that may have contributed to the blood cell disease. We have therefore generated another mouse model in which this inflammatory substance has been deleted, allowing us to determine whether the blood cell disease still persists or not. We have determined that this blood cell disease does indeed still persist in the absence of the inflammation-related substance. We are now determining how the MPS occurs in order to develop better treatments for such blood cell diseases.	We anticipate that research following on from these studies will provide insight into how the bone marrow microenvironment cells regulate blood cell production and in turn blood cell diseases.
GNT0508046	2007	Prof Cory Xian	Project Grants	Standard Project Grant	Mechanisms and prevention of chemotherapy-induced bone growth defects	University of South Australia	SA	University	1/01/2008	31/12/2011	$622,598.08	Clinical Medicine and Science	Orthopaedics	bone growth defects | childhood cancer chemotherapy | growth plate and bone defects | pathophysiological mechanisms | prevention treatment strategies | bone growth arrest | chemotherapy toxicity | childhood cancer | osteoporosis | treatment strategies |	Childhood chemotherapy often causes growth arrest, osteoporosis, and fractures in cancer patients and survivors. Using a rat model, this project will study how the most commonly used chemotherapy drug methotrexate causes bone growth defects and examine any protective effects of two natural-derived substances. This work will increase our knowledge on chemotherapy-induced bone growth defects, and will be useful for developing a preventative treatment.	Work in this grant has shown that bone growth defects in young rats caused by treatment with the commonly used anti-metabolite methotrexate (MTX) are associated with dysfunctions in both growth plate and metaphyseal bone, resulting from (1) arrest of cell growth, induction of apoptosis, reduction in synthesis of cartilaginous template for bone formation, (2) an increase in osteoclast formation and aggravated resorption of newly formed trabecular bone, (3) a decrease in osteogenic potential but an increase in adipogenesis in the bone marrow, and (4) alterations in NF-kB, Wnt/b-catenin and CXCR4 signalling pathways. In addition, supplementary treatments with folinic acid or genistein can potentially protect bone growth during MTX chemotherapy.	Our increased mechanistic understanding for cancer chemotherapy-induced bone defects will open new windows and opportunities to explore novel therapeutic preventative treatments. Effectiveness of bone protection with supplementary treatments of folinic acid or genistein could lead to potential therapies in clinical practice.
GNT0508047	2007	Prof Cory Xian	Research Fellowships	Research Fellowship	Uncoupled Research Fellowship	University of South Australia	SA	University	1/01/2008	31/12/2012	$617,878.82	Basic Science	Orthopaedics	childhood bone growth | injury and repair | injury responses | osteoporosis, development of treatments | skeletal toxicity |	"I am a biomedical scientist undertaking basic and clinical research on the pathophysiology of growth plate injury and repair, which critically impacts on children's bone growth and growth disorders. I aim to investigate the underlying mechanisms and deve	Musculoskeletal conditions including skeletal fractures are major burdens on individuals and health systems. Childhood bone health is critical for ensuring healthy development, and the peak bone mass achieved in adolescence and early adulthood also profoundly influences adult bone health. During 2008-2012 with NHMRC SRF support, I have made following research achievements in three major areas. Injured growth plate is often "faultily" repaired leading to bone growth defects. My laboratory has identified a sequential injury repair response and potential targets which could lead to development of a biological treatment. Cancer chemotherapy unfortunately causes significant bone defects (osteoporosis, marrow adiposity and fractures). My laboratory has identified that these defects result from reduced bone formation, increased bone resorption, and increased marrow fat formation, as well as involvement of major signalling pathways (Wnt/b-catenin and NF-?B). Our work also showed that supplementation with folinic acid (a folate analogue) or genistein (a soy	oPotential development of the first in situ biological regenerative therapy for children's growth plate trauma injury-induced bone growth defects;oPotential identification of novel preventative strategies for bone and bone marrow damage caused by chemotherapy;oPotential identification of dietary interventions for optimising bone growth and bone mass accrual in early life.
GNT0510113	2007	Prof Hazel Mitchell	Project Grants	Standard Project Grant	The role of mucus-associated bacteria in inflammatory bowel disease.	University of New South Wales	NSW	University	1/01/2008	30/06/2011	$431,764.08	Clinical Medicine and Science	Medical Infection Agents (incl. Prions)	crohn's disease | fish | bacteria | host-pathogen interaction | crohn's disease | aetiology | bacterial pathogens | children |	The role of bacteria in Crohn's disease is well accepted however to date no conclusive agents have been identified. Recent animal studies have implicated mucus-associated bacteria. We have recently shown that such bacteria, the Helicobacteriaceae, are present in humans and children with Crohn's disease. The aim of this project is to determine in children and young adults the role of these bacteria in IBD thus providing information that could be used to design improved therapies for IBD.	This study investigated the possible role of mucus-associated bacteria (Helicobacter and Campylobacter species) in Crohn's disease (CD). While the prevalence of Helicobacter species was increased in children with newly diagnosed CD as compared with controls without CD, no specific Helicobacter species was associated with CD. In contrast, the prevalence of Campylobacter concisus, a mucus associated bacterium that has been associated with gastroenteritis, was significantly higher in biopsy and faecal samples of CD children as compared with non-CD controls. Furthermore C. concisus was grown from biopsy specimens of a number of PCR positive CD children, and PCR positive CD children were shown to mount an immune response to C. concisus. Investigation of the pathogenic potential of C. concisus using attachment and invasion assays and scanning electron microscopy showed that a C. concisus isolate from CD children could attach to and invade Caco-2 cells, while strains from patients with gastroenteritis and a healthy control (HC) had reduced or no invasive ability.	If these findings are confirmed in a larger population of patients with newly diagnosed CD, screening tests to detect the presence of C. concisus strains with increased virulence potential will be developed and the effect of antibiotic therapy directed against C. concisus determined.
GNT0510230	2007	Prof Hazel Mitchell	Project Grants	Standard Project Grant	Nutritional therapy in Crohns	University of New South Wales	NSW	University	1/01/2008	30/09/2011	$364,549.81	Clinical Medicine and Science	Gastroenterology and Hepatology	crohn's disease | children | gastroenterology | inflammation | nutrition | treatment | children | inflammatory bowel disease |	Crohn's disease occurs at any age, even in young children. One treatment for CD involves the use of a special drink (nutritional treatment). This works well for CD in children, helping to settle symptoms and heal the bowel surface. Despite being established as a treatment for 20 years, it is not yet clear how it works. These studies aim to work out how nutritional treatments work in CD. This should expand our knowledge about CD and may lead to further ways to prevent or manage CD.	The work undertaken during the course of this grant has further defined mechanisms by which nutritional therapy modulates gut inflammation in the context of Crohn disease in children. Key aspects are the profound effects that exclusive enteral nutrition has upon the gastrointestinal flora, and the effects of this intervention upon epithelial and mucosal innate defence mechanisms (including barrier function).	The data arising from this work will provide a foundation for further and ongoing work exploring the interactions between diet and the gut. This includes current studies focusing upon optimising the effects of nutrition in paediatric Crohn disease (to ensure even better clinical outcomes).
GNT0565081	2008	Dr Sharon Byers	Project Grants	Standard Project Grant	Gene therapy for bone and cartilage disease in MPS.	University of Adelaide	SA	University	1/01/2009	31/12/2011	$383,783.50	Clinical Medicine and Science	Paediatrics	gene therapy | inherited metabolic disease | orthopaedics | skeletal dysplasia | degenerative joint disease | lysosomal storage disorder | mucopolysaccharidoses | musculoskeletal disease |	Skeletal disease is a major problem for children with mucopolysaccharidoses (MPS). Patients suffer from early onset osteoporosis and osteoarthritis, severely affecting their quality of life. We will evaluate a lentiviral gene therapy vector developed in-house for its capacity to transduce bone, cartilage, synovial and ligament cells in a mouse model of MPS VI. Our goal is to generate high level, sustained expression of the deficient MPS enzyme and alter the course of skeletal disease in MPS.	We have shown that neonatal gene therapy prevents the development of the high bone mass phenotype characteristic of MPS VII, via an increase in osteoclast number and attachment to bone. Established bone disease also responds rapidly in mice treated at an older age. Conversely growth in bone length is unchanged by gene therapy. Thus this mode of therapy has future application to disorders of high bone mass phenotype but does influence bone length discrepancies arising from growht plate cartilage dysfunction.	Oucomes can be developed to provide a gene therapy approach to disorders of high bone mass.
GNT0572638	2008	Prof David Joyce	Project Grants	Standard Project Grant	Macrophage uncoupling protein-2 regulation and expression in inflammatory joint disease and hyperoxic lung damage	University of Western Australia	WA	University	1/01/2009	31/12/2011	$270,013.24	Clinical Medicine and Science	Respiratory Diseases	hyperoxic lung damage | inflammation | macrophage | reactive oxygen species | uncoupling protein 2 | oxidative stress | anti-inflammatory drug therapy | hyperoxic lung damage | inflammatory arthritis | inflammatory bowel disease |	Oxygen radicals (OR) are made by white blood cells (WBC) when they protect against microbes and cancer cells. However, excessive production also damages normal tissue, for example in lungs that receive too much oxygen (hyperoxic lung damage) or in inflamed joints. One type of WBC, the macrophage has a protein named UCP2, that limit the amount of OR formation. This project aims to find out how macrophages activate UCP2 and whether they do so in inflammatory arthritis and hyperoxic lung damage.	The body sends macrophages to some sites of infection, inflammation or tissue damage, to defend and repair. There, they need oxygen and nutrients for energy. These may be limited in infected or damaged tissue, but macrophages are equipped to gain energy from a range of nutrients. In the process of oxidising nutrients for energy, macrophages produce oxygen radicals (reactive oxygen species: ROS) from cell mitochondria. ROS assist in clearing some infectants, but can also damage cell components. Macrophages can mount a protective response to ROS. In the work funded by this grant, we have examined situations where macrophages are under particular ROS stress, in the clinical conditions of hyperoxia-associated lung injury (HALI) and endotoxaemia caused by gram-negative bacteria. We found that macrophages responded in each condition by expressing uncoupling protein-2 (UCP2) in mitochondria, which served to contain mitochondrial ROS generation. In HALI, we found evidence that ROS themselves initiated UCP2 expression. In endotoxaemia models, it	We will explore whether UCP2 expression makes macrophages better at immune functions, more resistant to ROS damage or more likely to retain M1 phenotype or adopt an alternative M2 phenotype. We are also exploring UCP2 regulation, observing links to central controllers of energy metabolism, including mTOR and AMP-kinase in macrophages.
GNT0595989	2009	Dr Joanne Reed	Early Career Fellowships	CJ Martin Biomedical ECF	Mechanisms of foetal cardiac injury by maternal autoantibodies	Garvan Institute of Medical Research	NSW	Research Institutes	1/01/2010	31/12/2015	$442,759.87	Basic Science	Autoimmunity	autoantibodies | cell death-apoptosis | cellular immunology |	Media Summary not available	Our immune system protects us from disease by producing antibodies that attack viruses and bacteria. However, 5% of Australians suffer from autoimmune diseases, where their immune system produces "auto"antibodies that attack their own cells/organs. This project studied autoantibodies that cause neonatal lupus, a permanent heart injury that affects foetuses born to mothers with autoimmune diseases Sjogren's syndrome and systemic lupus erythematosus. The first half of the fellowship, done at New York University, utilised the Research Registry for Neonatal Lupus, the largest collection of clinical samples from affected families. Reed established that levels of a blood protein, called b2-glycoprotein, were reduced in newborns with neonatal lupus compared to their healthy siblings. She then showed that b2-glycoprotein binds to cardiac cells and blocks binding of autoantibody. Having established that b2-glycoprotein protected against autoantibody-mediated injury, the next goal was to define factors that damage cardiac cells. Reed established an experimental	Autoantibody-mediated disorders account for a large burden of chronic disease and can be difficult to diagnose and treat due to heterogeneous symptoms, ranging from joint pain, dry eyes and mouth to kidney failure, lymphoma, or giving birth to a child with neonatal lupus. The unpredictability of disease reduces patient quality of life, while posing significant costs to healthcare systems for monitoring large populations of patients. Current diagnostic tests confirm the presence of autoantibodies but have limited value for predicting disease outcome. For example, autoantibodies that react with a protein called "Ro" are associated with neonatal lupus such that weekly echocardiograms from 12-22 weeks gestation are recommended for all pregnant women with Ro autoantibodies. However only 2% of these pregnancies result in disease. This project identified a subset of autoantibodies, present in mothers of children with neonatal lupus,
GNT0607347	2009	A/Pr Carl Kirkwood	Career Development Fellowships	RD Wright Biomedical CDF	Role of infectious agents in gastrointestinal diseases of children	Murdoch Childrens Research Institute	VIC	Research Institutes	1/01/2010	31/12/2013	$436,312.91	Clinical Medicine and Science	Medical Virology	crohn's disease | gastroenteritis | infectious disease | viral pathogenesis |	Media Summary not available	During the fellowship I have led an internationally recognised research programme directed towards improving our understanding of infectious causes of gastrointestinal disease. During this period, I have had a sustained high level of research productivity, with 48 publications, including 39 peer reviewed articles, 4 reviews, 3 book chapters/book editorship and 2 research reports since 2010. The majority of my publications are in the leading virology and infectious diseases specialty journals, such as PLOS, IBD, EID and J. Virology , I have made substantial and fundamental contributions to the field that have enabled me to obtain competitive research funding from NHMRC, and from national and international NGO and philanthropic organisations in excess of $6,000,000 since 2010., I have developed an excellent international profile, and play key role in strategic research direction, thorugh roles as;-, o Director of WHO Collaborating Centre for Child Health (Research in Human Rotavirus),, o Director of WHO Regional Rotavirus Laboratory, o Director of Australian	In the future, i intend to lead a highly effective and innovative research team acknowledged internationally for cutting edge microbial and genomic technologies, with the aim to significantly improve our knowledge of gut infections and develop preventative and treatment strategies. The program will ultimately improve the health of children in Australia and globally.
GNT0607382	2009	A/Pr Carl Kirkwood	Project Grants	Standard Project Grant	Infectious agents that trigger Crohns disease	Murdoch Childrens Research Institute	VIC	Research Institutes	1/01/2010	31/12/2012	$570,876.85	Clinical Medicine and Science	Gastroenterology and Hepatology	crohn's disease | enteric infections | gastroenterology | chronic inflammatory diseases and infection | crohn's disease | gastrointestinal disease |	Crohn's disease is a major cause of illness throughout the world. There is no cure and current therapies carry substantial risks. An infectious agent has been suggested as the trigger for disease but research has been inconclusive. Our study focuses on the characterisation of a novel virus we have identified that may trigger Crohn's disease in children at disease onset.	This study aimed to characterise viruses that may be involved as a trigger for early onset Crohn's disease (CD) in children. The project initially explored the differential gene expression between ileal tissue from CD and controls. Several genes were either expressed only in intestinal tissue, or have roles in processes relevant to CD pathogenesis or in microbial processes. Molecular screening of a culture-adapted virus from CD tissue identified sequences that were predominantly assigned to human endogenous retroviruses (HERV). Efforts to generate a complete viral genome were unsuccessful, with sequences confined to 2 genomic regions. To further explore an association between HERV and CD, PCR based assays targeting several target regions of the HERV genome was performed. This prevalence study showed no significant differences in these HERV regions between CD and control tissues. High throughput sequence analysis was conducted to explore the viral communities present in mucosal and stool samples from CD patients. The majority of viral hits belonged to	In this study, we have identified differences in the diversity and distribution of the phage viral population between CD and non-IBD, and novel information regarding development of early onset CD. If developed further this data has the potential to be used in treatment therapies as well as diagnostic assays.
GNT0997502	1998	Dr Helen Woodhead	Postgraduate Scholarships	Medical Postgraduate Scholarship	The skeletal adaptaions to exercise in prepubertal athletes and normal children	Children's Hospital at Westmead	NSW	Health	1/01/1999	31/12/2000	$52,386.00	Clinical Medicine and Science	Endocrinology	exercise | bone density | bone architecture | children | osteoporosis |	Media Summary not available	Data not available	Data not available

GNT1003339	2010	Prof Louise Purton	Research Fellowships	Research Fellowship	Regulation of haemopoiesis and bone by retinoids	St Vincents Institute of Medical Research	VIC	Research Institutes	1/01/2011	31/12/2015	$601,483.97	Basic Science	Haematology	haematopoietic stem cells | bone cancer | retinoic acid | osteoporosis | haematopoietic stem cells | osteosarcoma | vitamin a | osteoporosis	My research has shown that vitamin A is very important to the normal function of blood and bone cells. I will further explore the uses of vitamin A products to improve the treatment of patients with a range of different blood and bone diseases. These studies may lead to better treatments of patients with a wide range of blood cell diseases. It may also reveal better treatments for patients with bone diseases such as cancer and osteoporosis.	This Senior Research Fellowship further delineated the roles of vitamin A receptors in regulating bone and blood. My research revealed a novel cell type in the thymus that helps to regulate T lymphocyte production, with a related cell type regulating B lymphocyte production in the bone marrow. We also identified how vitamin A receptors regulate bone production. My fellowship also contributed to research that has resulted in a clinical trial currently being prepared in USA to test the use of a vitamin A compound in leukaemia. Another clinical trial is also currently being performed in USA to prevent bone loss in cancer patients, and this trial resulted directly from my senior author research performed and published during my fellowship period. This fellowship resulted in invitations to speak at 6 International and 6 National conferences, in addition to numerous seminars in Australia and internationally. During this Fellowship I was on the Scientific organising committee of two National conferences, the Organising committee of one National conference and I initiated the Gender	The delineation of the roles of each of the vitamin A receptors (retinoic acid receptors) has significant benefit in identifying therapies that will have better outcomes than those currently existing, where all vitamin A receptors are activated (by use of the vitamin A derivative, all-trans retinoic acid, ATRA). For example, my research has now resulted in a clinical trial currently being prepared at the John Hopkins Hospital in Baltimore, USA, to trial the use of a retinoic acid receptor alpha (RARalpha) agonist in place of ATRA in patients who have leukaemia (separate from acute promyelocytic leukaemia patients). Our studies on how retinoic acid receptor gamma regulates haematopoiesis via microenvironment cells identified key microenvironment regulators of B and T lymphopoiesis. Further delineation into how this occurs may lead to new therapies to improve immune cell number and function in aging people, in addition to patients with a range
GNT1021148	2011	Prof Carola Vinuesa	Research Fellowships	Research Fellowship	Research Fellowship	Australian National University	ACT	University	1/01/2012	31/12/2016	$675,736.67	Basic Science	Cellular Immunology	t cell response | b cells | antibody | microrna | ubiquitin | autoimmunity initiation | lupus	I am an immunologist focusing on understanding how can we combat chronic infections while preventing autoimmunity. This proposal aims to investigate how a poorly understood subset of lymphocytes called Tfh cells are regulated to promote the formation of protective antibodies, and prevent development of harmful antibodies that go on to cause or exacerbate diseases such as lupus, rheumatoid arthritis and type 1 diabetes. Our discoveries will illuminate novel drug targets for these diseases and help generate more potent vaccines.	My team has made several discoveries on two fronts: A) Discovery of novel mechanisms that control the growth and function of follicular helper T cells. These T cells help B cells make antibodies and as such regulate responses to infection, autoimmunity and Tfh-derived neoplasms. The novel mechanisms discovered include metabolic pathways, regulation of homeostasis of small non-coding RNAs known as microRNAs, and micro-RNA-mediated regulation of the expressionof molecules important for follicular T cell function such as ICOS. B) Identification of the genetic basis of autoimmune diseases. We have identified the causal mutations in several patients with autoimmune disease. The first case to be solved revealed paediatric cerebral lupus could be caused by rare variants in the gene TREX1, causing impaired degradation of DNA and an exacerbated type I IFN response. Solving similar cases is helping refine the diagnosis of a complex disease like lupus, and illuminating more targeted therapies.	Collectively, my team's findings have established the importance of Tfh cells in the control of infection and the need to regulate their numbers and function to prevent autoimmune diseases and transplant rejection. Our work has provided a rationale and novel targets for treatments that block Tfh cell growth or function in transplantation and in the treatment of autoimmune diseases. It also underscores the importance of designing vaccines that can boost Tfh numbers. Our work on elucidating the contribution of gene mutations to human lupus is providing us with clues as to the molecular heterogeneity of SLE and clues on how to design more targeted therapies.
GNT1026349	2011	A/Pr Justine Ellis	Project Grants	Standard Project Grant	Vitamin D and JIA risk	Murdoch Childrens Research Institute	VIC	Research Institutes	1/01/2012	31/12/2015	$586,485.81	Public Health	Epidemiology	vitamin d | sun exposure | autoimmune disease | gene expression | juvenile arthritis	Juvenile Idiopathic arthritis (JIA) is an autoimmune disease that occurs in up to 1/250 Australian children. Growing evidence suggests that low vitamin D increases risk of autoimmune disease, yet no-one has looked at its effect on JIA. We will compare vitamin D in blood, and also exposure to sun through life, between children with and without JIA. We will also look to see if vitamin D interacts with autoimmune disease risk genes. The outcomes of this study will help to inform policy on the importance of sun exposure to health.	This study aimed to understand the role of vitamin D in determining susceptibility to juvenile idiopathic arthritis (JIA). Vitamin D is involved in the development of the immune system, and has been associated with risk of other autoimmune diseases such as multiple sclerosis. The role of vitamin D in JIA had not been examined in any detail prior to our project. The three main outcomes of this study are as follows: 1. Exposure to sun (ultraviolet radiation) across the life course and prior to disease onset does not appear to be strongly associated with JIA susceptibility (manuscript in preparation). We hypothesised that increased exposure to the sun during gestation, and through childhood, would protect against the development of JIA. We found some evidence that increasing time spent in the sun in the summer prior to disease onset is associated with a decreased risk of JIA (test for trend p = 0.034), but no other life course measures of sun exposure showed association with JIA. 2. Established JIA susceptibility genes interact with genes in the vitamin D pathway to determine	This project and its findings are significant because this is the most comprehensive, multidisciplinary examination of the role of vitamin D in development of JIA to date. Understanding the role of environment, and how environment interacts with genes in a disease like JIA is crucial to being able to translate basic science findings to improvements in clinical care. In particular, in moving towards a personalised approach to medicine, looking at genes and environment in isolation will not allow for sufficient understanding of an overall individual susceptibility profile. Here, we have shown that just by examining environmental determinants of circulating vitamin D, patterns of association did not provide a clear picture of the role of vitamin D in disease risk. However, when we considered interactions between known JIA susceptibility genes and genes in the vitamin D pathway known to regulate vitamin D, we discovered clear associations that were able to be
GNT1029116	2011	Dr Qingju Wang	Project Grants	New Investigator Grant	Does trabecular structure in childhood determine metaphyseal bone strength in adulthood?	University of Melbourne	VIC	University	1/01/2012	31/12/2013	$165,339.32	Clinical Medicine and Science	Paediatrics	bone architecture | growth | osteoporosis | bone development | bone markers	Skeletal fragility is common is elderly people but has its origin in childhood. Strong bone established during growth will provide more protection against occurrence of fragility fracture in old age. Identifying individuals during childhood who are at high risk of skeletal fragility, and early intervention is a strategic approach managing the burden of skeletal fragility on the ageing population.	We have shown that children with forearm fractures have lower bone mineral density of the outer cortical shell of the wrist because the shell is more porous than healthy children without fractures. Children with fractures had a slightly wider bone but the cortical shell around the wider bone was thin as well as being more porous. These findings indicate that children with forearm fractures (30% of all children suffer these fractures) do not build the bone architecture normally when they are growing. In addition, girls with forearm fractures had thinner and fewer trabeculae that form the inner spongy bone of the wrist. The explanation for this we believe also relates to how the bone grows in early life. The growth plate produces spicules of spongy or trabecular bone formed from cartilage. As the bone grows the spicules on the outer zone of the growth plate fuse together to form the cortex while the inner spicules form the trabeculae. When deficient both the cortical shell becomes thin and the spongy bone has fewer and thinner trabeculae. We also found that the architecture	Bone is most amenable to change during growth. Once improvements in bone structure and mineral content are established, and if maintained until completion of growth, they will positively affect fracture risk during childhood and into adulthood. Exercise may alter bone structure, and diet, mineral content during growth so future work is needed to determine the optimal type of intervention.
GNT1042105	2012	Prof Cory Xian	Research Fellowships	Research Fellowship	Bone growth for healthy development: physiology, pathophysiology, and regeneration	University of South Australia	SA	University	1/01/2013	31/12/2017	$621,458.93	Clinical Medicine and Science	Orthopaedics	growth plate | cancer chemotherapy | regeneration | bone cells | bone growth | bone loss | osteoporosis | wnt signalling | cell therapy | micronutrients	Musculoskeletal damage is a major burden on individuals and our health care system. My research program will focus on improving bone health in three important areas: (1) children's growth plate injury and growth defects; (2) bone loss and bone marrow defects from cancer chemotherapy; (3) ensuring that bone grows healthily in early life. The overall intent of this research is to develop new therapies when bone doesn't grow well, or is damaged.	My research program during 2013-2017 SRF funding period (GNT1042105) has obtained considerable achievements: I made major research contributions (shown in 88 publications including in leading journals eg Endocrinology, J Bone Miner Res), uncovering functions/mechanisms of NT-3 in bone and growth plate repair, mechanisms and potential prevention strategies for cancer chemotherapy induced bone loss, MACF1 gene in controlling bone homeostasis, PI3K/AKT signaling in osteoarthritis, and microRNAs in osteoporosis. I expanded research impact in 2013-17 vs the previous 5-yr period: (1) increased numbers of publications: 88 (2013-now) vs 26 (2007-11); (2) increased citations/year (Google Scholar): 560 cites in 2017 alone vs 451 in 2013; (3) invest grants/funding awarded: $2.5M in 2013-17 vs $2.0 M in 2008-12; (4) 6 PhD completions in 2013-17 vs 5 in 2008-12. I consolidated my position as a leading/competitive researcher. I am recognised as an international leader in 2 research areas: growth plate/bone repair and cancer chemotherapy-induced	During 2013-2017, my research has been focused on (i) addressing novel questions relating to, and (ii) testing targeted interventions for, 3 major orthopaedic conditions. To date, trauma-induced bone growth defects can only be treated by highly invasive, costly and often ineffective corrective surgeries. We do not yet know enough about the pathobiology of, and lack preventative therapies for, bone defects caused by chemotherapy. Finally, healthy bone in adulthood has its origins, in part, in early life; thus optimising healthy bone growth and development in early life will be an important component of childhood and adult bone health. During 2013-2017, my research findings made strong impact. Some were highlighted in international media (US Endocrine News; Int Bone Miner Soc Update). My editorial (2014) was cited in JBMR, Orthop Trauma, Nutr Res Rev by leading researchers, influencing latest research directions and impacting on
GNT1045408	2012	Prof Graeme Jones	Project Grants	Standard Project Grant	T Bone study: 25 year follow up	University of Tasmania	TAS	University	1/01/2013	31/12/2015	$386,313.11	Clinical Medicine and Science	Medical and Health Sciences not elsewhere classified	bone | barker hypothesis | paediatric | fracture | growth	This study will follow up a birth cohort for 25 years with the aim of looking at critical periods for bone development including the role of in utero exposures, early infancy, age 8 and age 16.	We have completed a 25 year follow up of a birth cohort studying bone development and fracture risk in younger life. Data are not fully analysed at this stage but we have had one oral at a major international meeting on genetics of bone structure.	When data are finalised, we expect a much better understanding of bone development and fracture risk in children
GNT1078879	2014	A/Pr Craig Harrison	Project Grants	Standard Project Grant	Physiological consequences of the loss of inhibin activity	Monash University	VIC	University	1/01/2015	31/12/2017	$613,035.09	Basic Science	Paediatrics and Reproductive Medicine not elsewhere classified	activin and inhibin | transforming growth factor beta (tgf-beta) | female menopause | muscle wasting | bone loss	Inhibin A and B are essential factors in mammalian reproduction, negatively regulating pituitary production of follicle stimulating hormone (FSH). Interestingly, declines in inhibin levels at menopause correlate with a rapid decrease in bone and muscle mass. We propose that inhibin A and B have important physiological roles in the stimulation of bone and muscle growth, and that inhibins could be utilised to treat postmenopausal complications, including osteoporosis and sarcopenia.	Our original aim for this proposal was to: (1) demonstrate that the gonadal hormones, inhibin A and inhibin B, have important physiological roles outside the reproductive axis, and (2) show that inhibin mimetics can be utilised as novel therapeutics to treat postmenopausal complications We had great success achieving these aims. Specifically, we generated a new mouse model of inhibin deficiency (previous models developed tumours and died of wasting), which allowed us to examine the long term consequences of the loss of inhibin. Female mice demonstrated the expected ovarian pathology, but surprisingly gained significant weight on both a standard and high fat diet. Thus, the loss of inhibin contributes to increased adiposity. This is very significant, because inhibin is lost in women at menopause. We also developed a novel method to produce highly potent inhibin A (patent-granted), which will form the basis for future pre-clinical and clinical studies. The outcomes of GNT1078879, enabled Dr Kelly Walton to successfully gain a New Investigator Grant this	Menopause affects all women and the need for novel interventions that can alleviate menopausal symptoms, many of which (e.g. osteoporosis, cardiovascular disease and metabolic disorders) persist for decades, is greatly required. Using a unique genetic model of inhibin insufficiency, we have for the first time characterised the actual physiological roles of inhibin A and B, and identified organs/tissues that are likely to be adversely affected by the loss of these hormones at menopause. One somewhat surprising physiological target of inhibin action was fat, which increased significantly in the absence of inhibin. This is a very exciting finding and suggests that the loss of inhibin at menopause may be a major contributing factor to weight gain during this period. Importantly, we have also engineered highly potent inhibin A in sufficient quantities for preclinical studies. Inhibin replacement therapy in ovariectomised mice will determine the
GNT1081858	2014	Prof Christopher Goodnow	Research Fellowships	Research Fellowship	Immunological diseases: understanding their cause and improving their treatment by human genome sequencing	Garvan Institute of Medical Research	NSW	Research Institutes	1/07/2015	10/05/2018	$507,201.90	Clinical Medicine and Science	Immunogenetics (incl. Genetic Immunology)	autoimmune disease | antibody | genomics | t cells | molecular biology	Prof Goodnow will develop a collaborative consortium of specialist physicians, laboratory researchers and bioinformaticians. This team will apply the new tools of large scale DNA sequencing to reveal the root cause of immune system diseases including: autoimmune diseases, congenital immune deficiency diseases, allergic disorders, and cancer. It aims to accelerate, simplify and unify the diagnosis of these diseases, and guide targeted, earlier and more effective treatment.	The vision of this fellowship was to initiate a fundamental change in the way our health system manages autoimmune diseases, enabling diagnosis not by the organs affected but based on underlying cause, guiding targeted, earlier, more effective treatment. The specific plan was to bring together a interdisciplinary collaborative team to implement a new bedside to bench to bedside strategy for tackling autoimmune diseases: 1. starting with patients with autoimmune diseases; 2. analysing their genomes for damaging mutations affecting the immune system; 3. experimentally introducing candidate mutations into the mouse genome to test if and how they damage the immune system; 4. use the laboratory information above to guide analysis of blood cells from the patient; 5. target new use of therapeutics based on diagnosis of cause. This plan was successfully executed in the 3.4 years of the Fellowship. Through a collaborative network – The Clinical Immunogenomics Research Consortium of Australia (CIRCA) - more than 100 children with severe autoimmune	The research has initiated a fundamental change in the way our health system manages autoimmune diseases, enabling diagnosis not by the organs affected but based on underlying cause, guiding targeted, earlier, more effective treatment. The research connected the best of lab-based genetic, molecular and cellular immunology with the best of clinical care in disciplines of paediatrics, clinical immunology, rheumatology, hematology, endocrinology, gastroenterology and neurology. It revealed paradigm-shifting discoveries about how the immune system normally distinguishes foreign invaders from normal body components, and how that breaks down in autoimmune diseases that collectively affect more than 12% of people as chronic debilitating disorders. This new way of approaching autoimmune disease transformed the lives of two Sydney children, one with life-threatening destruction of his blood platelets and the other
GNT1122744	2016	A/Pr Jane Munro	Project Grants	Standard Project Grant	Towards a diagnostic test for juvenile idiopathic arthritis	Murdoch Childrens Research Institute	VIC	Research Institutes	1/01/2017	31/12/2021	$683,621.67	Basic Science	Autoimmunity	juvenile arthritis | rheumatology | diagnosis | genetic markers | prediction	Childhood arthritis is an autoimmune disease that affects around 6000 Australian children. It can be difficult to diagnose, but quick diagnosis is important to prevent ongoing pain and limit long term damage to joints. We have been able to use genetic information to predict which people have autoimmune celiac disease. In this project, we will find out how well genetic information can predict which children have childhood arthritis, and whether genetics can be used as a diagnostic test.	Final report due 30 June 2022	Final report due 30 June 2022

Notes:
Attachment A provides details of all of the grants that we were able to identify as being relevant to childhood rheumatic disease, that add up to the $12 million in total research funding.
All of these grants have now been completed. Columns J and K of the attached spreadsheet provide the start date and end date for each grant.
Column P (Media Summary) provides an overview of the proposed research as provided by the applicant at the time of application.
Columns Q and R provide a description of the research achievements and the expected future benefits, both provided by the grantee following the completion of the grant. Unfortunately we are unable to provide links to publications or published reports.

PARLIAMENTARY INQUIRY QUESTION ON NOTICE

Department of Health and Aged Care

Standing Committee on Health, Aged Care and Sport

Inquiry into Childhood Rheumatic Diseases

17 February 2022

PDR Number: IQ22-000028

Commonwealth plan to manage emerging treatments for juvenile rheumatoid arthritis

Spoken

Hansard page number: 3

Member: Mike Freelander

Question:

Dr FREELANDER: Could you take that on notice and see whether there is some Commonwealth mechanism that could be used to fund training positions, even if it's through supporting the colleges to do it?

Ms Wallbank: Yes. A scholarship or something along those lines?

Dr FREELANDER: Yes. Is there some Commonwealth plan to deal with the emerging treatments for childhood juvenile rheumatoid arthritis?

Ms Wallbank: There is an area of the department that looks at new treatments. Let me find the notes so I use the right words on that.

Dr FREELANDER: While you're looking: we've had a lot of submissions about workforce issues and new emerging treatments, but there doesn't seem to be any plan to deal with all of this.

Ms Wallbank: Workforce and emerging treatments are probably dealt with separately—in the department, at least. There's the health technology assessment process, which is undertaken by a particular part of the department. They do look at emerging technology. You'd be pleased to know there are a lot of doctors who work there, unlike myself, and so they're very technical experts. They're the people who also work with PBAC, BAC and those groups.

Answer:

The House of Representatives Standing Committee on Health, Aged Care and Sport *Inquiry into Approval Processes for New Drugs and Novel Medical Technologies* was tabled on 25 November 2021. The report's 31 recommendations address matters including the assessment process for new medicines, access to emerging treatments, and support for clinical trials for new medicines and technologies within Australia. The Government is currently in the process of responding to these recommendations.

The Government currently works with state and territory governments to consider new and emerging treatments through arrangements developed under Schedule C to the Addendum to the National Health Reform Agreement 2020-2025 (Long Term Health Reform Principles).

Under the *National Health Act 1953*, the Government may fund a medicine through the Pharmaceutical Benefits Scheme (PBS) if the Pharmaceutical Benefits Advisory Committee (PBAC), an independent and expert advisory body, makes a recommendation in favour of PBS listing.

When considering a medicine proposed for PBS listing, the PBAC is required to consider the clinical effectiveness (how well it works) and cost-effectiveness (value for money), compared with other available treatments.

The PBAC also takes into account whether the product has been approved by the Therapeutic Goods Administration (TGA), Australia's regulator of medicines. Medicines are not generally made available on the PBS to treat conditions for which they have not been approved by the TGA.

The Government has committed to list all medicines on the PBS following a positive recommendation by the PBAC.

The Australian Government's Specialist Training Program (STP) supports around seven per cent of specialist medical training in Australia, with the remainder of specialist training supported by state and territory governments and the private sector. Commencing on 1 January 2010, the STP funds extended training for specialist registrars into settings outside traditional metropolitan public teaching hospitals, including regional, rural and remote and private facilities. The program was developed to positively influence on future specialist medical workforce distribution, providing a contribution to trainee salary with state and territory government and/or the private sector meeting any residual trainee costs.

The STP funds 13 non-GP specialist medical colleges, including the Royal Australasian College of Physicians (RACP) which oversees the specialty of paediatric rheumatology. The Australian Government does not determine which subspecialties are allocated training positions under the STP – this is a matter for colleges. All posts approved for funding under the STP require approval of colleges, state and territory governments and the department.

Across 2022-2025, $708.6 million will be provided under the STP, supporting 920 fulltime equivalent (FTE) specialist training places and an additional 100 FTE places under the Integrated Rural Training Pipeline annually. All places are fully allocated across colleges.

Existing Rheumatology places under the STP

In 2020, 4.93 FTE places for rheumatology positions are funded under the STP. There are no specific paediatric rheumatology positions.

PARLIAMENTARY INQUIRY QUESTION ON NOTICE

Department of Health and Aged Care

Standing Committee on Health, Aged Care and Sport

Inquiry into Childhood Rheumatic Diseases

17 February 2022

PDR Number: IQ22-000030

Emerging treatments for childhood rheumatic diseases

Spoken

Hansard page number: 2

Member: Trent Zimmerman

Question:

CHAIR: The final question from me was about emerging treatments. Again, I'm not quite sure whether this is your area of expertise. I'm wondering whether the department is aware of emerging treatments that are not yet available in Australia.

Ms Wallbank: I'll have to take that one on notice, unfortunately. Sorry.

CHAIR: Okay, thank you.

Answer:

As part of the *Strategic Agreement in relation to reimbursement, health technology assessment and other matters*, the Commonwealth and Medicines Australia have agreed to share and develop greater insight into the new medicines, vaccines, and new and emerging technologies, coming through development pipelines, in order to facilitate faster access for Australian patients.

As pharmaceutical companies are in the best position to advise on emerging treatments in development, Medicines Australia committed to convene an annual forum with Government and the innovator medicines sector to:

- identify major therapeutic advances which may enter the regulatory or reimbursement systems (or both) over the following 18-24 months and which may represent a significant disruption in the treatment paradigm and/or require innovation in health care system planning, and
- understand the potential implications for the Commonwealth from the introduction of these advances in terms of resources, systems and processes.

The House of Representatives Standing Committee on Health, Aged Care and Sport *Inquiry into Approval Processes for New Drugs and Novel Medical Technologies* was tabled on 25 November 2021. The report's 31 recommendations address matters including the assessment process for new medicines, access to emerging treatments, and support for clinical trials for new medicines and technologies within Australia. The Government is currently in the process of responding to these recommendations.