### Project Title: Identifying CKD-specific therapeutic pathways for reducing CKD-related cardiovascular events in vitro

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**Host School / Institute:** Westmead Institute for Medical Research  
**Address:** 176 Hawkesbury Road, Westmead

**Certificates & Clearances required:** No

**Primary Supervisor:** A/Prof Natasha Rogers  
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**Co-Supervisor/team:** Dr Oshel Julovi (research scientist)

**Project Type:** Laboratory based

**Project Category:** Ageing; Bone

**Skills / Attributes of a successful student:** Students with prior laboratory experience will be at an advantage. However, prior experience is not a pre-requisite and students who are new to basic science research will be taught all the skills during their rotation. Students will be expected to be punctual with a desire to learn and develop their skills rapidly. No out-of-hours work is expected, but students will be supported if they wish to complete experiments in this manner. Students will be well-supported by the lab head and research scientist leading the project; other lab staff are always available for help or trouble-shooting.

**Project Keywords:** Chronic kidney disease; Osteoarthritis; Ageing

**Project Description:** Chronic kidney disease (CKD) has been reported to alter joint cartilage. Osteoarthritis (OA) patients have a high prevalence of renal disease. A recent clinical study reported that mean cartilage thickness is less in CKD patients than in controls, suggesting that patients with CKD are at increased risk for developing early knee osteoarthritis. The reasons for this comorbidity is not known. Despite the substantial morbidity and health costs attributed to osteoarthritis, no treatment has been approved to prevent or slow disease progression, largely because the underlying pathogenic mechanism remains elusive.

Most of the preclinical studies in the literature target single disease models to elucidate the pathogenesis of OA and CKD pathogenesis. To the best knowledge of our there are no preclinical models of combined disease in the literature. In order to overcome these limitations, it is important to develop new models that mimic the clinical scenario.

Thrombospondin-1 (TSP1) is a matrix protein. TSP1 binding to the receptor CD47 regulates cellular responses to injury or repair. TSP-1 is known to be present in cartilage, but detailed analysis in OA has not been reported. This project involves establishing a new model of CKD and OA in mice and testing the hypothesis that the protein thrombospondin-1 can alter the development of osteoarthritis. Students will work with supervisors who have expertise in these areas. You will learn many useful and transferable research skills including experimental design, standard molecular biology techniques (cell culture, western blot, PCR), basic laboratory bench work (ELISA, immunohistochemical staining), and data analysis. We will also be using cutting-edge micro-CT and MRI scanning to analyse joints in mice.

Students who generate data will be rewarded with co-authorship on any resulting publication. There are significant opportunities to develop and extend this topic into further projects suitable for MPhil or PhD work.