Principal Investigator
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Applicant Institution
Imperial College London, National Heart and Lung Institute, London

Application Number / Title
20342 - Biomarkers and mechanisms of cardiovascular side effects caused by COX-2 inhibitors

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Keywords
COX2, coxib, cardiovascular, NSAID

Application Lay Summary

1a: Nonsteroidal anti-inflammatory drugs (NSAIDs) are amongst the most commonly used medications including for arthritis. NSAIDs can also prevent ~50% of some cancers. However NSAIDs cause cardiovascular adverse events, estimated to result in 30,000-100,000 extra heart attacks and strokes each year in the UK. The concern surrounding NSAID-induced cardiovascular adverse events has led to an arrest in drug development, patient anxiety, cautious prescribing of COX-2 selective drugs and the withdrawal of celecoxib for the prevention of cancer. We aim to identify genetic biomarkers that can predict those susceptible to NSAID induced cardiovascular adverse events.

1b: The purpose of UK Biobank is 'to improve the prevention, diagnosis and treatment of a wide range of illnesses and to promote health throughout society'. Our research seeks to identify genetic biomarkers that predict cardiovascular adverse drug reactions in people taking these common anti-inflammatory pain medications. Cardiovascular adverse events are increased by around a third in people taking these drugs which impacts on people with (i) arthritis, (ii) heart disease and, because the medicine can prevent cancer, (iii) people at risk of cancer. In this way, our work is entirely in line with the stated purpose of UK Biobank.

1c: We will look for genetic variants that are different between people with arthritis taking NSAIDs that did or did not have heart attacks or strokes. To see if the differences in genotypes that we find are present in everyone that has heart attacks or strokes regardless of if they take these drugs, we will also assess these associations with genetic variants amongst people not taking NSAIDs. When these data sets are combined, we will be able to identify any genetic variants that specifically predict people are susceptible to cardiovascular side effects trigged by NSAID use.

1d: We are requesting genotyping data from the full cohort which will be analysed in the following groups:
(i) arthritis patients who report NSAID use who have had an acute myocardial infarction or stroke ~1,000 individuals.
(ii) arthritis patients who report NSAID use and who have NOT had an acute myocardial infarction or stroke ~40,000 individuals.
(iii) patients without arthritis or NSAID use but have had an acute myocardial infarction or stroke –~9,000 individuals.
(iv) patients without arthritis or NSAID use and who have NOT had an acute myocardial infarction or stroke ~450,000 individuals.