Opportunity 2017012

# Using n-3 DPA-derived Resolvins to Treat, Assess the Risk of, or Monitor Treatment of Cardiovascular Diseases

A novel therapeutic strategy, using n-3 DPA-derived resolvins to treat or prevent cardiovascular disease. Using patient samples, it was demonstrated that N-3 DPA-derived resolvins reduce leukocyte and platelet activation. Furthermore, due to the negative correlation found between plasma and immune cell activation, n-3 DPA-derived resolvins can be used to assess the risk of cardiovascular diseases and the efficacy of therapeutic treatments.

## Background

Specialised pro-resolving mediators (SPM) are molecules produced by leukocytes that play a key role in counter-regulating inflammation and promoting the resolution of inflammatory responses. n-3 docosapentaenoic (DPA)-derived resolvins are a class of SPMs crucial for cardiovascular health, shown to reduce the activation of platelets and leukocytes thereby decreasing the formation of platelet-leukocyte aggregates. Platelet-leukocyte aggregates play a significant role in cardiovascular disease (CVD) and reducing their activation can help maintain vascular integrity and prevent the excessive activation of immune cells in response to inflammatory stimuli.

## The Problem

Circadian rhythms play a key role in regulating various physiological functions, including cardiovascular health and the immune system. There is evidence linking disturbances in circadian responses to inflammatory conditions, including myocardial infarction, and platelet activation is shown to be at its peak during the early morning hours, potentially increasing the risk of thrombosis. Recent studies have shown that N-3 DPA-derived resolvins are also regulated in a diurnal manner and are markedly altered in patients at risk of myocardial infarct.

## Invention: Benefits & Application

QMUL researchers have developed a method for assessing a patient's risk of cardiovascular disease, including myocardial infarction, related to an inadequate control of platelet and leukocyte activation. The method involves assessing the levels of multiple N-3 DPA-derived resolvins in biological samples, particularly in the early morning. This is based on research which showed a significant negative correlation between plasma N-3 DPA-derived resolvins and markers of platelet, monocyte and neutrophil activation. Our researchers showed that incubation of N-3 DPA-derived resolvins with peripheral blood from healthy volunteers and patients with CVD significantly (and dose-dependently) decreased platelet and leukocyte activation (Figure 1). These results provide evidence that higher levels of N-3 DPA-derived resolvins may help mitigate excessive immune cell activation and reduce the risk of cardiovascular events. This can allow for patient stratification and researchers to tailor treatments or interventions to specific patient groups.

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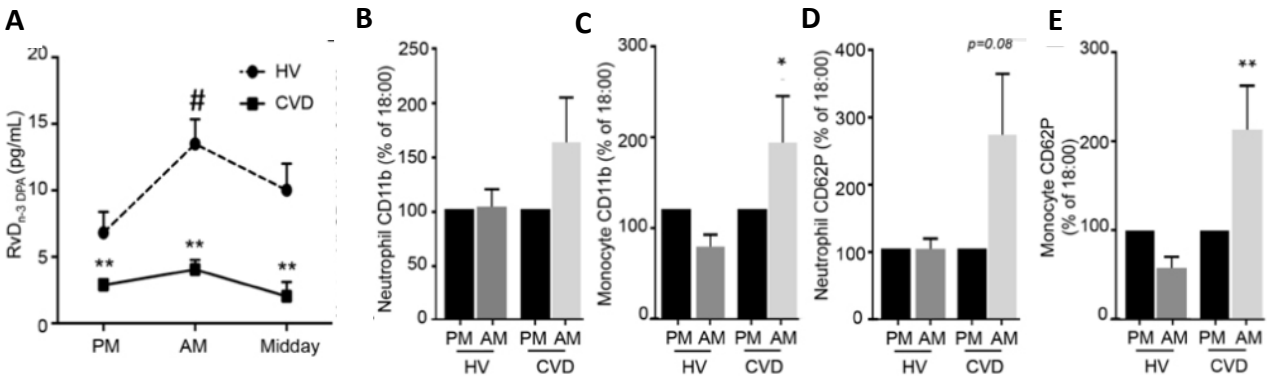


**n-3 DPA-derived SPM are reduced and leukocyte activation is increased in patients with CVD**

Peripheral blood was collected for healthy volunteers (HV) and patients diagnosed with cardiovascular disease (CD) (A) Plasma RvDn-3 DPA concentrations were markedly decreased in CVD patients. (B-C) CVD patients had an increase in the expression of CD11b on both neutrophils and monocytes (D-E) CVD patients had an increase in increases in platelet-neutrophil and platelet-monocyte aggregates.

A similar approach, in which the levels of multiple N-3 DPA-derived resolvins in patient samples are determined at differing time points throughout the day, can be utilised to assess the efficacy of therapeutic treatments for cardiovascular diseases. The observed negative correlation between plasma N-3 DPA-derived resolvins and immune cell activation markers provides a potential biomarker for assessing the effectiveness of preventative treatments targeting cardiovascular disease. This method can identify therapies designed to elevate these specialized pro-resolving lipid mediators that could be valuable in reducing the risk of cardiovascular events, such as myocardial infarction.

## Patent

A patent has been filed in UK, USA, Europe and Japan.
Patent application: WO 2019/057756 A1

## Lead Inventor

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## Publications

Impaired Production and Diurnal Regulation of Vascular RvDn-3 DPA Increases Systemic Inflammation and Cardiovascular Disease.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5924694/

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