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## **First Contact Initiative Grant: Report**

To the ESC Council on Basic Cardiovascular Science,

I would like to start this report by sincerely thanking the ESC Council on Basic Cardiovascular Science for providing me with the First Contact Initiative Grant in 2020. I feel honored to receive this award as it gave me the opportunity to join the Liverpool Centre for Cardiovascular Science under the supervision of Professor Gregory Lip during 2021.

During this period, I had the pleasure to establish a fruitful collaboration with one of the main leaders in several cardiovascular diseases worldwide, and take part of an institution with wide experience in translational research, which has allowed me to improve my skills in the cardiovascular field overall.

Initially, we published a short report showing that citrate samples may be used for the determination of GDF-15 in AF given the positive and good correlation with EDTA and serum matrices. This should be the first step for starting a project on GDF-15 but the hard impact of COVID-19 during 2021 made impossible to carry out such a project. However, one of the most important goals of the First Contact Initiative Grant was to establish a collaboration and research network with international colleagues and this has been successfully completed. Hence, my stay in the Liverpool Centre for Cardiovascular Science with Professor Lip allowed me to lead and participate in other projects in the field of biomarkers for risk prediction in atrial fibrillation (AF) and COVID-19.

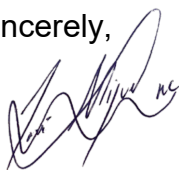
For example, in one of the papers published together with Prof. Lip, we showed that the ABC-stroke and ABC-bleeding scores had similar predictive ability for outcomes beyond stroke and bleeding in AF patients, including myocardial infarction, acute heart failure, a composite of cardiovascular events,

and all-cause deaths. We can therefore conclude that many biomarkers are non-specific and predict “sick” patients or poor prognosis overall. In another study, we demonstrated that high particulate matter 10 (PM<sub>10</sub>) and low temperature were associated with increased risk of ischemic stroke, cardiovascular events, major bleeding and mortality in AF patients. These markers should be considered also when assessing the risk of worse clinical outcomes in AF and during decision-making process. Finally, we published an interesting review about the role of gut microbiota on the quality of oral anticoagulation with vitamin K antagonists (VKAs). We suggested that the potential effects of gut microbiota may be mediated first, by an indirect effect of metabolites produced by gut microbiota in the availability of VKAs; second, by an effect of vitamin K-producing bacteria; and finally, by the structural modification of the molecules of VKAs.

However, the emergence of COVID-19 and its relationship with thromboembolic events motivated our interest in this disease. Thus, we worked in a couple of studies showing that, on the one hand, previous direct-acting oral anticoagulant (DOAC) therapy at time of COVID-19 diagnosis was not associated with improved clinical outcomes or lower hospitalization/re-hospitalization rate compared to patients not taking oral anticoagulants; and on the other hand, in COVID-19 outpatients with cardiometabolic diseases, prior use of DOAC therapy compared to VKA therapy at the time of COVID-19 diagnosis demonstrated lower risk of arterial or venous thrombotic outcomes, without increasing the risk of bleeding.

I would like to express again my gratitude to the ESC Council on Basic Cardiovascular Science for this opportunity and to all Liverpool Centre for Cardiovascular Science members for their kind help and reception. Particularly, I would like to thank Prof. Gregory Lip for his predisposition and assistance during this process. For sure we will continue working together on several projects, and this is just the beginning of a fantastic journey.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'José Miguel Rivera Caravaca', with a stylized flourish at the end.

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