PhD Programme in Molecular and Experimental Medicine

Research Topic

Title:

Role of platelet heterogeneity and platelet-leukocyte interactions in coronary syndrome

Principal Investigator and Supervisor:	Prof. Condorelli Gianluigi
Research Supervisor:	Dr. Dario Bongiovanni
Department:	Biomedical Sciences
Disciplinary Sector:	Cardiovascular diseases

Abstract

Platelets play a key role in vascular homeostasis and in non-hemostatic fields, including immune response, tumor progression and other nonvascular diseases. Human platelets are a heterogeneous cell population differing with respect to their size, surface receptor expression, granule density and RNA-content. Recently, attention raised on a distinct pro-thrombotic subgroup of platelets: the immature or reticulated platelets (RPs). RPs are young, hyper-reactive platelets that are larger and contain more RNA compared to older platelets. RPs have emerged as promising biomarkers but the reason for their intrinsic hyper-reactivity and their association with ischemic adverse events is unknown as the biology of RPs still needs to be elucidated. Moreover, platelet-leukocyte aggregates (PLAs), which participate in cardiovascular diseases and are increased in acute and chronic coronary syndromes, could also be a potential marker of platelet activity, for monitoring antiplatelet therapy and possible predictors of adverse events. However, knowledge concerning the pathophysiology of PLAs is limited and further studies and methods are needed to shed light on PLAs role in cardiovascular disease.

Humanitas University
Via Rita Levi Montalcini 4
20090 Pieve Emanuele (Milano) Italy
Tel +39.02.8224.1 - Fax +39.02.8224.2394
info@hunimed.eu
Website: www.hunimed.eu
C.F. 97692990159

The main purpose of our project is to investigate the biomolecular features and heterogeneity of platelet, leukocyte, and platelet-leukocytes aggregates in coronary artery disease. Specifically, we aim to characterize the expression phenotype of the prothrombotic platelet subgroup defined as Reticulated Platelets, and to determine which cell subpopulations are more prominent in coronary artery disease and whether they correlate with the disease and inflammatory state, or prothrombotic states which could increase the risk for major adverse cardiovascular events in coronary syndromes. To achieve this, we will employ a range of experimental techniques, including fluorescence-activated cell sorting (FACS), mass cytometry, single-cell RNA sequencing, and platelet function testing. To facilitate the research, the successful candidate will spend up to 18 months in a laboratory in Germany to gain access to specialized equipment and expertise in platelet biology.

Our experimental design will provide a detailed characterization of platelet and leukocyte subpopulations and will allow us to identify potential biomarkers and therapeutic targets in coronary artery disease.

Main Technical Approaches to carry out the present project:

- Peripheral Blood handling and analysis
- FACS/Sorting
- RNA Isolation
- RNA-sequencing
- Single-cell RNA-Sequencing
- Mass Cytometry/Time of flight mass cytometry
- Platelet Function Testing

Scientific References related to the project:

Immature Platelet Fraction Predicts Adverse Events in Patients With Acute Coronary Syndrome: the ISAR-REACT 5 Reticulated Platelet Substudy.
Bongiovanni D, Schreiner N, Gosetti R, Mayer K, Angiolillo DJ, Sibbing D, Holdenrieder S, Anetsberger A, von Scheidt M, Schunkert H, Laugwitz KL, Schüpke S, Kastrati A, Fegers-Wustrow I, Bernlochner I.
Arterioscler Thromb Vasc Biol. **(ATVB)** 2022 Dec 22. doi: 10.1161/ATVBAHA.122.318614. Online ahead of print.

Role of Reticulated Platelets in Cardiovascular Disease
D Bongiovanni, J Han, M Klug, K Kirmes, G Viggiani, M von Scheidt, N Schreiner, G Condorelli, KL Laugwitz and I Bernlochner
ATVB, 24 Mar 2022, Ahead of print, doi: 10.1161/ATVBAHA.121.316244

Mass cytometry of platelet-rich plasma: a new approach to analyze platelet surface expression and reactivity
M. Klug, K. Kirmes, J. Han, O. Lazareva, M. Rosenbaum, G. Viggiani, M. von Scheidt, J. Ruland, J. Baumbach, G. Condorelli, K-L Laugwitz, M. List, I. Bernlochner and **D. Bongiovanni**
Platelets 2021, Dec 27:1-8. doi: 10.1080/09537104.2021.2009453. Online ahead of print.

Humanitas University
Via Rita Levi Montalcini 4
20090 Pieve Emanuele (Milano) Italy
Tel +39.02.8224.1 - Fax +39.02.8224.2394
info@hunimed.eu
Website: www.hunimed.eu
C.F. 97692990159

SARS-CoV-2 infection is associated with a pro-thrombotic platelet phenotype
D Bongiovanni, M Klug, O Lazareva, S Weidlich, M Biasi, S Ursu, S Warth, C Buske, M Lukas, C Spinner, M von Scheidt, G Condorelli, J Baumbach, KL Laugwitz, M List and I Bernlochner
Cell Death & Disease 2021 12, 50. https://doi.org/10.1038/s41419-020-03333-9

Sorting and magnetic-based isolation of reticulated platelets from peripheral blood
I Bernlochner, M Klug, D Larasati, M Von Scheidt, D Santovito, M Hristov, C Weber, K-L Laugwitz
& D Bongiovanni
Platelets 2020 Feb 11:1-7. doi: 10.1080/09537104.2020.1724923.

Transcriptome Analysis of Reticulated Platelets Reveals a Prothrombotic Profile.
Bongiovanni D, Santamaria G, Klug M, Santovito D, Felicetta A, Hristov M, von Scheidt M, Aslani M, Cibella J, Weber C, Moretti A, Laugwitz KL, Peano C, Bernlochner I.
Thromb Haemost. 2019 Nov 1, 119(11), 1795-1806, doi: 10.1055/s-0039-1695009.

Humanitas University
Via Rita Levi Montalcini 4
20090 Pieve Emanuele (Milano) Italy
Tel +39.02.8224.1 - Fax +39.02.8224.2394
info@hunimed.eu
Website: www.hunimed.eu
C.F. 97692990159