Medical University of Graz

Pregnancy-primed platelets

Summary

Martin Gauster, Gottfried Schatz Research Center, Division of Cell Biology, Histology and Embryology, Medical University of Graz, Austria

Supervisor:	PD Dr. Martin Gauster
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between August 03, 2022 00:00 and September 20, 2022 23:59 (Europe/Zurich)

Description

Background:

Platelets are small, discoid-shaped blood circulating cells, which originate from megakaryocytes in the bone marrow, with a life span of eight to ten days in the circulation before they are finally degraded in the spleen, liver and lung. Despite their importance in hemostasis, wound healing and tissue regeneration, inappropriate activation of platelets is associated with various pathologies, including thrombosis, inflammation, diabetes, and cancer. Recently, aberrant RNA- and protein profiles have been described for platelets under pathological conditions, including cardiovascular disease and solid tumors [1]. In the latter case, platelets modify their content and function in response to local or systemic signals from the tumor tissue, which led to the recently proposed concept of tumor-educated platelets (TEPs) [2,3].

In human pregnancy, circulating maternal platelets leave the endothelium-lined maternal vasculature during their passage through the placenta, where they come in contact with fetal epithelial-like trophoblasts at the placental barrier [4]. There, activation and subsequent release of granules-stored mediators can seriously affect the fine-balanced immune-cross talk at the maternal fetal interface [5–8]. However, they may also get primed by the placental milieu, i.e. the trophoblast and/or its derived mediators, and thereby may get adapted to pregnancy when returning into maternal vasculature. Based on the concept of TEPs, it is tempting to speculate that maternal platelets get primed to ongoing pregnancy either through direct transfer and storage of placenta-derived vesicles and biomolecules, placenta-induced alterations in platelet RNA processing, and/or altered platelet production by megakaryocytes in the maternal bone marrow and lung niche.

Hypothesis and Objectives:

In this project the hypothesis will be tested whether placenta-derived vesicle- and biomolecule sequestration by maternal platelets can affect their transcriptome- and proteome landscape. Moreover, placental endocrine communication with the bone marrow and its impact on the transcriptional profile of megakaryocytes and generation of platelet subpopulations will be studied. Finally, the hypothesis will be tested whether or not placenta-associated pregnancy pathologies such as preeclampsia involve abnormal priming of maternal platelets into distinct subpopulations.

Methodology:

Beside standard molecular biology techniques and conventional cell culture, the candidate will be trained in human placental explant culture, trophoblast-platelet co-culture, fluidic flow culture of cells and tisse, isolation of human platelets and rodent megakaryocytes.

References:

[1] A. Supernat, M. Popeda, K. Pastuszak, M.G. Best, P. Gresner, S.I. Veld, B. Siek, N. Bednarz-Knoll, M.T. Rondina, T. Stokowy, T. Wurdinger, J. Jassem, A.J. Zaczek, Transcriptomic landscape of blood platelets in healthy donors, Scientific Reports. 11 (2021) 15679-z. https://doi.org/10.1038/s41598-021-94003-z [doi].

[2] S.G.J.G. In 't Veld, T. Wurdinger, Tumor-educated platelets, Blood. 133 (2019) 2359–2364. https://doi.org/10.1182/blood-2018-12-852830 [doi].

Medical University of Graz

[3] M.G. Best, N. Sol, I. Kooi, J. Tannous, B.A. Westerman, F. Rustenburg, P. Schellen, H. Verschueren, E. Post, J. Koster, B. Ylstra, N. Ameziane, J. Dorsman, E.F. Smit, H.M. Verheul, D.P. Noske, J.C. Reijneveld, R.J.A. Nilsson, B.A. Tannous, P. Wesseling, T. Wurdinger, RNA-Seq of Tumor-Educated Platelets Enables Blood-Based Pan-Cancer, Multiclass, and Molecular Pathway Cancer Diagnostics, Cancer Cell. 28 (2015) 666–676. https://doi.org/10.1016/j.ccell.2015.09.018.

[4] J. Guettler, D. Forstner, G. Cvirn, S. Maninger, B.A. Brugger, O. Nonn, N. Kupper, E. Pritz, S. Wernitznig, G. Dohr, H. Hutter, H. Juch, B. Isermann, S. Kohli, M. Gauster, Maternal platelets pass interstices of trophoblast columns and are not activated by HLA-G in early human pregnancy, Journal of Reproductive Immunology. 144 (2021) 103280. https://doi.org/S0165-0378(21)00010-3 [pii].

[5] D. Forstner, J. Guettler, M. Gauster, Changes in Maternal Platelet Physiology during Gestation and Their Interaction with Trophoblasts, International Journal of Molecular Sciences. 22 (2021) 10.3390/ijms221910732. https://doi.org/10732 [pii].

[6] J. Guettler, D. Forstner, M. Gauster, Maternal platelets at the first trimester maternal-placental interface - Small players with great impact on placenta development, Placenta. (2021). https://doi.org/S0143-4004(21)00658-5 [pii].

[7] G. Moser, J. Guettler, D. Forstner, M. Gauster, Maternal Platelets-Friend or Foe of the Human Placenta?, International Journal of Molecular Sciences. 20 (2019) 10.3390/ijms20225639. https://doi.org/E5639 [pii].

[8] D. Forstner, S. Maninger, O. Nonn, J. Guettler, G. Moser, G. Leitinger, E. Pritz, D. Strunk, K. Schallmoser, G. Marsche, A. Heinemann, B. Huppertz, M. Gauster, Platelet-derived factors impair placental chorionic gonadotropin beta-subunit synthesis, Journal of Molecular Medicine (Berlin, Germany). 98 (2020) 193–207. https://doi.org/10.1007/s00109-019-01866-x [doi].