

Joint Meeting of the Austrian Neuroscience Association (16th ANA Meeting) and the Austrian Pharmacological Society (25th Scientific Symposium of APHAR) Innsbruck, 25–27 September 2019

MEETING ABSTRACT

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A role for platelets in Alzheimer's disease?

Diana M. BESSA DE SOUSA^{1,2,*}, Kathrin M. KNIWALLNER^{1,2},
Michael S. UNGER^{1,2}, Heike MROWETZ^{1,2}, Christian HUMPEL³,
Bettina M. FOIDL³ and Ludwig AIGNER^{1,2}

¹Institute of Molecular Regenerative Medicine, Paracelsus Medical University, Salzburg, Austria; ²Spinal Cord Injury and Tissue Regeneration Center Salzburg (SCI-TReCS), Paracelsus Medical University, Salzburg, Austria; ³Laboratory of Psychiatric and Experimental Alzheimer's Research, Department of Psychiatry and Psychotherapy, Medical University of Innsbruck, Austria

Background: Alzheimer's disease (AD) is a neurodegenerative disease and the most common form of dementia. It is largely recognized that AD is a multifactorial and complex pathology, but its exact aetiology remains elusive. In the last years, increasing evidence suggests that platelets might contribute to AD pathology, particularly in the onset and development of cerebral amyloid angiopathy (CAA). Nevertheless, it remains unclear whether platelets might as well have a role in AD independent of CAA. To better comprehend the potential involvement of platelets in AD pathology, we investigated the spatial distribution of platelets within the brain as well as the activation status and morphology of circulating platelets in APP Swedish PS1 ΔE9 mice (APP-PS1), an AD transgenic mouse model with a severe amyloid plaque formation but no CAA pathology.

Methods: Platelet spatial location in relation to cerebral blood vessels was assessed by immunohistochemistry in brain tissue of 14-months-old APP-PS1 mice and wild-type (WT) age-matched control animals. Characterization of platelet morphology and activation status was performed in blood isolated platelets by transmission electron microscopy and flow cytometry, respectively.

Results: In APP-PS1 mice, a significantly higher percentage of platelets was observed outside the cerebral blood vessels in comparison with WT age-matched controls. In the brain, APP-PS1 platelets displayed typical features of platelet activation, *i.e.* expression of CD62P activation marker and membrane elongations, and were observed in tight interaction with astrocytes. Importantly, platelets in the bloodstream of APP-PS1 mice were already activated. Moreover, compared to WT platelets, APP-PS1 circulating platelets had significantly smaller surface area and presented abnormalities at the ultrastructural level, showing a trend towards an enlarged open canalicular system (OCS).

Discussion: These results demonstrate that platelets in the context of AD are activated, extravasate and invade the brain. Whether platelets have a beneficial or a detrimental function in AD brains remains completely unknown, but these findings certainly provide a base for future developments.

Acknowledgements: This study was supported by the Austrian Science Fund (P24734-B24), the PMU Rise Project (PMU-FFF) (R17/04/097-KNI) and the PMU postgraduate students support program DISCITE! (D-19/01/008-BES).

Keywords: platelets – Alzheimer's disease – ageing – vascular pathology

*Corresponding author e-mail: diana.bessa@pmu.ac.at