A104 TRANSIENT RECEPTOR POTENTIAL (TRP) CHANNELS CONTRIBUTE TO NEUTROPHIL CHEMOTAXIS DURING THE INFLAMMATORY RESPONSE

O Lindemann,[1] D Umlauf,[2] S Mally,[1] J Bertrand,[2] A Fabian,[1] A Dietrich,[3] A Schwab,[1] T Pap[2] *[1]Institute of Physiology II, University of Münster, Germany; [2]Institute of Experimental Musculoskeletal Medicine, University of Münster, Germany; [3]Institut for Pharmacology and Toxicology, Philipps-University Marburg, Germany*

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Objective Neutrophils (polymorphonuclear leucocytes; PMNs) are one of the earliest cell types to be observed within diseased joints in rheumatoid arthritis and possess a considerable capacity to evoke tissue damage. The recruitment of PMNs to inflamed joints involves a sequence of complex cellular events including directed chemotaxis to the inflammatory site. Owing to the crucial role of Ca^{2+} transients in chemotactic signalling and responses, the authors assessed the role of the potential Ca^{2+} entry channels TRPC1 and TRPC6, members of the transient receptor potential (TRP) channel family, in PMN chemotaxis.
Methods For experiments addressing the impact of TRP channel knockout on PMN migration, the authors used primary neutrophils from both TRPC1- and TRPC6-deficient mice. Neutrophils from the bone marrow of 8-week-old mice were purified by density gradient centrifugation. Chemotaxis was performed in three-dimensional collagen I matrices (2.5 mg/ml) on fibronectin coated (1 µg/cm^2) microslides and quantified by time-lapse videomicroscopy. PMN migration was elicited using gradients of either N-formyl-methionyl-leucyl-phenylalanine (fMLP) or a cell-free inflammatory exudate obtained from acute phases of mice peritonitis.
Results In three-dimensional collagen matrices, TRPC6-deficient PMNs exhibited reduced chemotaxis along an inflammatory exudate gradient. Time-lapse videomicroscopy analyses also revealed decreased migration velocity and translocation of these PMNs. However, their chemotaxis towards fMLP was not affected by the lack of TRPC6. PMNs from TRPC1-deficient mice showed reduced chemotaxis in fMLP gradient assays. In addition, they exhibited diminished migration velocity and translocation in the time-lapse videomicroscopy-based analyses.
Conclusion The reduced migratory capacity of TRPC knockout PMNs in the different chemotaxis assays indicates a contribution of both TRPC1 and TRPC6 to chemotactic signalling pathways of murine neutrophils. Further investigations will lead to a better understanding of their role in cell migration and may provide new therapeutic strategies for the treatment of inflammatory diseases such as rheumatoid arthritis.

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