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In search for mediators of dendritic cell recruitment to the cornea during inflammation

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Purpose: Dendritic cells play an important role in the immune response in cornea in inflammation as well as in graft rejection. It has been previously shown by other groups that there is a clear correlation between corneal vascularization and graft rejection. Corneal vasculature mediates the recruitment of leukocytes to corneal surface by interactions between adhesion molecules on leukocytes and on endothelial cell on vascular beds. We have previously shown the recruitment of Cs to the cornea is partially mediated by vascular cell adhesion molecules (VCAM)-1 and P-selectin. In this study we showed the contribution of MAdCAM-1, a molecule previously not described on the ocular surface, is another molecular target mediating DC homing to cornea.

Methods: We studied the rolling and adhesion behaviour of fluorescently-labeled DCs, adoptively transferred to BALB/c mice by intravital microscopy (IVM, 500 Mikron Instruments) in steady state and in inflammation in vivo. To study the contribution of MADCAM to the recruitment behaviour of DCs in corneal vasculature, anti-MAdCAM-1 blocking antibody or controls antibody were injected intravenously (i.v.) 30 minutes before IVM recordings. Homing (recruitment) of DC to normal or inflamed corneas were studied by ex vivo. Also, 24 hours after i.v. injection of fluorescently-labeled DC, recruitment were studied by confocal microscopy (Olympus Fluoview 1000) of the corneas.

Results: While VCAM-1 and P-selectin contributed partially to the recruitment of DCs to the corneal vasculature, MAdCAM-1 is found to be an important candidate target regulating recruitment to the corneal surface. MAdCAM-1 significantly reduced the rolling fraction (4.1 % vs. controls (20.7%; $p<0.001$)) and the sticking of DCs (0.4% vs. (3.4%; $p<0.001$) in inflamed corneas as compared to controls. This effect of MAdCAM on DC recruitment was further supported by the blockade of anti-MAdCAM-1 (18.4 cells/mm2; $p=0.005$) or its ligand $\alpha4\beta7$ (4.5 cells/mm2; $p=0.003$), $\alpha4$ (12.1 cells/mm2, $p=0.032$) and $\beta7$ (3.2 cells/mm2, $p=0.007$), treatment showing significant reduction of DC homing to the inflamed cornea as compared to controls (51.5 cells/mm2). This effect was supported by studying $\alpha4\beta7$ and L-selectin expression on CD11c-high DC population by flow cytometry.

Conclusions: Our study demonstrated, for the first time that MAdCAM-1 played a role in leukocyte recruitment to the cornea through limbal vessels in inflamed corneas. MAdCAM 1 might be a good candidate as a new molecular target for pharmacological intervention for conducting leucocyte recruitment in response to inflammation in cornea.

Biography

Aslihan Turhan is a PhD in Immunology. Worked as an Instructor at Harvard Medical School in Surgery department and in Ophthalmology department. Dr. Turhan is currently serving as an assistant professor in Gaziantep University, Medical School, Turkiye. During her studies in MSSM and in HMS she designed live imaging techniques for intravital imaging of cremaster muscle, colonic mucosa and cornea. She is an expert in cell trafficking, inflammation and imaging. Dr. Turhan is experienced in target identification for drug development, in inflammatory conditions and intravascular cellular interactions. Her primary interests are cell-cell interactions in response to inflammation, target identification for drug development for manipulating cell trafficking. She has identified targets for cellular interactions in sickle cell disease and DC trafficking in cornea in response to inflammation. Her work on sickle cell disease is currently in clinical trial. Dr. Turhan has published in peer-reviewed journals, is in editorial board of Journal of Infectious Diseases and Therapy. She has patent applications for treatment approaches in sickle cell disease and corneal inflammation.

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