Functional differences between human CR3 (CD11b/CD18) and CR4 (CD11c/CD18): CD11b dominates iC3b mediated phagocytosis, while CD11c prevails adherence

Sándor N.[1], Lukácsi Sz.[2], Salánki R.[3], Orgován N.[4], Szabó B.[3], Horváth R.[4], Erdei A.[1,2], Bajtay Zs.[2]

1 MTA-ELTE Immunology Research Group, Budapest, Hungary

2 ELTE TTK Institute of Biology Department of Immunology, Budapest, Hungary

3 ELTE TTK Institute of Physics Department of Biological Physics, Budapest, Hungary

4 MTA TTK Nanobiosensorics "Lendület" Group, Budapest, Hungary

Complement receptors CR3 (CD11b/CD18) and CR4 (CD11c/CD18) belong to the family of beta2 integrins and are expressed by several, mainly myeloid cell types in humans. Their function is to mediate iC3b opsonized phagocytosis and adherence to ICAM-1 and fibrinogen. These functions were so far analysed under experimental conditions, where the contribution of CD11b/CD18 and CD11c/CD18 could not be separated. Although very little is known about the features of CR4, it is supposed that the two integrins exert similar functions, since they bind the same ligands. From an evolutionary aspect however it does not seem rewarding to maintain two receptors with similar ligand specificity for the same functions. Therefore our goal is to reveal what separate functions might be exerted by CR3 and CR4

We used both classical and high throughput label free optical biosensor and single cell analysis methods to decipher the distinct role of CD11c. Previously we demonstrated that on human monocyte-derived dendritic cells (MDCs) CD11b is responsible for iC3b mediated phagocytosis, while CD11c is dispensable. In our recent work we analysed how CD11b and CD11c participate in adherence to their ligands. We employed human monocytes, monocyte-derived macrophages (MDMs) and MDCs which highly express CR3 and CR4 and adherence is their natural property.

First we determined the exact number of CD11b and CD11c on these cell types by a bead based technique, and found that the ratio of CD11b/CD11c is 1.2 for MDCs, 1.7 for MDMs and 7.1 for monocytes, suggesting that CD11c is most important for MDCs and less for monocytes. By analyzing the kinetics and force of adherence of the different cell types to immobilized fibrinogen ligand, we found that attachment of MDCs is stronger than that of monocytes. Using antibody blocking and RNA silencing techniques we proved that adherence to fibrinogen – the common ligand of CR3 and CR4 – is mediated by CD11c. When we previously analyzed iC3b mediated phagocytosis, we found that blocking CD11c does not impair this function. In contrast to this, in the case of adherence, we found that blocking CD11b even enhances attachment to fibrinogen, suggesting a competition between CD11b and CD11c for this ligand.