Dynamic regulation and differential compartmentaliztion of C-type lectin receptors in the dendritic cell membrane

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Dendritic cells (DCs) are important antigen-presenting cells in the immune system. They are responsible for the recognition and internalization of pathogens, followed by the induction of antigen specific $CD4^+$ and $CD8^+$ T cell responses, but also for the maintenance of peripheral T cell tolerance. DCs express a variety of endocytic receptors such as C-type lectin receptors (CLRs), which are important for the defense against invading pathogens. CLRs are able to bind and internalize a variety of different pathogens, which can then lead to DC maturation (activation and migration). These receptors are potential candidates for immunomodulatory therapeutic intervention as the delivery of chimeric antigen-targeting antibodies to such receptors (e.g. DEC205 or DCIR) induced strong $CD4^+$ and $CD8^+$ T cell responses (Dudziak et al., 2007, Neubert et al., 2014). Here, we want to further investigate the distinct antigen uptake and presentation properties of the most common antigen-targeting receptors DEC205 and DCIR. In multi-color confocal microscopy (up to 6 different fluorochromes) of human monocyte-derived DCs (moDC) we found that the receptors DEC205 and DCIR demonstrated a distinct and mutually exclusive distribution in the membrane. This expression pattern might indicate that recognition and uptake of pathogenic material into endosomal compartments might not only be directed by the endocytic receptor itself, but also by the localization of the receptor in the membrane of a phagocytic active cell. To further elucidate if this spatial distribution might be valid also for other receptors, we have tested the mannose receptor MMR as well as DC-SIGN and found that MMR showed a similar profile than DCIR while DC-SIGN was only partially overlapping with DEC205, DCIR, or MMR. In order to obtain a more detailed picture of the biological cell environment of the receptors, we investigated the lipid composition of moDCs within Lipidomics and lipid packing imaging. Interestingly, the membrane of immature moDCs is more ordered than of mature moDCs. This finding could also be confirmed with our Lipidomics results. Furthermore, mature moDCs express higher levels of di- and triacylglycerides, which is important for activation of the cells and signaling pathways (Cantrell et al., 2015).