Role of membrane lipids in the organization of TCR dimers

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Summary

The TCR is a multiprotein complex, which forms nanoclusters independently of antigen binding. However, the mechanism of primary TCR clustering is poorly understood. We showed that the monomeric TCR dimerizes upon integration into liposomes composed of PC, cholesterol and SM, whereas in liposomes of binary mixtures or PC the TCR stays monomeric. Both in liposomes and giant plasma membrane vesicles the TCR was localized in the liquid ordered domain. We found that the TCR specifically interacts with cholesterol through its TCRβ subunit. Moreover, cholesterol extraction from the plasma membrane and from purified TCR disrupted the TCR nanoclusters. We propose a novel model for transmembrane protein clustering; a liquid ordered islet arises upon the binding of cholesterol and SM to the transmembrane region of TCRβ. Consequently, TCR dimerization is energetically favourable as it shields the liquid ordered islet from the surrounding liquid disordered phase.