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The tight junction plague a dynamic condensate for sequestering effector proteins.

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Tight junctions form a border between the apical and basolateral plasma-membrane domains and are linked to the machinery that controls apicobasal polarization. This achieved by adhesion/polymerization of the claudin protein family and the interactions with the scaffold proteins on the cytoplasmic side. The main proteins family in the scaffold is the MAGUK family, especially the zona occludens proteins (ZO) which play a key role in the tight junction formation and establishment cellular polarity but it is still unclear how the ZO proteins are involved in this process. We discovered a possible molecular basis of tight junction formation and sequestering of interaction partners to the tight junction. We could show ZO proteins can undergo condensation into dynamic liquid condensates in vitro and in vivo. This condensed ZO scaffold recruits efficiently interaction partners via ZO multiple protein-protein interaction domains which have a low affinity towards their interactions partners. Our findings provide a new molecular function inside for the complex structure of ZO-proteins. It can explain the supra-molecular structure and function of the tight junction as a self-organization process which has a direct impact in the role of the tight junction in cell polarity.

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