IQGAP-related protein IqgC involved in large-scale endocytosis regulates cell-substratum adhesion and migration in Dictyostelium

P-02.5-12

L. Mijanović[I], D. Putar[I], V. Filić[I], I. Weber[I]

[I]Ruder Boškovic Institute, Division of Molecular Biology, Zagreb, Croatia

The same building blocks and regulatory modules of the actin cytoskeleton are often utilized by the cell to perform multiple functions, but how their use is balanced between often competing processes is not well understood. Involvement of small GTPases from the Ras superfamily in the regulation of a variety of cellular processes, e.g. cell migration, large-scale endocytosis, cell division, and membrane trafficking, is a case in point. In *Dictyostelium* amoeba and other cells, Ras GTPases regulate the formation of transient actin-based assemblies such as pseudopodia, filopodia, ruffles and endocytotic cups by alternating between inactive (GDP-bound) and active (GTP-bound) forms. Thereby, they are primarily deactivated by GTPase-activating proteins RasGAPs. We recently characterized an untypical IQGAP-related protein from *Dictyostelium*, IqgC, as a RasG-specific GAP. Furthermore, we showed that IqgC localizes to macropinosomes and phagosomes and supresses RasG signaling during macropinocytosis and phagocytosis. Since it has been suggested that macropinocytosis and cell migration are negatively correlated, we proceeded to check whether IqgC has an effect on cell migration. Indeed, we determined that the speed of migration is positively correlated with overexpression of IqgC, which is exactly opposite to what we have previously shown for macropinocytosis. Interestingly, IqgC-null cells displayed a strongly diminished strength of the cell-substratum adhesion, as shown in a detachment assay using a rotary shaker. Consistent with this finding, TIRF microscopy showed that fluorescently labelled IqgC is localized to the stationary puncta at the ventral plasma membrane, which are known to harbour other proteins involved in cell-substratum adhesion such as talin and paxillin. Since RasG has previously been shown to positively regulate cell adhesion, our results indicate that IqgC regulates cell adhesion via a mechanism independent of its RasG-GAP activity.