**Membrane elasticity and polymerization energy modulate the shape of spherical clathrin coats**

Mohammed Saleem

Department of Life Science, National Institute of Technology, Rourkela, India- 769008 email: saleemm@nitrkl.ac.in

Clathrin mediated endocytosis is the most widely used means of vesicular trafficking and membrane bending is the first step involved, believed to be facilitated by clathrin polymerization. The polymerization of clathrin is thought to force the membrane to adopt the shape of the clathrin coat by scaffolding mechanism. However the variety of clathrin lattice shapes found in vivo has challenged this model. The mechanism of membrane bending by clathrin is still highly debated1-3. Addressing this question, in this study, we have reconstituted clathrin budding in vitro with giant unilamellar vesicles (GUVs), purified adaptors and clathrin. By changing the osmotic conditions, we found that clathrin coats caused extensive budding of GUVs under low membrane tension, while polymerizing as a flat lattice under moderate tension. High tension and bending rigidity of the membrane fully inhibited polymerization. We hypothesize that membrane tension could oppose polymerization energy of clathrin. Using theoretical modeling, we predict that a transition between different shapes of clathrin coats depends on membrane tension and clathrin polymerization energy. We then experimentally validated the theoretical model by estimating the transition values by measuring the polymerization energy of clathrin for the first time. The measured membrane tension and clathrin polymerization energy were found to be of the same order as in vivo tension regimes, suggesting a physiologically critical control of the shape of clathrin mediated budding by membrane elasticity4.

References

1. Ford, M.G., Barbara M.F. Pearse, Mathew K. Higgins, Yvonne Vallis, David J. Owen, Adele G, Colins R Hopkins, Philip R Evans, Harvey T McMahon. Simultaneous binding of PtdIns(4,5)P2 and clathrin by AP180 in the nucleation of clathrin lattices on membranes. Science 2001, 291:1051-1055.

2. Boulant, S., Kural, C., Zeeh, J.C., Ubelmann, F. & Kirchhausen, T. Actin dynamics counteract membrane tension during clathrin-mediated endocytosis. Nat Cell Biol 2011, 13:1124-1131.

3. Dannhauser, P.N. & Ungewickell, E.J. Reconstitution of clathrin-coated bud and vesicle formation with minimal components. Nat Cell Biol 2012, 14:634-639.

4. Saleem, M. et al. A balance between membrane elasticity and polymerization energy sets the shape of spherical clathrin coats. Nat. Commun. 2015, 6:6249.