Macropinocytosis is non-selective actin-dependent type of endocytosis. It is important for the normal physiology of some cell types. However, it is used by intracellular parasites which internalise themselves into host cells in this way and also play a role in the nutritional supply in some type of cancer cells.

During macropinocytosis a self-organized subdomain of plasma membrane is separated by a diffusion barrier named macropinocytic cup. RAC1-driven actin polymerization is required for membrane protrusion at the cup periphery, where a narrow ring of the actin nucleating factors is present. In contrast, actin dissociation occurs at the base of the cup due to RAS-controlled formation of phosphatidylinositol trisphosphates (PIP3). During cup closure sequential breakdown of PIP3 to phosphatidylinositol and acquisition of the endosomal identity of the newly formed vesicle is necessary. As a result of tubulation in the early stages of macropinocytosome maturation the vesicle decreases in diameter and stabilizes. At late stages the macropinocytic vesicle may fuse with the lysosome, allowing internalized material to enter this degradative organelle.

Throughout the process specific types of phosphatidylinositols are part of the membrane providing signal transduction and membrane identity. These phospholipids control the entire macropinocytosis and regulate the metabolism of the cell.