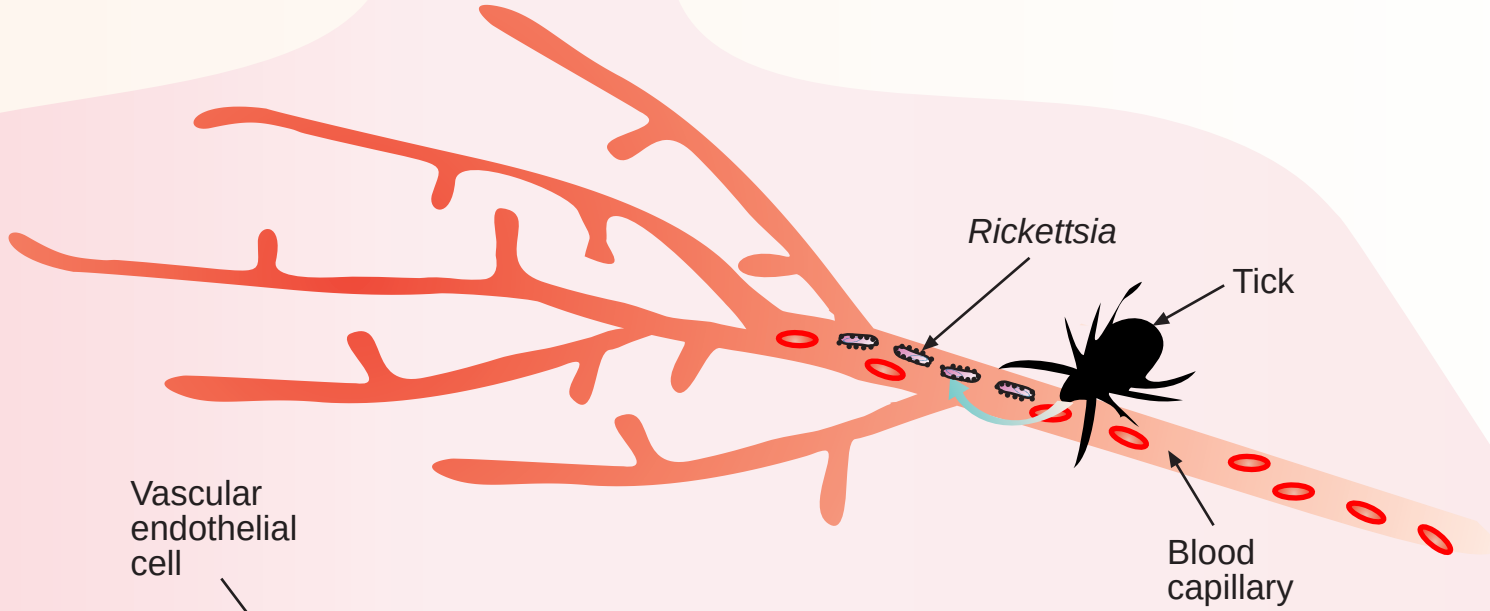
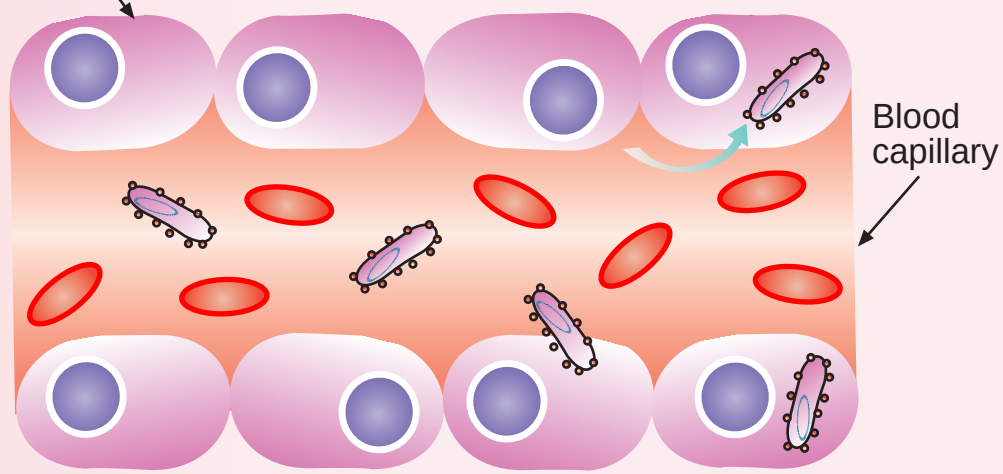
Transmission of *Rickettsia* to humans

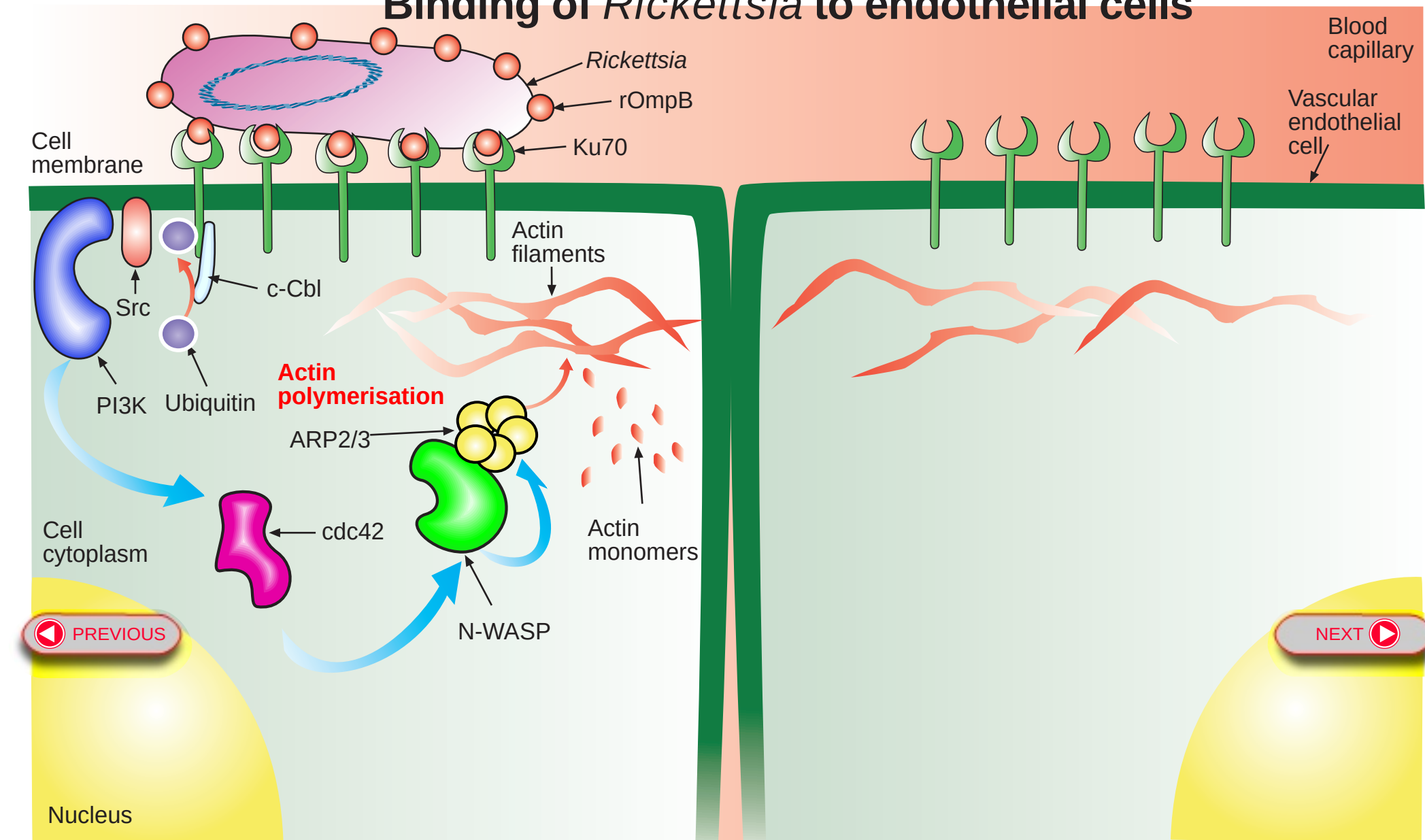




NEXT

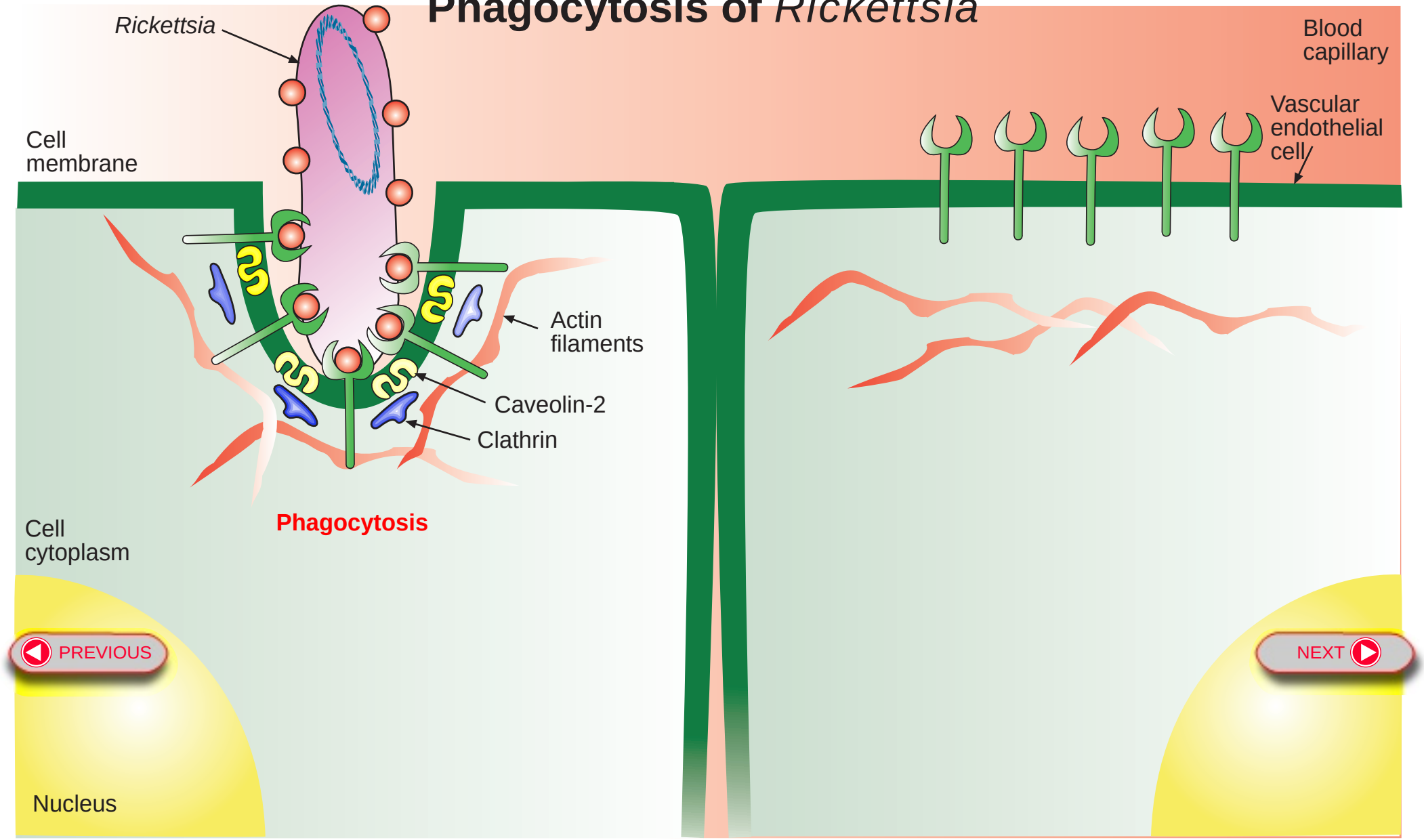
Humans are infected by *Rickettsia* bacteria by direct inoculation into the blood by infected feeding ticks. In Africa, two species of Rickettsia can cause disease; *Rickettsia conorii* transmitted by *Rhipicephalus sanguineus* and *Rhipicephalus pumilio* tick species and *Rickettsia africae* transmitted by *Amblyomma hebraeum* and *Amblyomma variegatum* tick species. Rodents and other animals are the reservoir for the bacteria which are taken up by feeding ticks.

Binding of *Rickettsia* to endothelial cells



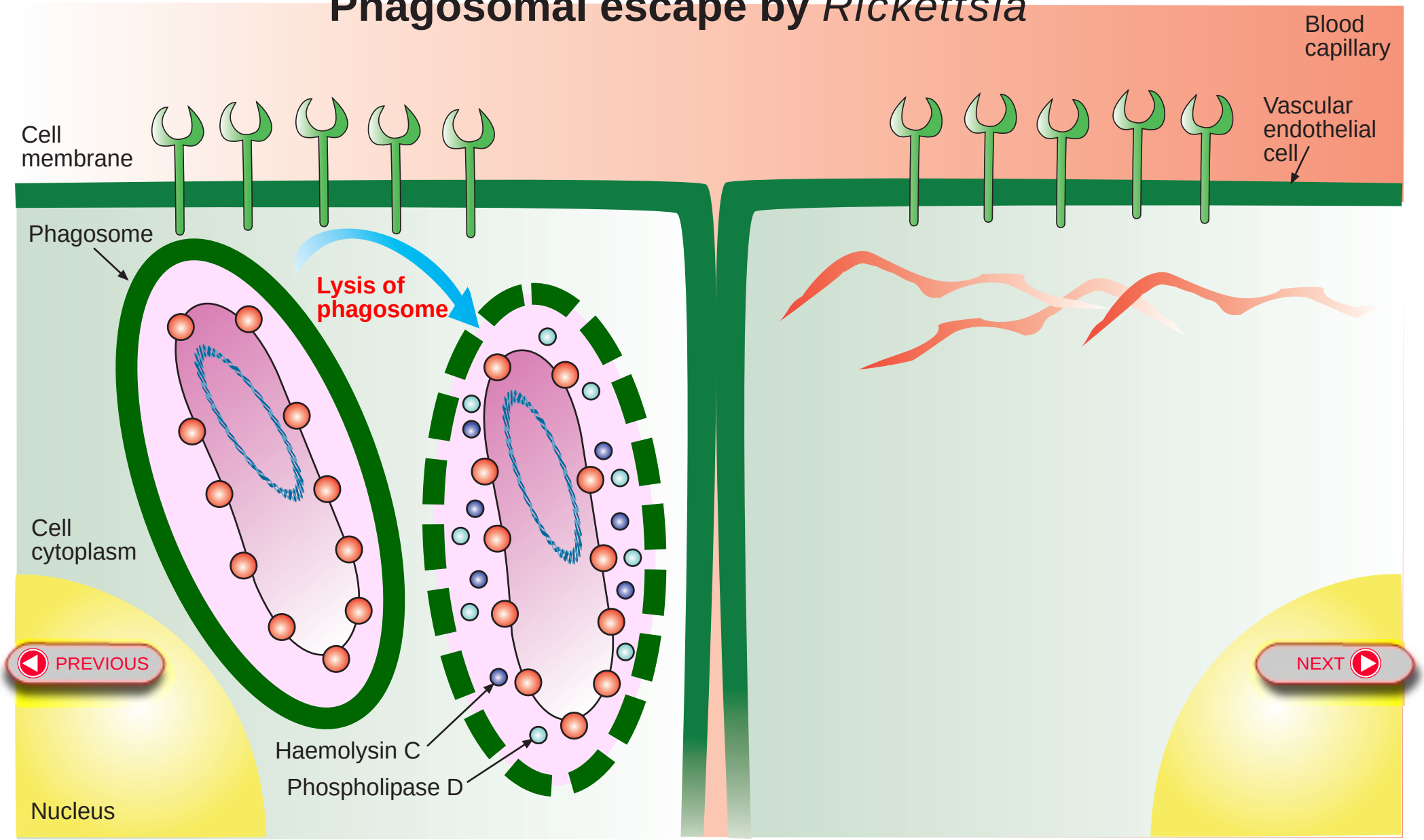
In the blood vessels *Rickettsia* bacteria penetrate vascular endothelial cells by a receptor-mediated endocytic pathway. Bacteria express outer membrane proteins rOmpB which bind to Ku70 membrane proteins expressed on the surface of vascular endothelial cells. Binding to Ku70 by rOmpB triggers a transduction signal which initiates an enzymatic cascade leading to the eventual phagocytosis of the bacterium. This process involves ubiquitination of Ku70 by ubiquitin ligase c-Cbl which activates phosphatidylinositol 3'-kinase (PI3K) and Src kinase. PI3K activates cdc42 which activates N-WASP. N-WASP activates ARP2/3 which induces the polymerisation of actin necessary for the internalisation of the bacteria.

Phagocytosis of *Rickettsia*



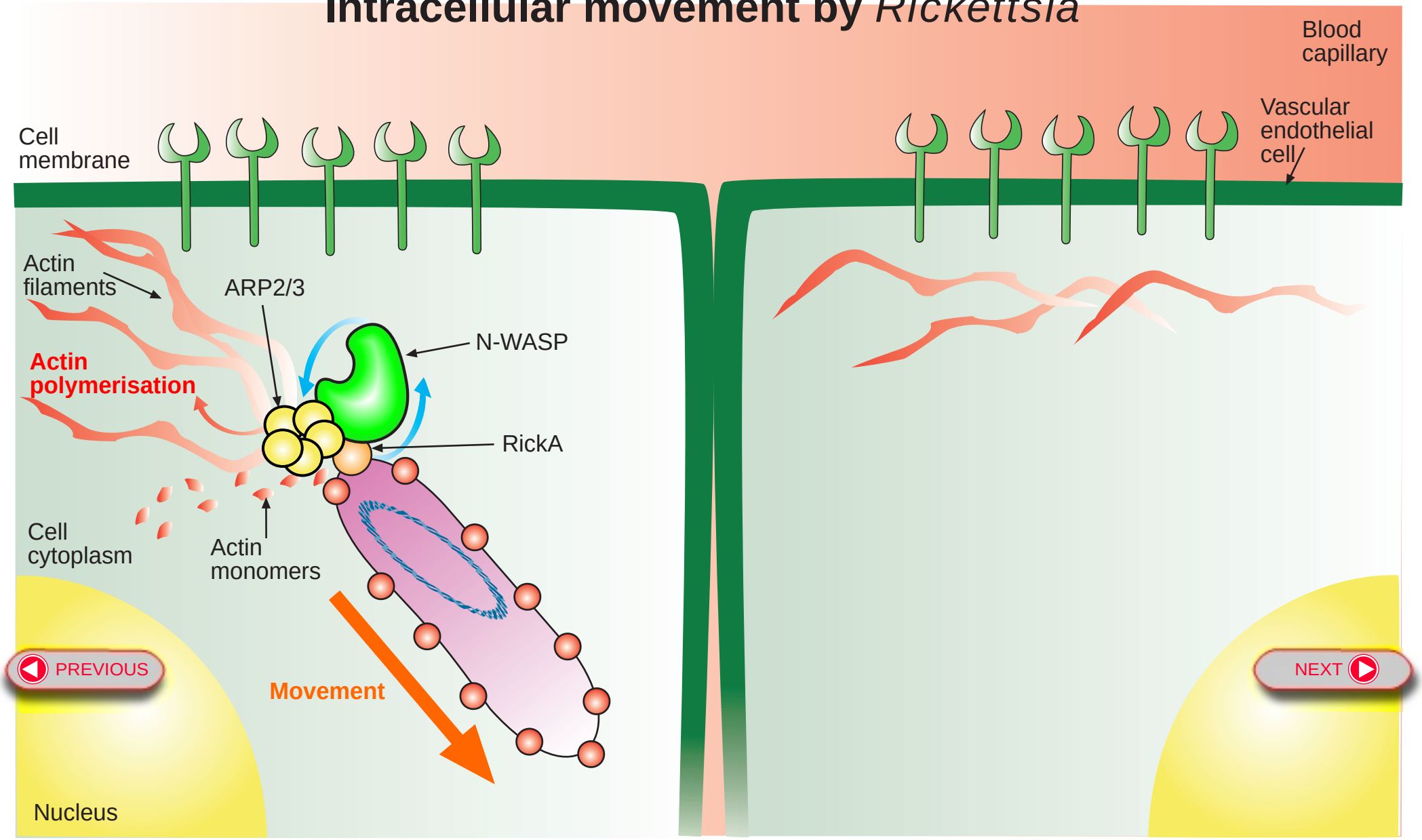
The internalisation process involves actin polymerisation and is also dependent on clathrin and caveolin-2. The cell-membrane becomes invaginated and internalises the bacteria into a phagosome. This is a natural biological process of endocytosis of cellular receptor molecules which *Rickettsia* has evolved a mechanism to exploit. Other intracellular bacterial species are known to penetrate cells in this way and the process is referred to as “zippering”.

Phagosomal escape by *Rickettsia*



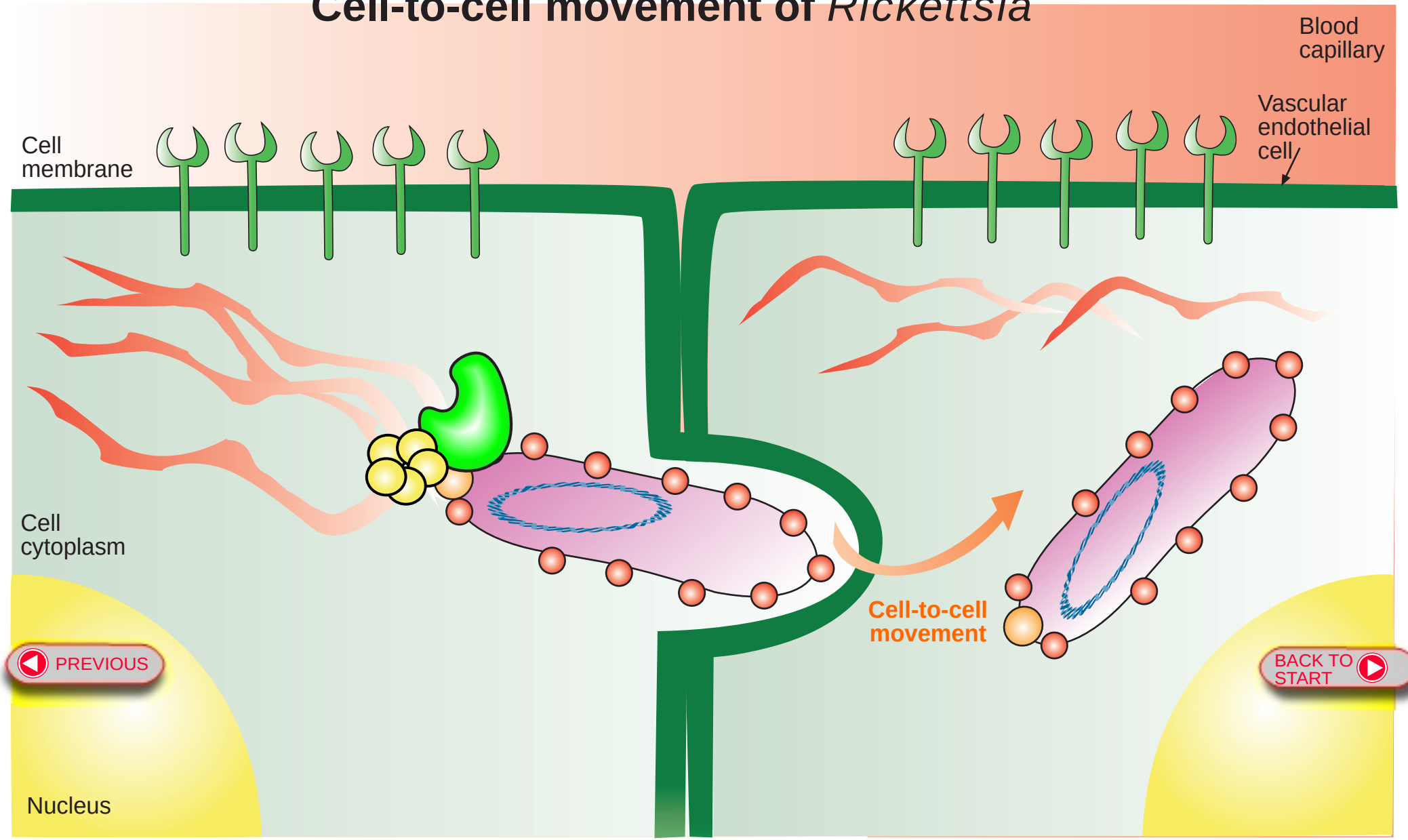
The cell membrane of the phagosome is lysed by secretion of bacterial membranolytic proteins Phospholipase D and Haemolysin C which permits the bacterium to escape into the cytosol before the phagosome can fuse with lysosomes for degradation of the contents.

Intracellular movement by *Rickettsia*



Movement within the cytosol is achieved by actin polymerisation at one of the poles of the bacterium. Bacterial protein RickA is responsible binding momomeric actin and recruiting N-WASP which mobilises the Arp2/3 complex to promote actin polymerisation. The actin filaments produced are long unbranched actin chains that propel the bacterium and allow movement within the cell.

Cell-to-cell movement of *Rickettsia*



Internalised bacteria also have the ability to penetrate into other cells through the adjacent plasma membranes and sometimes enter the cell nucleus. Bacteria can also exit the cell by targetting membrane structures known as filopodia.