Physical characteristics of phagocytic uptake and transport

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Abstract

Phagocytosis of bacteria by macrophages is a key cellular process of the mammalian immune system. When bacteria bind to phagocytic receptors, e.g. Fc• receptors, in the plasma membrane of a macrophage, induced signaling events lead to a wrapping of the membrane around the bacteria and as a consequence to their engulfment into the cell. Subsequently, molecular motors transport the newly formed membrane organelles, called phagosomes, along the cytoskeleton as part of the phagosomal maturation process. This maturation process leads in general to a degradation of the bacteria. However certain pathogenic bacteria are able to interrupt the maturation process and therefore their degradation. Although a large number of molecules that are involved in the phagocytic uptake and transport are known already, a quantitative physical understanding of this process is still lacking and basic questions concerning its physical characteristics are still open: What are the fundamental length and time scales of the spreading of the phagocytic signaling? Which parameters determine the intracellular transport of the phagosomes?

We will present various experimental approaches to address the abovementioned questions. We are using polystyrene microparticles coated with the antibody Immunoglobulin G (IgG) to investigate Fc• receptor-mediated phagocytosis in macrophages. Our experimental approaches include the use of holographic optical tweezers (HOT), magnetic tweezers (MT) and correlative light and scanning electron microscopy (CLSM). We will show how HOT and CLSM can be used to investigate the spreading of the phagocytic signaling on length scales between about one hundred nanometers and several micrometers. In addition, we will present how MT can be applied to measure phagosomal transport forces to estimate the number of molecular motors that are involved in the transport. Furthermore, we will present how HOT can be used to study the characteristics of intracellular transport paths. We will show that in contrast to common textbook knowledge not all phagosomes are transported directly from the cell periphery to the perinuclear region, but that they exhibit more complex transport characteristics depending on the size of the phagosomes. This transport behavior might be the foundation for a basic size-dependent cellular sorting mechanism for organelles.