Macrophages play a pivotal role in several physiological processes. Their functions include immune surveillance, defending the host from a variety of exogenous threats, and scavenging for necrotic and apoptotic bodies as well as toxic substances. The encounter of macrophages with exogenous bodies and materials results in cell activation, leading to the so-called M1 macrophages. M2 macrophages, on the other hand, are activated through different pathways and have mainly anti-inflammatory properties [1]. The equilibrium between these two phenotypes is critical in regulating the systemic immune response, as the excess M1 macrophages can lead to chronic inflammation and autoimmune disease. This is the case of atherosclerosis, where circulating monocytes are recruited at the diseased site, activated and differentiated into foam cells, and eventually die amplying the local inflammatory state [2]. In Alzheimer’s disease, microglia undergo a M1-phenotype transformation to induce neuronal loss [3].

In this issue, Dr. Paolo Decuzzi and his collaborators present their study on the nanoparticle-assisted systemic delivery of rosiglitazone (RSG), an important agonist for peroxisome proliferator-activated receptors [4]. RSG is a member of the thiazolidinedione class of drugs, which reduces glucose, fatty acid, and insulin blood concentrations. It can also efficiently modulate macrophage inflammation. Unfortunately, RSG has also been found to increase fatality from heart dysfunction, dramatically limiting its clinical use. The Decuzzi group was able to increase the delivery of RSG to immune cells in circulation as well as the cells residing in different tissues, including the WAT and liver. This alleviates macrophage inflammation without altering lipid metabolism and cardiac function. The macrophage-selective delivery of RSG represents a means of attenuating inflammation without causing the known side effects associated with systemic drug exposure. The same NPs can be used to deliver other classes of nuclear receptor agonists and therapeutic molecules for modulating macrophage phenotype and inflammation. The reduced side effect observed by the Decuzzi group is another example demonstrating the usefulness of nanoparticulate drug delivery systems can be found in reducing the drug side effects, rather than in addition to increasing the drug efficacy.

References


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