Synergistic effect of swarms of enzyme-powered nanomotors for enhancing the diffusion of macromolecules

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In recent decades, nanotechnology has made significant progress in drug delivery systems. The goal is to improve therapy effectiveness by precisely releasing drugs to specific tissues. However, there are still challenges to overcome. One major challenge is the presence of biological barriers,[1] such as viscoelastic fluids like synovial fluid in joints, which mainly contain hyaluronic acid. The complex network of these fluids hinders the transportation of nanosystems, causing conventional particles to get trapped and limiting their ability to reach the target area.[2,3] Therefore, there is a need for innovative technologies that can enhance the delivery of therapeutic agents.

To overcome the obstacles presented by complex media, one promising approach is the development of "active" nanoparticles or nanomotors (NMs).[4–6] However, the exploration of enzyme-powered nanomotors capable of navigating and influencing viscous fluids is still in its early stages. These enzyme-powered nanomotors offer great potential, as their coordinated movement can be driven by enzymatic reactions, effectively utilizing the biofuels present in the human body. Furthermore, some of these enzymatic nanomotors can modify the characteristics of the extracellular matrix by reducing its viscosity, thus facilitating improved diffusion of therapeutic agents.

In this study, we introduce a nanotechnological strategy using two swarms of nanomotors, namely hyaluronidase NMs (HyaNMs, Troop 1) and urease NMs (UrNMs, Troop 2), which synergistically enhance the diffusion of macromolecules within the synovial fluid. Troop 1 demonstrates the capability to break down the intricate network of synovial fluid, both in vitro and ex vivo, thereby reducing its viscosity. This enables Troop 2 to navigate more effortlessly through the viscous media. Moreover, the collective movement of Troop 2 significantly enhances the diffusion of Dextran macromolecules. These findings offer promising prospects for utilizing enzyme-powered NMs in the treatment of joint injuries, augmenting therapeutic effectiveness, and facilitating faster and more efficient delivery of therapeutic agents compared to conventional approaches.

References

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Figures

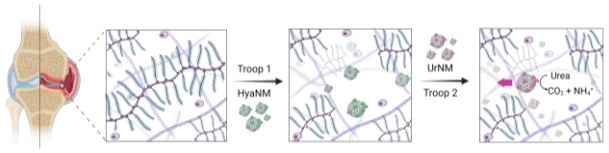

Figure 1. Conceptual idea of the novel approach using hyaluronidase NMs (HyaNMs) to interact with and reduce the viscosity of synovial fluid and urease NMs (UrNMs) for a more efficient transport of therapeutic agents in joints.