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Swarms of enzyme-powered nanomotors enhance the diffusion of macromolecules in viscous media

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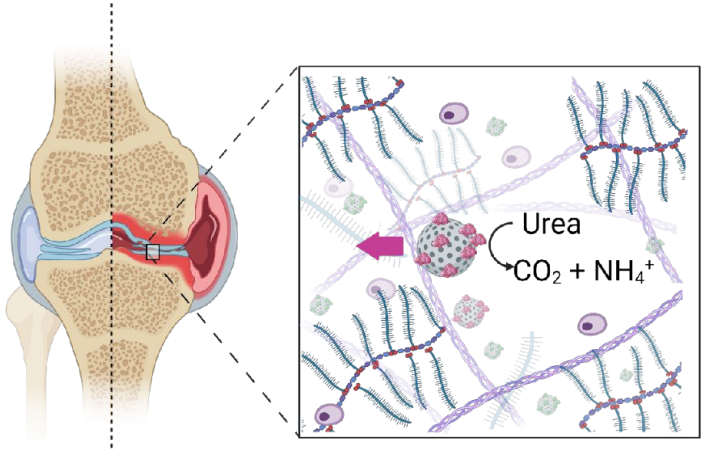

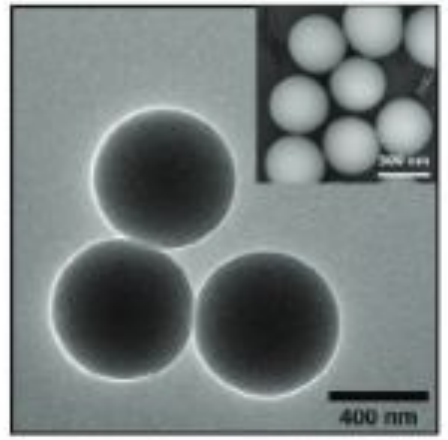

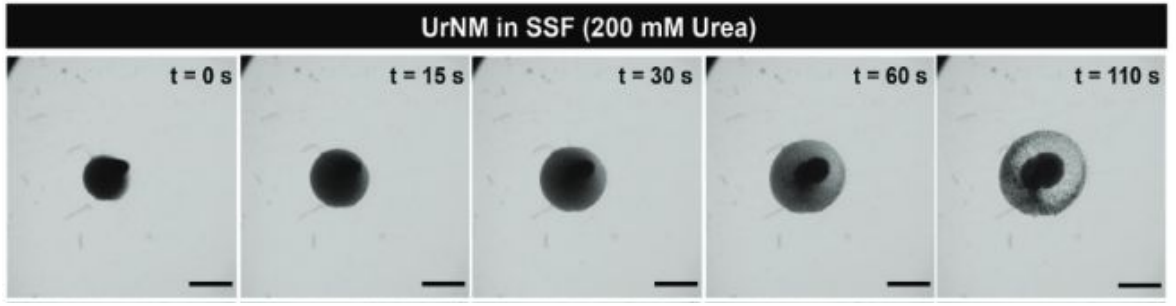

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Nanobots for knee injuries

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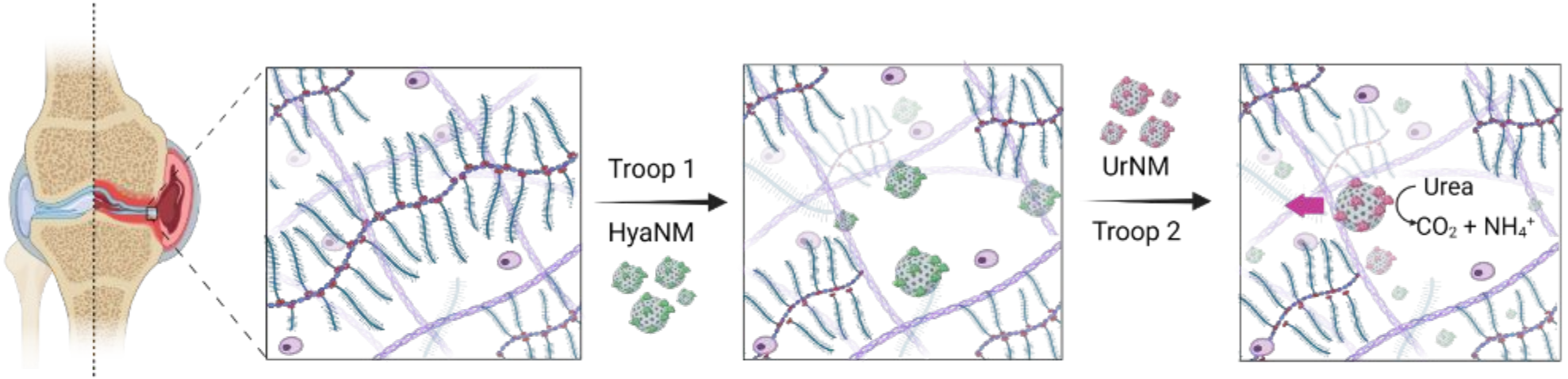

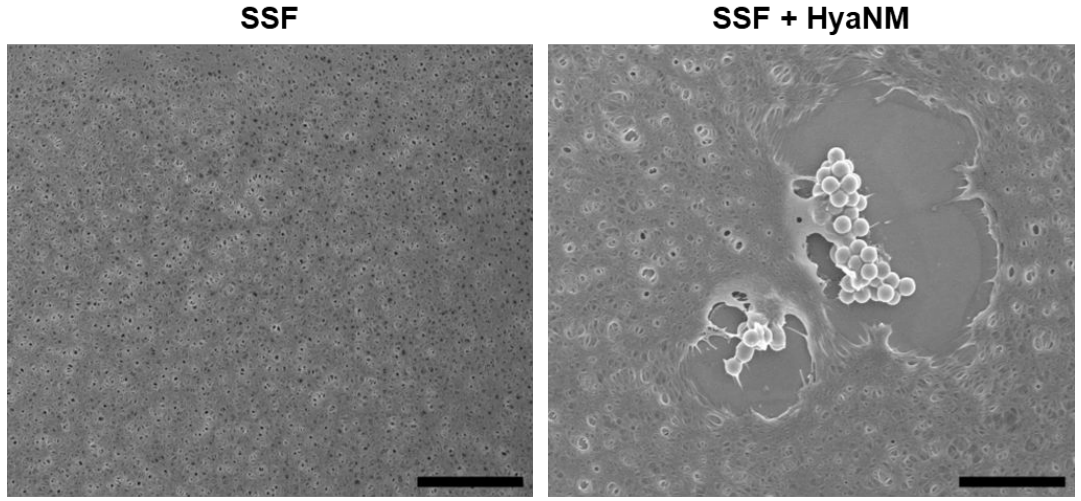

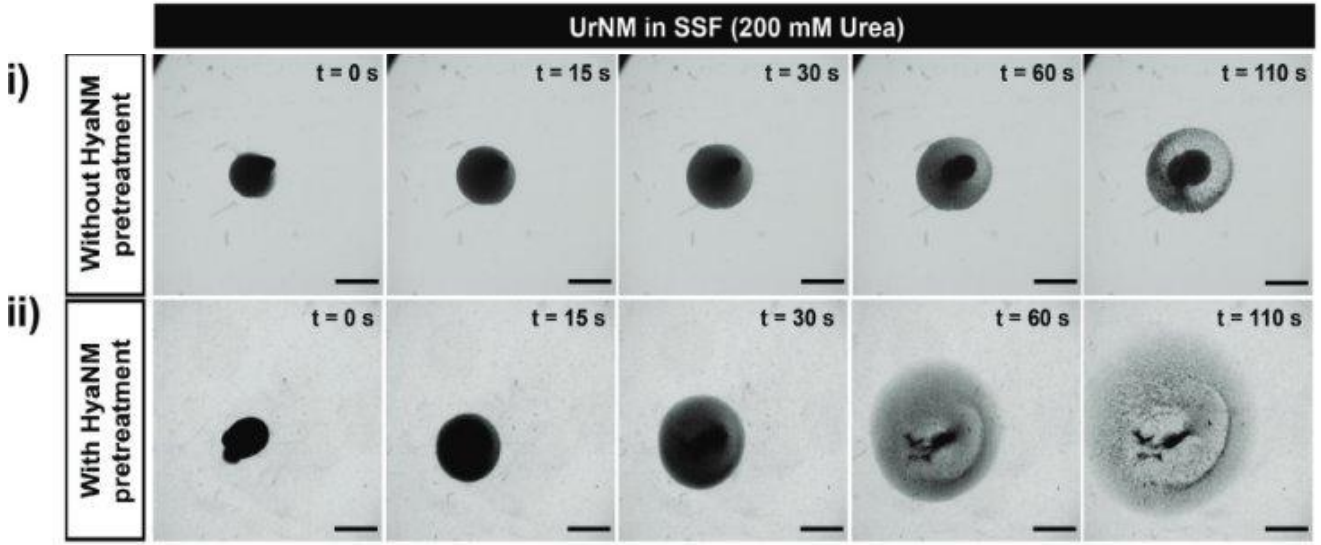

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More information in:

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RESEARCH ARTICLE

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Swarms of Enzyme-Powered Nanomotors Enhance the Diffusion of Macromolecules in Viscous Media

*Noelia Ruiz-González, David Esporrín-Ubieto, Ana C. Hortelao, Juan C. Fraire, Anna C. Bakenecker, Marta Guri-Canals, Ramón Cugat, José María Carrillo, Montserrat Garcia-Batlletbó, Patricia Laiz, Tania Patiño, and Samuel Sánchez**

Over the past decades, the development of nanoparticles (NPs) to increase the efficiency of clinical treatments has been subject of intense research. Yet, most NPs have been reported to possess low efficacy as their actuation is hindered by biological barriers. For instance, synovial fluid (SF) present in the joints is mainly composed of hyaluronic acid (HA). These viscous media pose a challenge for many applications in nanomedicine, as passive NPs tend to become trapped in complex networks, which reduces their ability to reach the target location. This problem can be addressed by using active NPs (nanomotors, NMs) that are self-propelled by enzymatic reactions, although the development of enzyme-powered NMs, capable of navigating these viscous environments, remains a considerable challenge. Here, the synergistic effects of two NMs troops, namely hyaluronidase NMs (HyaNMs, Troop 1) and urease NMs (UrNMs, Troop 2) are demonstrated. Troop 1 interacts with the SF by reducing its viscosity, thus allowing Troop 2 to swim more easily through the SF. Through their collective motion, Troop 2 increases the diffusion of macromolecules. These results pave the way for more widespread use of enzyme-powered NMs, e.g., for treating joint injuries and improving therapeutic effectiveness compared with traditional methods.

1. Introduction

challenge in biomedicine.[1] Particularly, passive nanoparticles (NPs) have been explored to act as drug carriers. Yet, they still need to overcome complex scenarios, such as viscous media,[2–4] the extracellular matrix (ECM), mucus, or synovial fluid (SF) in the joints, to name a few. These structures are highly complex and are mainly composed of hyaluronic acid (HA), glycoproteins, and collagen, with a high viscosity that reduces the ability of conventional nonmotile carriers to reach their target site. Hence, there is a clear need for novel, disruptive, and more efficient nanomedicine technologies capable of increasing the penetration and diffusion efficiency facing biological environments. In this context, self-propelled NPs, namely nanomotors (NMs), hold great potential to overcome the low diffusion problem. However, NMs have mostly been studied in liquids such as water, phosphate buffer solution (PBS), or Newtonian fluids, while their actuation in complex biofluids remains poorly explored. In this context, most studies based on micro- and nanomotors capa-

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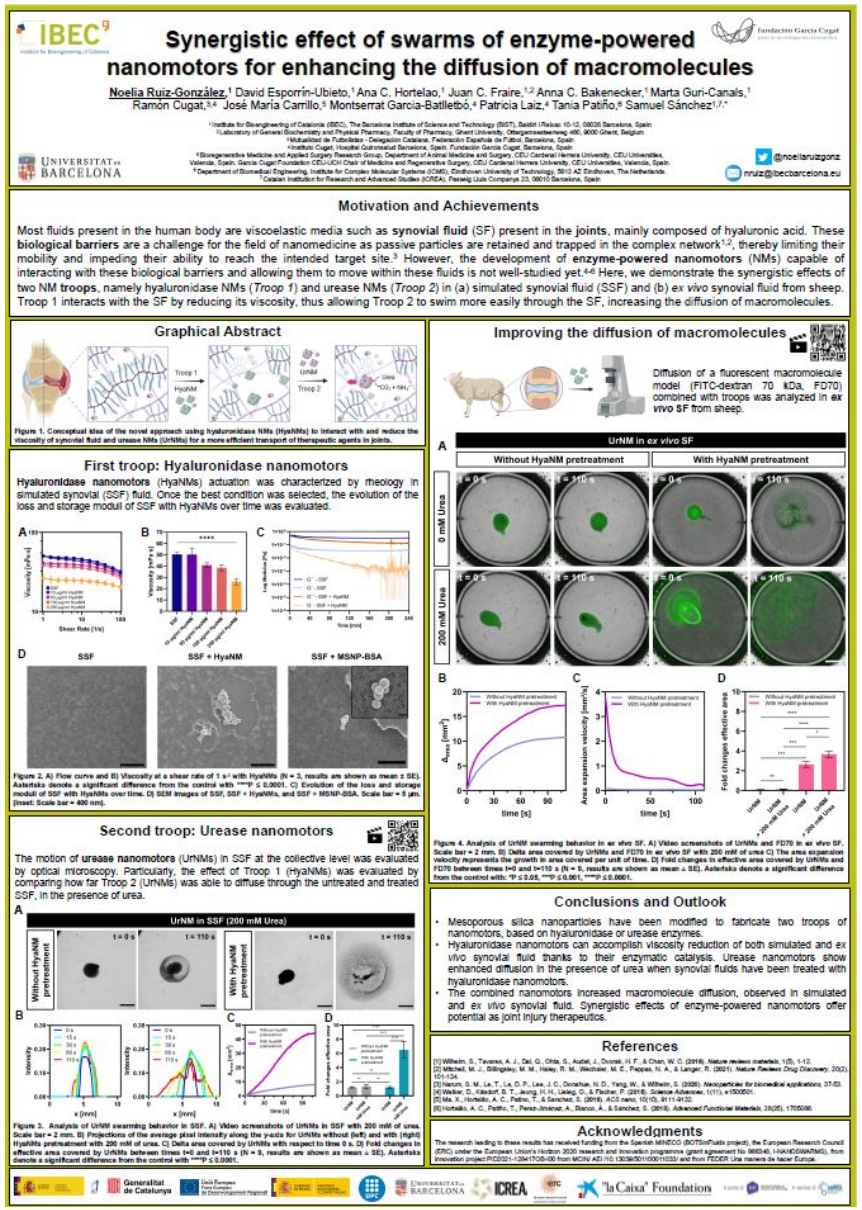

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