

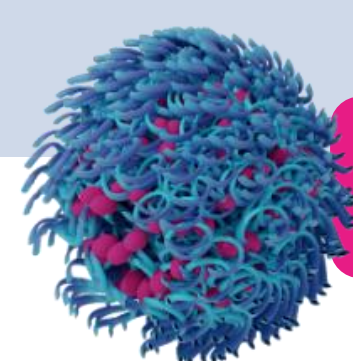
# FR-JET® modular mixer: A scalable solution for optimizing nanoparticle size and functionality

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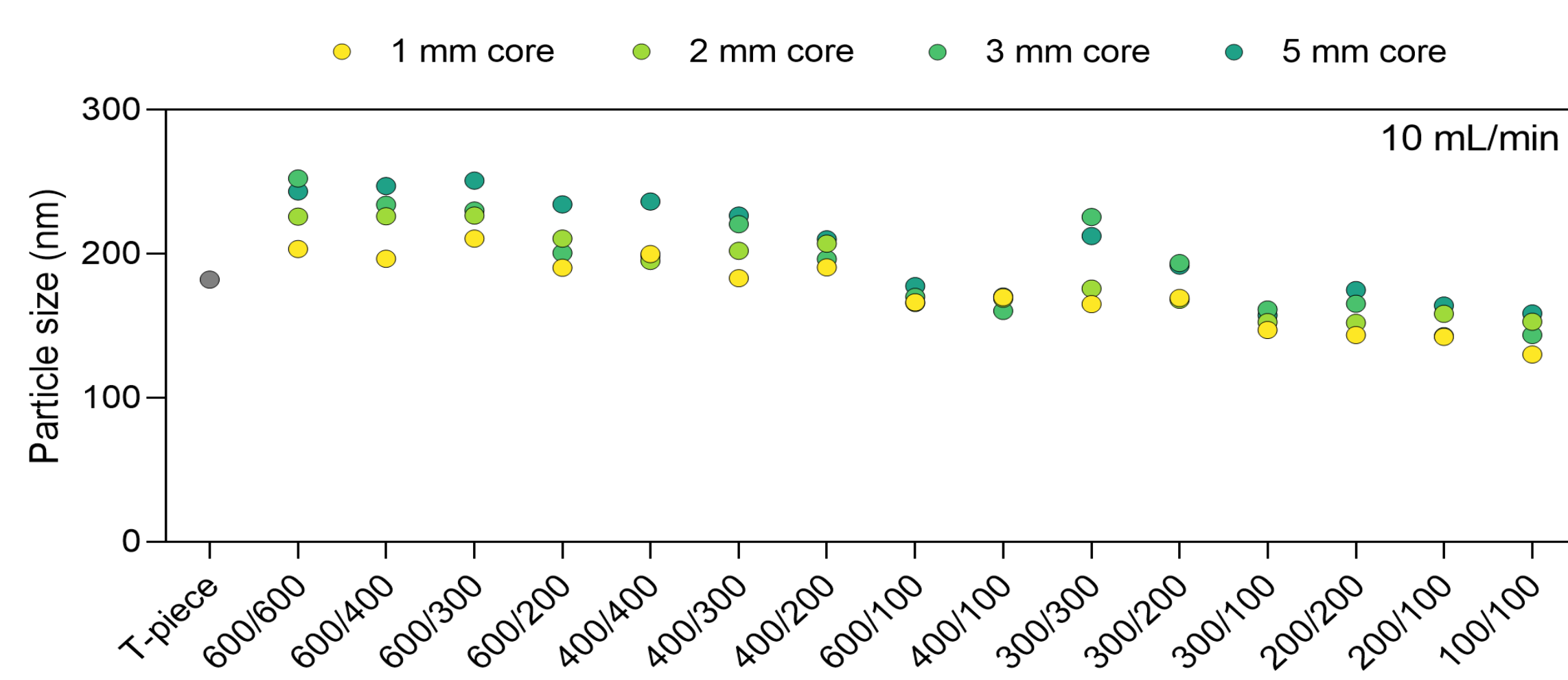
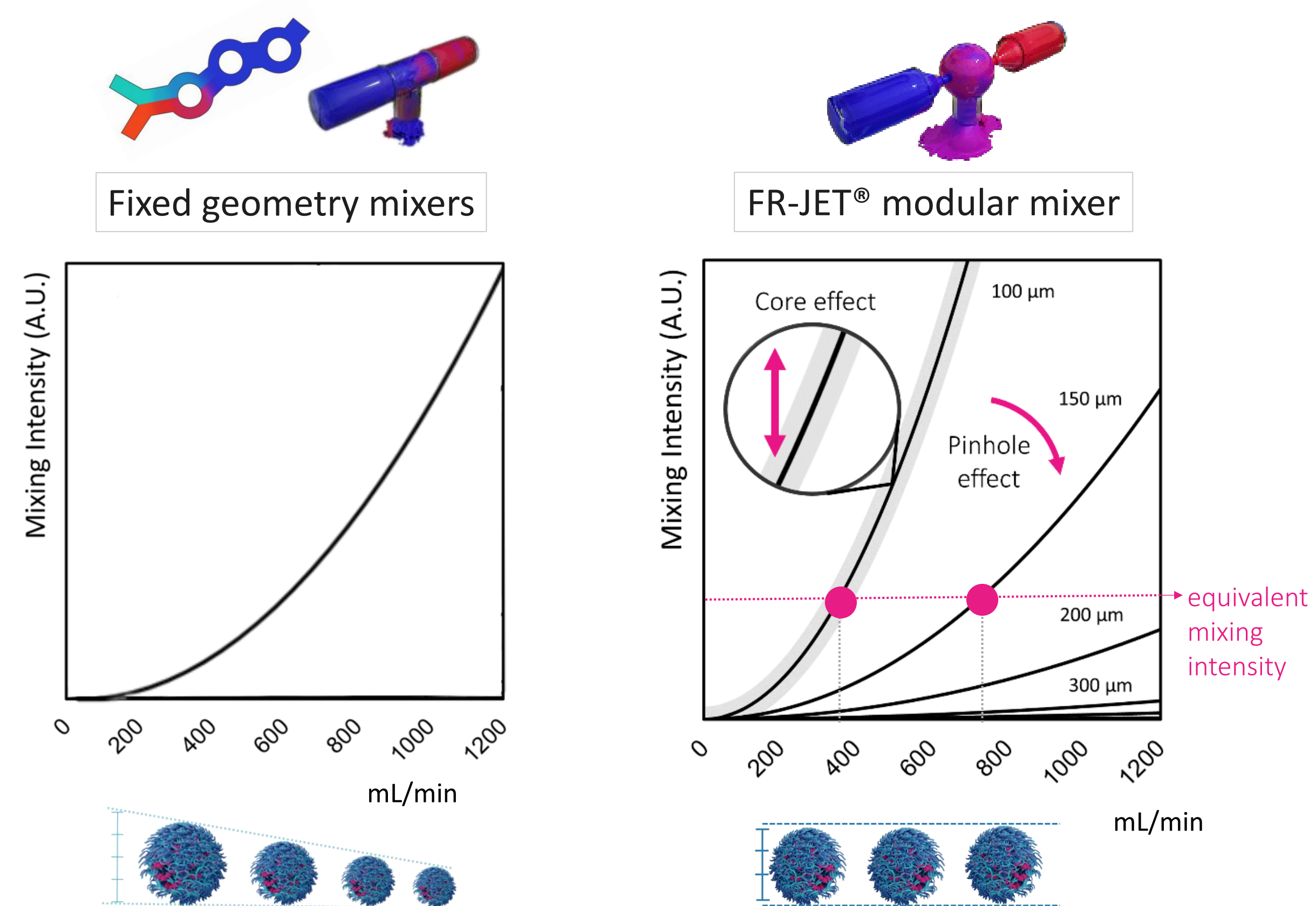


## INTRODUCTION

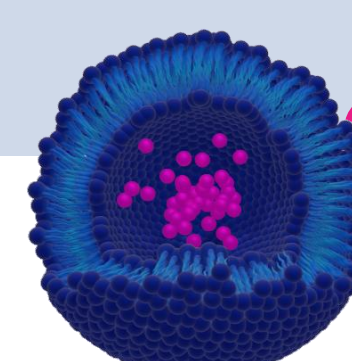
The case studies presented highlight the performance of the FR-JET® modular mixer in nanoparticle (NP) production, demonstrating its ability to precisely modulate particle size and enhance gene expression in H1299-eGFP cells. Comparative data against fixed geometry mixers, such as bifurcating mixers and conventional T-mixers, evaluate critical parameters such as particle size, polydispersity, and cellular uptake. The goal was to assess how mixing intensity impacts NP uniformity and biological efficiency, and to show how FR-JET® optimizes these factors to improve in vitro performance.



### FR-JET® tunes size by modulating mixing

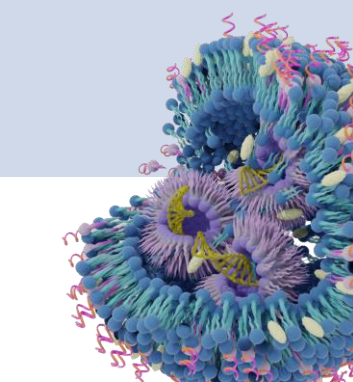
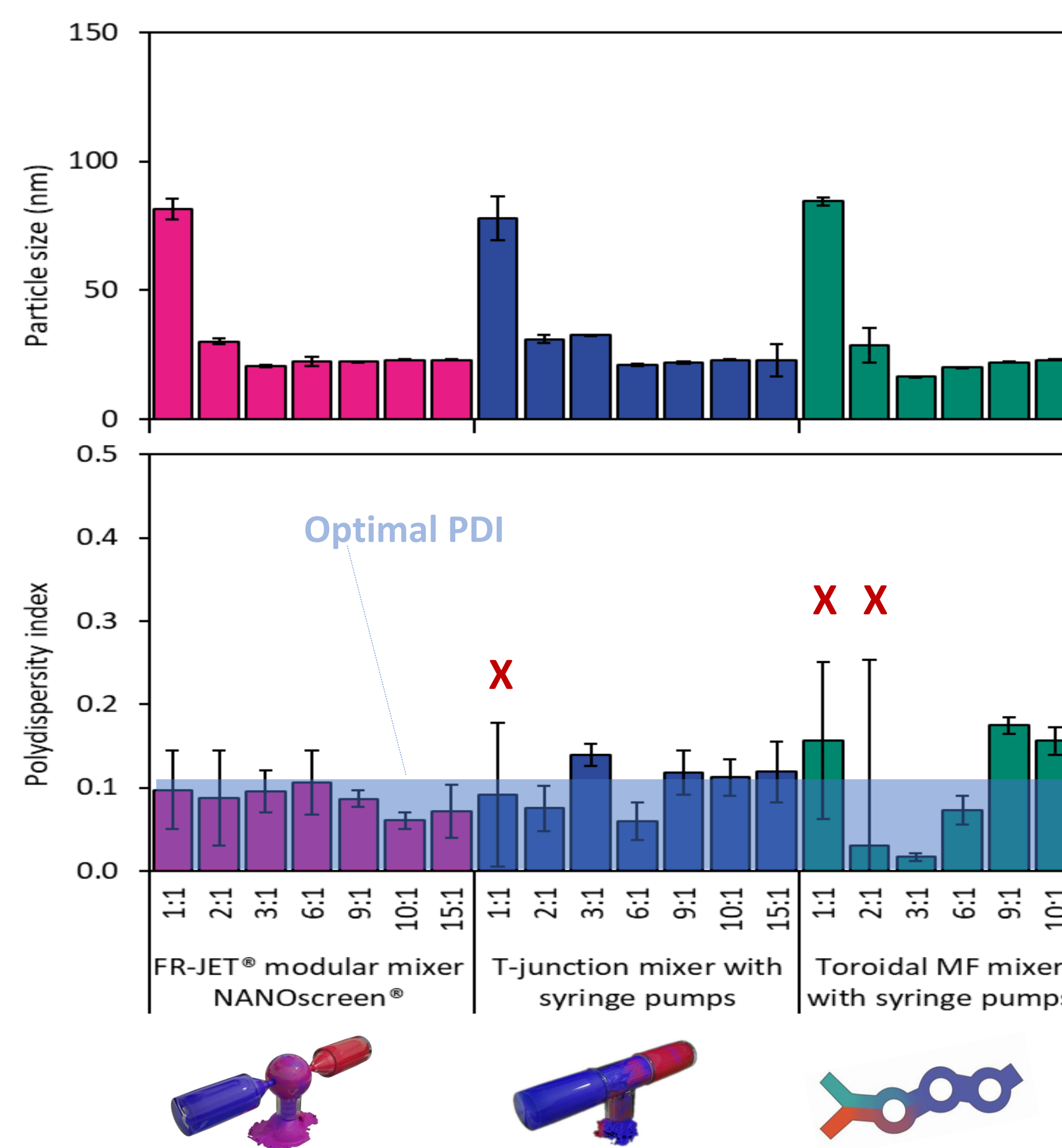


The FR-JET® modular mixer features two key innovations: a **spherical chamber** (1–5 mm diameter) that optimizes mixing dynamics, and **modular inserts** (100–600 µm) that allow precise control of mixing intensity across scales. The interchangeable core and inserts enable fine-tuning of flow conditions, ensuring consistent particle size distribution at different process scales. Modeling the interplay between flow, geometry, and performance reveals predictable trends, including the effects of chamber size, pinhole configuration, and flow rate on mixing efficiency. This level of control provides drug developers with a broader design space to tailor NP size as well as ensure product quality during scale-up.

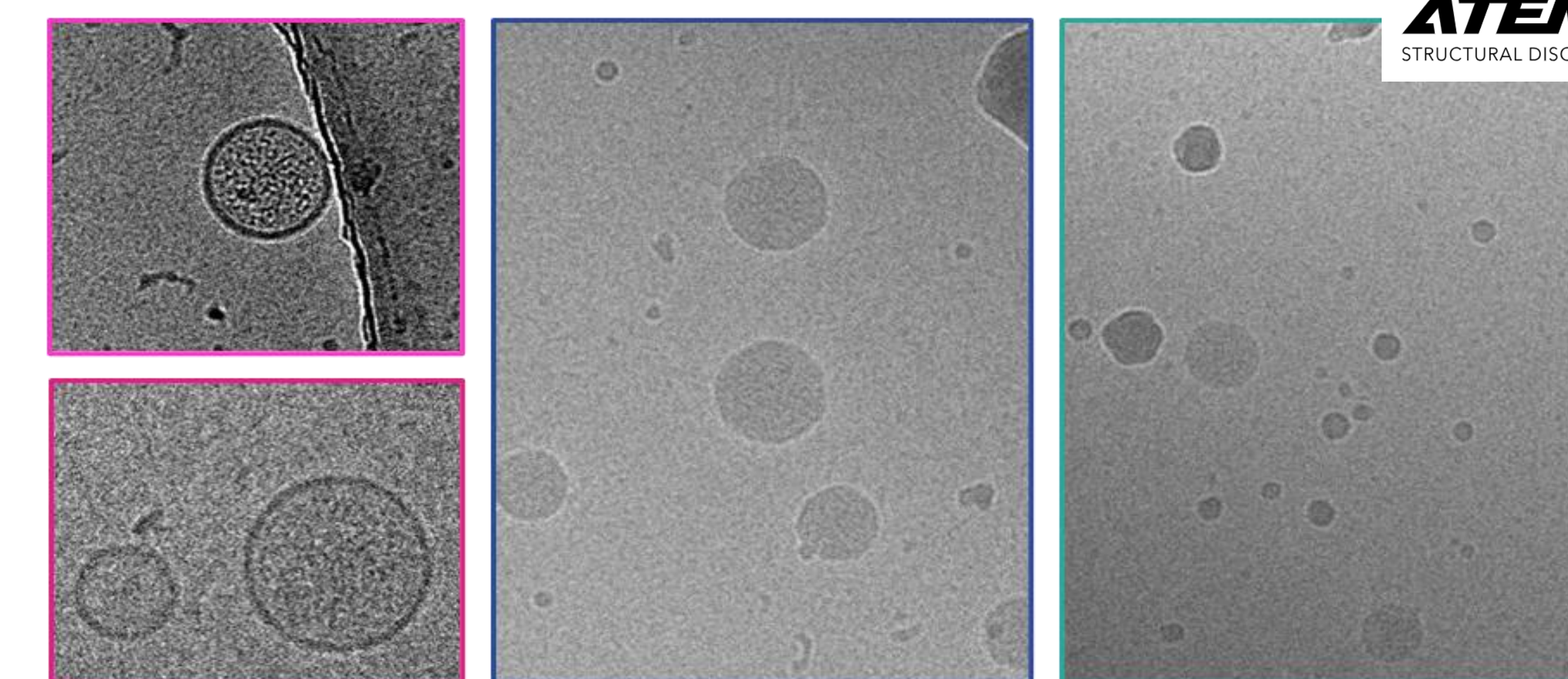
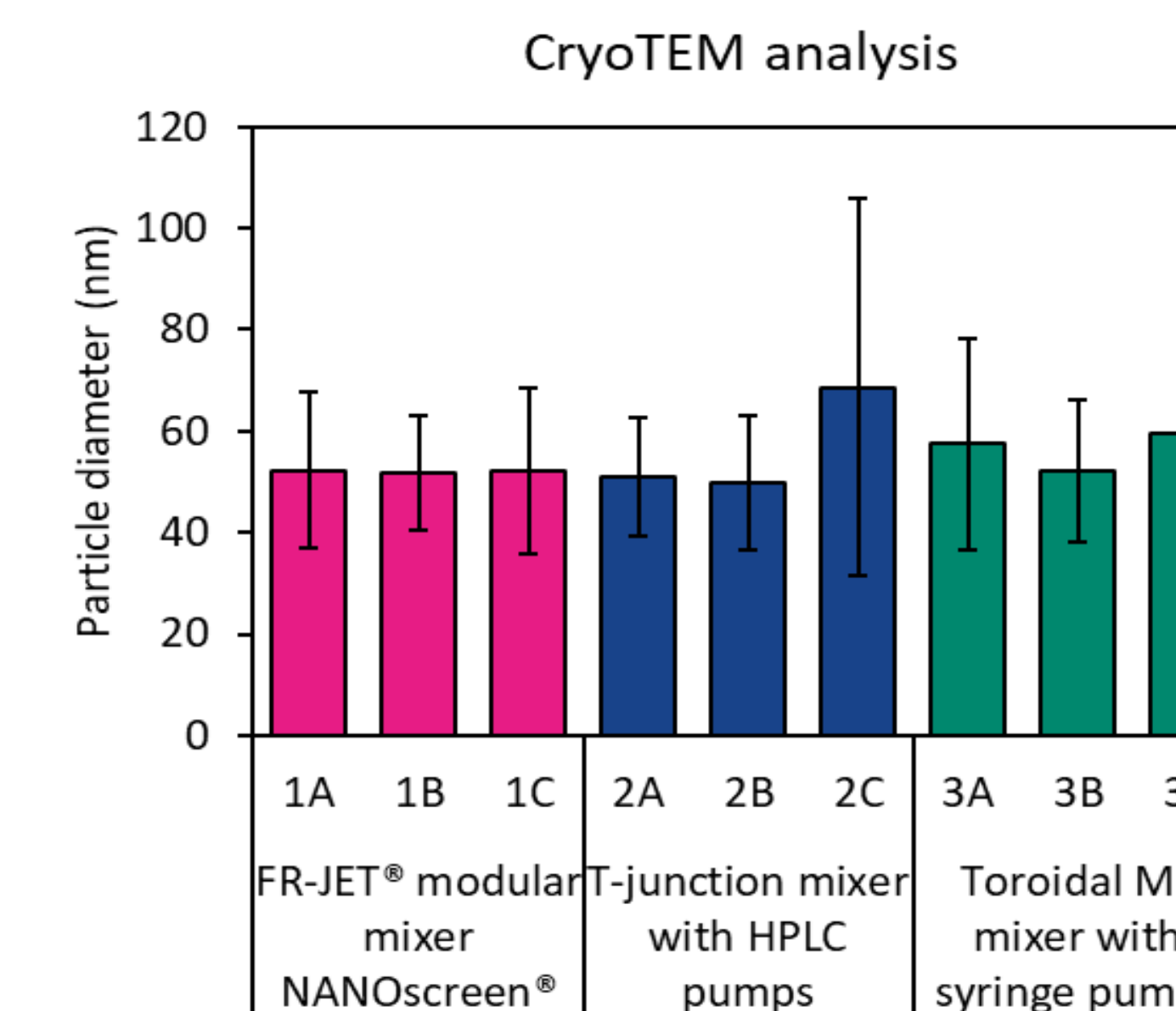
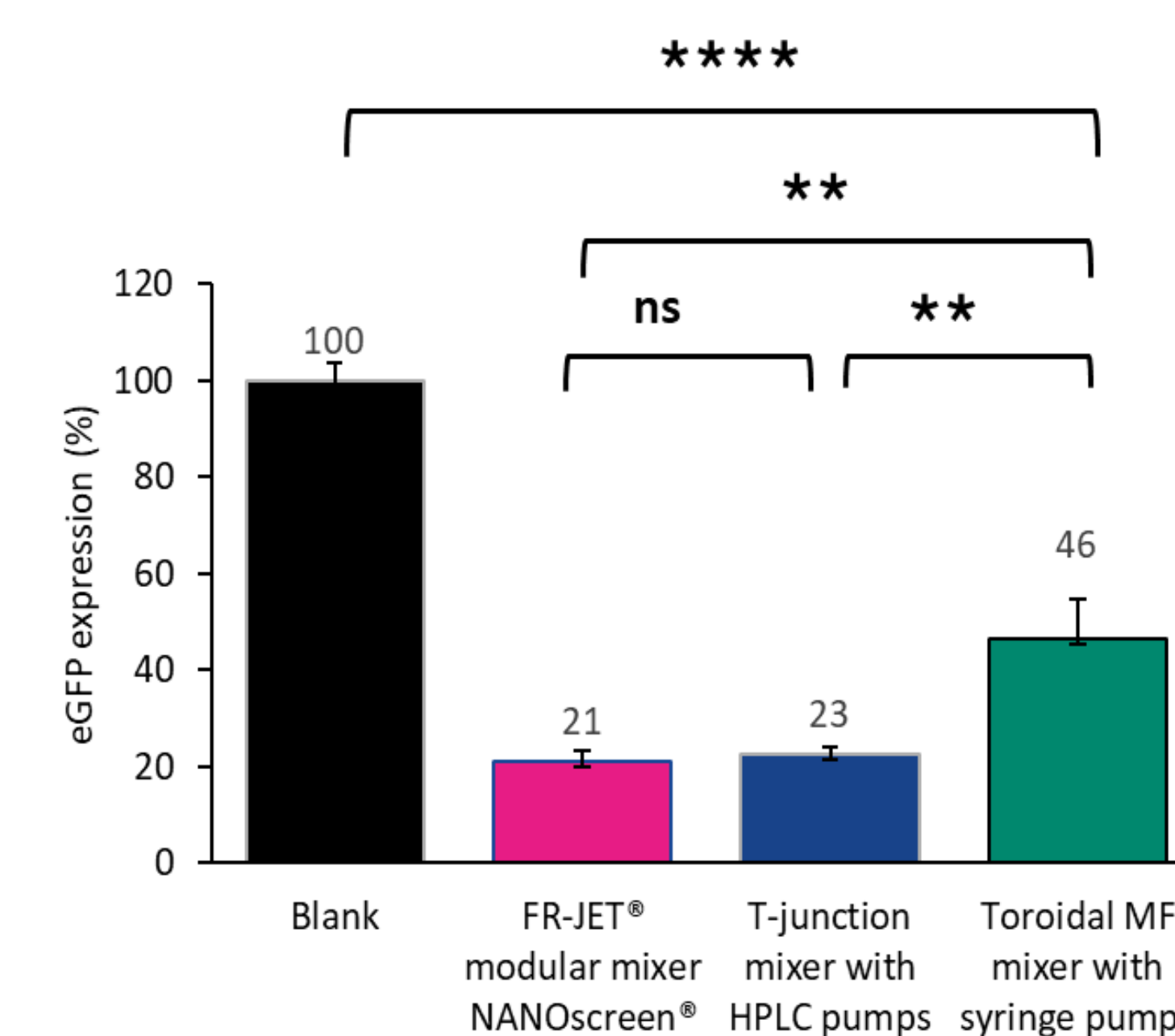


### FR-JET® delivers consistent liposomes

The case study compares production of liposomes composed of SoyPC/cholesterol/DMG-PEG2000 (mol% 52/45/3) using the FR-JET® modular mixer, a bifurcating microfluidic mixer, and conventional T-junction mixer. Liposomes were produced at various flow rate ratios (FRR) of the aqueous phase to organic phase. Results revealed that the FRR influenced the particle size (top graph). Particle size decreased with increasing portion of the aqueous phase. Meanwhile, results showed that liposomes produced with the FR-JET® modular mixer consistently produced liposomes with the lowest and most consistent polydispersity index (PDI < 0.1), indicating highly uniform particles. By contrast, liposomes produced with the bifurcating microfluidic mixer and T-junction mixer displayed a higher variability between various FRR, yielding particles with higher PDI values, thus reflecting less uniform size distributions.



### FR-JET® enhances siRNA-LNP biological activity



eGFP siRNA was encapsulated in LNPs using the same lipid composition (SM-102/Chol/DSPC/DMG-PEG2000) at a total flow rate of 20 mL/min, N/P ratio of 3, and FRR of 3:1. LNPs were prepared using three mixing technologies: the FR-JET® modular mixer, a toroidal microfluidic mixer, and a conventional T-junction mixer. Particle counts were  $2 \times 10^{12}$ /mL for FR-JET®,  $4 \times 10^{12}$ /mL for the toroidal mixer, and  $5 \times 10^{12}$ /mL for the T-mixer. Despite the lower particle count, FR-JET®-prepared LNPs showed superior in vitro biological activity compared to the toroidal mixer and slightly better performance than the T-mixer. CryoTEM imaging revealed that the FR-JET® LNPs exhibited a distinct bilayer structure at the particle surface, not observed with the other mixers, suggesting improved interactions with cellular membranes. These findings demonstrate that, even with fewer particles, the FR-JET® modular mixer enhances the functional performance of LNPs.

## CONCLUSION

The FR-JET® modular mixer demonstrates superior control over nanoparticle production, consistently producing highly uniform liposomes (PDI < 0.1) and LNPs with enhanced in vitro biological activity. Its unique spherical chamber and modular insert of various diameters, allow precise tuning of mixing intensity across scales, enabling predictable modulation of particle size distribution. Compared to fixed-geometry mixers, the FR-JET® modular mixer not only improved particle uniformity but also enhances functional performance, even at lower particle counts. These results highlight the FR-JET® modular mixer as a versatile, scalable, and efficient platform for optimizing nanoparticle formulation and performance.