

# Photoresponsive Bridged Silsesquioxane Nanoparticles with Tunable Morphology for Light-Triggered Plasmid DNA Delivery

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Bridged silsesquioxane (BS) nanomaterials with chemical structures  $O_{1.5}Si-R-SiO_{1.5}$  with organic R groups are emerging as the next generation of organosilica nanocomposites.<sup>1</sup> Consequently, the BS matrix photophysical, chemical, thermal and mechanical properties can be governed by the nature of homogeneously distributed organic fragments within the siloxane network.<sup>2</sup> Nonetheless, due to the synthetic challenge to control the kinetic in sol-gel processes, most non-porous BS materials that have been extensively studied in the past two decades were macroscaled.<sup>3</sup> Ideally, for biomedical purposes BS NPs should be non-aggregated sub-200 nm nanomaterials to benefit the enhanced permeation and retention (EPR) effect and, thus, accumulate in cancerous tissues and organs.

Photoresponsive bridged alkoxysilane precursor was used to synthesize nanomaterials (sub-200 nm) with tunable size and morphology, affording non-aggregated dense or hollow nanospheres. The organic-inorganic nanomaterials possessed a very high organic content (50%) of photoresponsive fragments which enabled the on-demand charge reversal from positive (+46 mV) to negative (-39 mV) values. Furthermore, this feature was harnessed to apply BS nanocarriers without further functionalization for the first time for light-triggered plasmid DNA delivery in cancer cells. The light-actuation was found to be effectively delivering DNA while the non-irradiated nanomaterials did not induce significant gene expressions (Figure 1). Dye-doped hollow BS NPs are envisioned for biomedical imaging while the use of a near-infrared fluorophore could extend its potential for in-vivo biomedical applications.

## References

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**Figure 1.** CLSM images on HeLa cells incubated with BS NPs binding DNA strands after 6 h of incubation. DNA is tracked via GFP fluorescing in green after translation in the nuclei, thus proving the DNA delivery from BS NPs. Scale bars of 40  $\mu$ m.

