

# 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 alkoxy silane 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.

