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LONG-TERM, IN SITU SENSING OF MICRORNAS ENABLED BY NANOCOMPOSITE FIBER NETWORKS SHELTERING DNA MOLECULAR BEACONS

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In vivo sensing applications demand extended residency time and localized release of the functional probes for overcoming the constraints of multiple interventions. It is especially challenging to endow tissue engineering scaffolds with sensing properties, as these often require residence times ranging from several days to months in order to perform their function. This currently limits the extent to which DNA-based probes can be deployed in tissue engineering and *in situ* molecular detection.[1] This work presents a strategy for bypassing the above limitations using hierarchically assembled platforms in which a DNA molecular beacon is incorporated in mesoporous nanoparticle carriers embedded in a polymer nanofiber matrix.[2] We show that these multiscale scaffolds can be engineered to provide controlled and sustained release of a DNA probe for long-term detection of a target microRNA marker. First, model synthetic DNA is loaded into porous silicon nanoparticles (pSiNPs) using a calcium-silicate trapping method, then incorporated into polymer nanofibers by means of a spray nebulization technique. The resulting hybrid nanofibers are characterized for their ability to release the oligonucleotide payload under under temperature and pH conditions mimicking physiological values. The amount of DNA released scales with the quantity of DNA-loaded pSiNPs and the chemical nature of the fiber matrix, which allows for arbitrarily tuning the release between 5 and 20 days. Next, we demonstrated that a DNA molecular beacon designed to recognize microRNA-21 (miR-21) can be used as a sensing payload retaining its functionality during extended timeframes. *In situ* detection of the target microRNA can be achieved at programmed time-points with defined signal gains spanning 20 days. This works shows that microRNA sensing can be performed in situ and in real time by combining miRNA-responsive DNA molecular beacons with hybrid polymer/porous silicon fiber scaffolds, suggesting that extracellular microRNA markers may be detected directly in cell culture over several weeks of incubation.

O1 BIO1

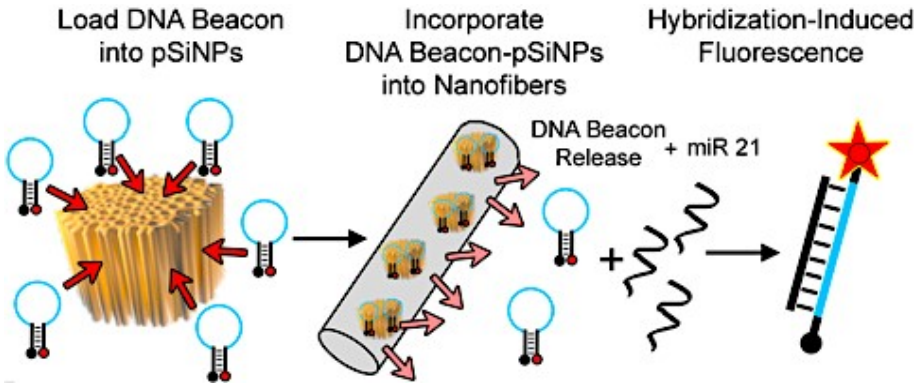

Figure 1. Hybrid polymer nanofibers containing DNA-loaded porous silicon nanoparticles allowing for long-term detection of a target microRNA.

References

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