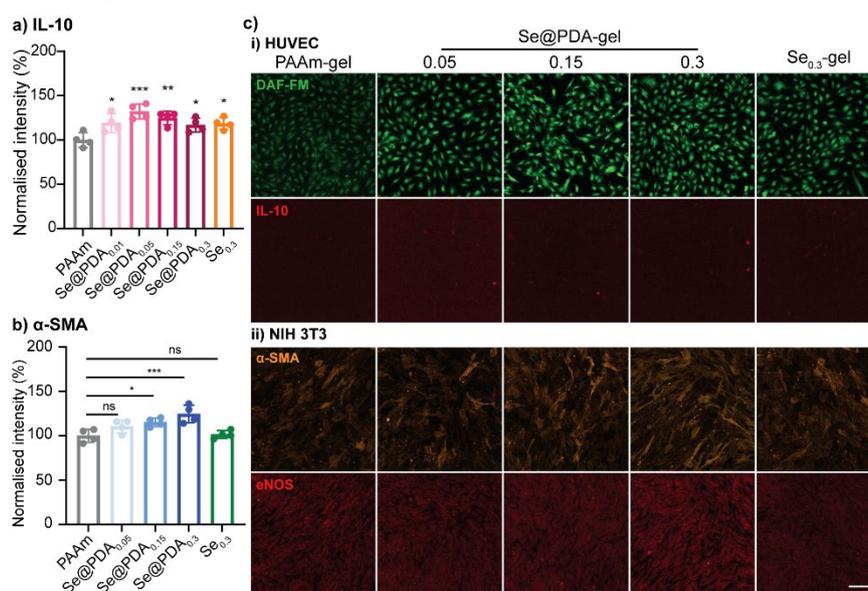


# Selenium nanoparticle-loaded hydrogel for stable and tuneable nitric oxide delivery with broad therapeutic potential

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Nitric oxide's (NO) crucial role in various physiological processes, such as vascular regulation, neurotransmission, and wound healing, has led to the development of various NO delivery platforms. However, achieving controlled and sustained NO delivery remains challenging due to its short half-life (< 5 s). To address this, catalytic approaches have emerged, employing nanomaterials as catalysts to decompose endogenous NO donors to generate NO *in-situ*. Our previous study established that selenium nanoparticles (SeNPs) are highly efficient NO-generating catalysts with low cytotoxicity, producing 7.5  $\mu\text{M}$  of NO within 30 min using as little as 0.1  $\mu\text{g}/\text{mL}$  of SeNPs.<sup>1</sup> Moreover, coating these nanoparticles with polydopamine (Se@PDA NPs) enhances their stability in physiological conditions and promotes cellular uptake, facilitating intracellular NO generation. Building on these advancements, we synthesised polyacrylamide (PAAm) hydrogels as a drug delivery platform, incorporating Se@PDA NPs to catalytically generate NO from both endogenous and exogenous NO donors. By adjusting the concentration of NPs loaded within the hydrogels, tuneable NO generation was achieved. Their excellent biocompatibility was evidenced through cytotoxicity tests with increased interleukin-10 (IL-10) and alpha-smooth muscle actin ( $\alpha$ -SMA) expression indicating anti-inflammatory effects and potential for wound healing, respectively (Figure 1). These findings suggest that Se@PDA-gel represents a promising platform for controlled and sustained NO delivery, offering therapeutic potentials in wound healing and anti-inflammatory therapies, particularly for cardiovascular and infectious diseases.



**Figure 1:** Evaluation of a) IL-10 expression of HUVEC and b)  $\alpha$ -SMA expression of NIH 3T3 cells after 48 h of incubation with hydrogels. c) Confocal images of i) HUVEC after 48 h of treatment stained with DAF-FM (green) and IL-10 (red), ii) NIH 3T3 cells after 48 h of treatment stained with  $\alpha$ -smooth muscle actin ( $\alpha$ -SMA, orange) and endothelial nitric oxide synthase (eNOS, red), (scale bar 100  $\mu\text{m}$ ).