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Genetically modified potato virus X nanoparticles functionalized with VEGF-derived peptide for enhanced angiogenesis in engineered tissues

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INTRODUCTION AND AIM

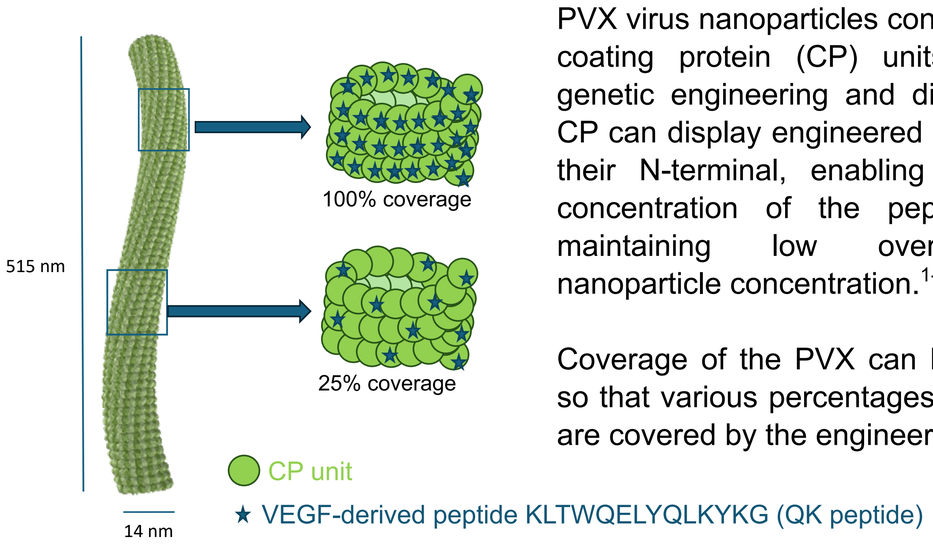


Figure 1. Potato Virus X (PVX) as a Peptide Display Platform

PVX virus nanoparticles consist of 1270 coating protein (CP) units. Through genetic engineering and direct fusion, CP can display engineered peptides on their N-terminal, enabling high local concentration of the peptide, while maintaining low overall virus nanoparticle concentration.[1-4]

Coverage of the PVX can be adjusted so that various percentages of the CPs are covered by the engineered peptides

In this study, PVX was genetically engineered to present proangiogenic QK peptides on its surface (PVX-QK). We hypothesized the dual action of PVX-QK nanoparticles as both an angiogenic media supplement and a hydrogel building block.

METHODS

PVX-QK as Angiogenesis enhancement supplement

Endothelial cells (ECs), were incubated with functionalized PVX-QK nanoparticles and interactions of the VEGFR2 receptors and PVX nanoparticles were confirmed with Immunostaining. (Figure 2.)

The effect of 30 fM (1 ng/mL) concentration of PVX-QK on angiogenesis-related parameters such as migration and FLT1, KDR and ITGB1 gene expression was investigated after 1 and 7 days of incubation with ECs (Figure 3.). All investigations were done with 3 human donor cells.

PVX-QK as a Hydrogel Building Block

Microstructure of PVX-laden collagen-fibrin hydrogels, crosslinked with microbial transglutaminase (mTG) was investigated with scanning electron microscopy (Figure 4.)

Their hydrolytic stability was tested in PBS for 1, 4 and 7 days. Their proteolytic stability was tested in 100 U/mL collagenase solution over a period of 60 minutes. (Figure 5.)

PVX nanoparticles were incubated with mTG, and the molecular weight distribution of the CP units was observed and compared to the single CP unit band at 25 kDa. (Figure 6.)

RESULTS

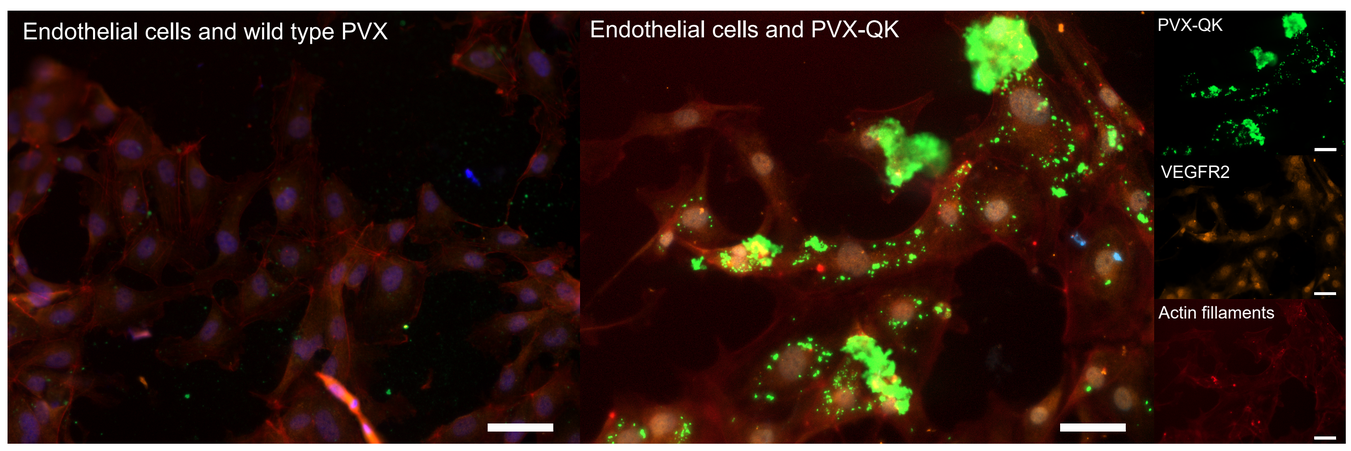


Figure 2. Immunostained interactions between the PVX nanoparticles and Endothelial cells. Scale bar is 50 µm

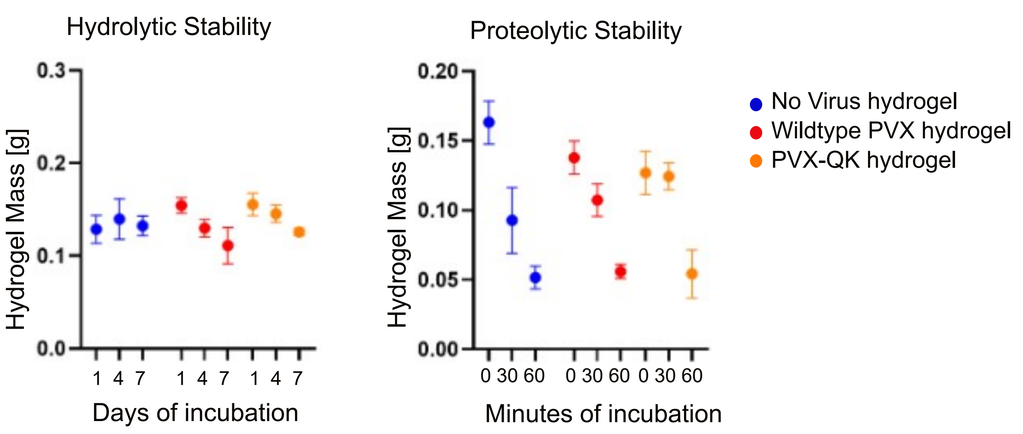


Figure 5. Hydrolytic and proteolytic stability of virus laden hydrogels.

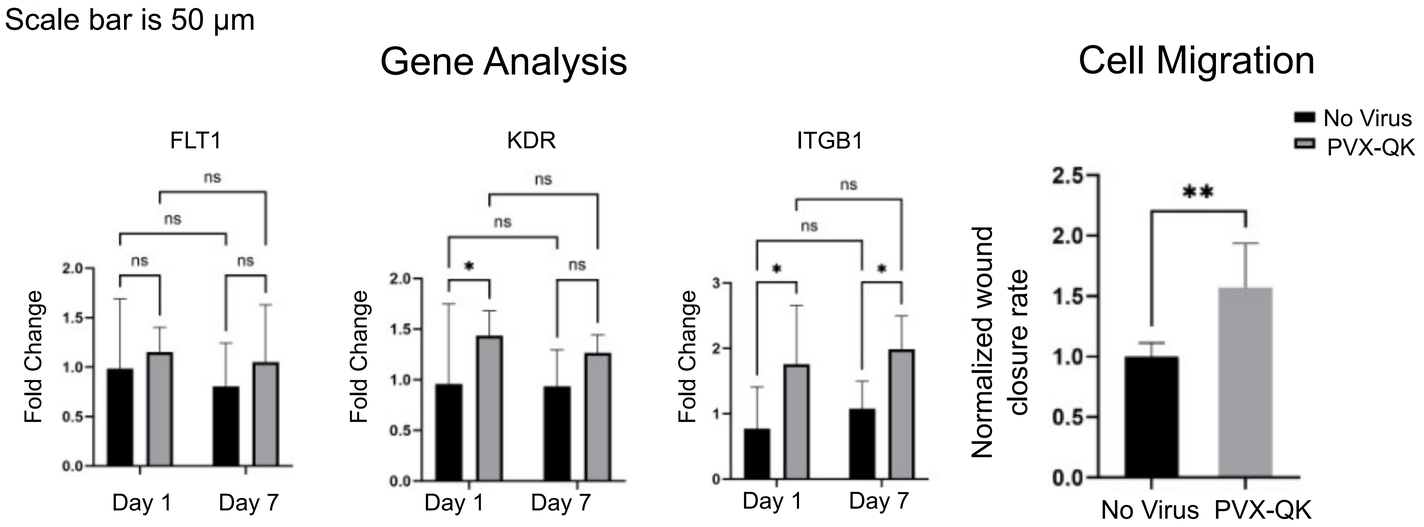


Figure 3. Gene analysis of angiogenesis related markers, and wound healing migration rate.

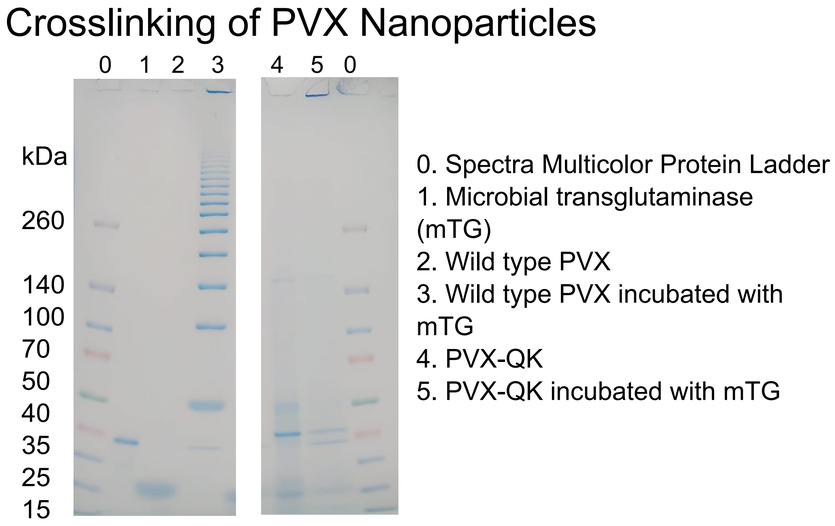
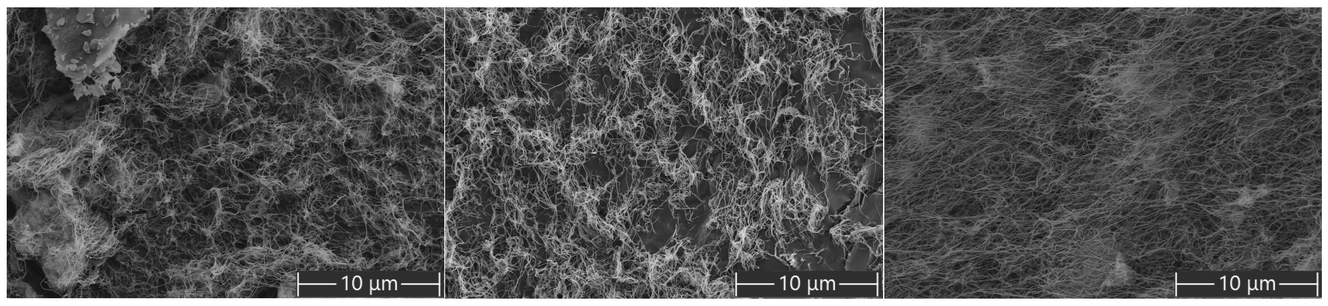


Figure 6. Crosslinked CP units of PVX wild type and PVX-QK

Microstructure of Virus-laden Hydrogels



No Virus wild type PVX PVX-QK

Figure 4. Scanning Electron Micrographs of Collagen-Fibrin, PVX-laden hydrogels. Scale bar is 10 µm

CONCLUSIONS

In conclusion, PVX-QK nanoparticles enhance angiogenesis parameters in endothelial cells while offering the potential to display a wide range of bioactive peptides, serving effectively as both media supplements and building blocks for stable 3D extracellular matrix hydrogels.

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