Background:

Stem cells possess immense wound healing potential. One of the common modes of delivering stem cells to the wound site is using stem cells-laden biomaterial scaffold. In this approach, stem cells are expanded before seeding onto the scaffold to generate a tissue-engineered construct. However, while expanding, the stem cells tend to lose their stemness. Currently, enhancing stem cells' stemness is one of the primary aims in generating stem cell-based products. Therefore, in this study, we sought to investigate if a collagen-based scaffold functionalized with an anti-aging β-klotho gene (gene-activated scaffold) could enhance the stemness and regenerative properties of stem cells.

Methods:

The gene-activated scaffold was first prepared by soak-loading nanoparticles of β-klotho plasmid/polyethyleneimine complex onto a freeze-dried porous collagen-chondroitin sulfate (coll-CS) scaffolds. Human adipose-derived stem cells (hADSCs) at passage 4 (5 x104 cells) were then seeded onto the gene-activated scaffold and cultured for two weeks. The cellular response was assessed on days 3 and 14 using qRT-PCR, secretome bioactivity assays and immunofluoroescene. hADSCs seeded onto gene-free coll-CS scaffold was used as control.

Results:

Figure 1 shows the graphical summary of the results. The hADSCs on the gene-activated scaffold showed prolonged expression of stemness factor Oct-4 and early activation of anti-fibrotic factor TGF-β3 relative to the control. Secretome bioactivity analyses showed that the hADSCs on the gene-activated scaffold could enhance angiogenesis and control fibrotic response in human adult dermal fibroblasts by reducing collagen I expression. Within the gene-activated scaffold, the hADSCs demonstrated a significant reduction in scar-associated α-SMA protein expression while enhancing the deposition of basement

membrane protein collagen IV by 8.8-fold than the control. The hADSCs on the gene-activated scaffold also deposited a relatively mature fibrous network of elastic protein elastin than the control.

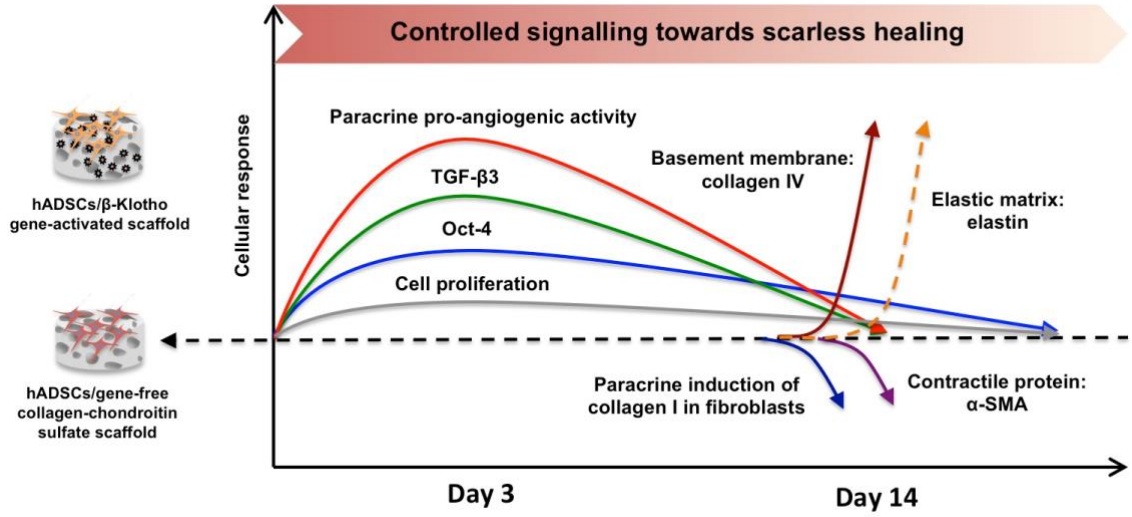

Figure 1: Impact of β-klotho gene-activated scaffold in hADSCs driven wound healing

Conclusion:

hADSCs/β-klotho gene-activated scaffold construct is a potential graft for scarless soft tissue repair.