18 - Title: Nanotech-Driven Angiogenesis: A Breakthrough in Plastic Surgery Recovery.

Background: Titanium dioxide nanoparticles (TiO_2 NPs) are highly regarded for their biocompatibility, antimicrobial effects, and light-scattering properties, making them promising candidates for various biomedical applications, particularly in regenerative medicine and wound repair. Previous studies indicate that TiO_2 NPs can enhance the activity of human umbilical vein endothelial cells (HUVECs) by upregulating adhesion molecules and inflammatory markers, suggesting a potential role in stimulating angiogenesis, a crucial process in effective wound healing. This study aims to examine the effects of TiO_2 NPs on angiogenesis in HUVECs, focusing on their role in vascular network formation and gene regulation.

Methods/Research Design. HUVECs were cultured with or without 0.1 mg/mL and 0.2 mg/mL Rutile TiO_2 nanoparticles for 24 hours to assess their impact on angiogenesis. Following treatment, cells were plated on 10 mg/mL Matrigel, and capillary formation was monitored every 20 minutes for 24 hours using EVOS fluorescence microscopy with a CO_2 on-stage incubator. Images from triplicate cultures were analyzed using Celleste Image Analysis software to quantify vascular network formation. Mechanical stress exerted by HUVEC networks on the substrate was evaluated using the Digital Image Speckle Correlation (DISC) method. To assess angiogenesis-related gene expression, RT-PCR was performed on TiO_2 NP-treated HUVECs at two time points: Day 0 (immediately after 24-hour exposure) and Day 1 (following an additional 24-hour incubation post-washing with PBS to remove excess NPs). Additionally, fluorescence-activated cell sorting (FACS) was used to determine TiO_2 NP uptake in HUVECs treated with 0.1 mg/mL TiO_2 NPs.

Results (or Preliminary Results, as applicable for a project in progress): HUVECs treated with TiO_2 nanoparticles exhibited more stable and extensive vascular networks, characterized by an increased number of branches, tubes, and nodes compared to the control group. Mechanical stress analysis indicated that TiO_2-treated cells applied less force on the substrate while forming these networks. SEM imaging confirmed the integration of TiO_2 nanoparticles within cellular structures, particularly within nodes and splines, while TEM analysis revealed that the nanoparticles were predominantly localized within vacuoles adjacent to mitochondria. Gene expression analysis via RT-PCR demonstrated a significant upregulation of VEGFR2 and HGF in HUVECs treated with 0.1 mg/mL TiO_2 over consecutive days. However, VEGF expression showed a delayed response, becoming upregulated only on the second day. These findings indicate that TiO_2 nanoparticles may indirectly enhance VEGF expression by first stimulating the production of other growth factors.

Conclusion (or Preliminary Conclusion, as applicable for a project in progress): This study demonstrates that TiO_2 nanoparticles enhance angiogenesis in HUVECs, suggesting potential applications in wound healing. Further research is ongoing to uncover the underlying mechanisms and confirm TiO_2's therapeutic potential in regenerative medicine.