

Nano-ink-mediated RNA therapy for non-invasive treatment of craniofacial disorders

Regenerative therapies for craniofacial disorders, including craniosynostosis (CS), remain a major clinical challenge due to the anatomical complexity of the craniofacial region and the limited availability of targeted, minimally invasive treatments. FGFR2-related CS is characterized by aberrant receptor activation, premature osteogenic differentiation of cranial suture cells, and early suture fusion.

In this context, we developed a bioactive nanocomposite ink for the localized and sustained delivery of small interfering RNAs targeting FGFR2 signalling. Patient-tailored siRNAs achieved up to 90% FGFR2 mRNA knockdown in CS-derived cells and reduced downstream activation of ERK1/2, and RUNX2, limiting pathological osteogenic differentiation and mineralized matrix deposition.

For controlled delivery, selected siRNAs were encapsulated into polymeric-based nanoparticles and embedded within a photocrosslinkable gelatin methacryloyl hydrogel. The resulting nano-ink was injectable, mouldable, and compatible with 3D printing. Printed constructs promoted nanoparticle retention and controlled siRNA release, maintaining functional gene silencing for up to 20 days.

By combining RNA nanomedicine and nanocomposite biomaterials, this platform provides a customizable strategy to locally modulate pathological osteogenesis, thereby supporting the restoration of the cranial suture niche in CS.