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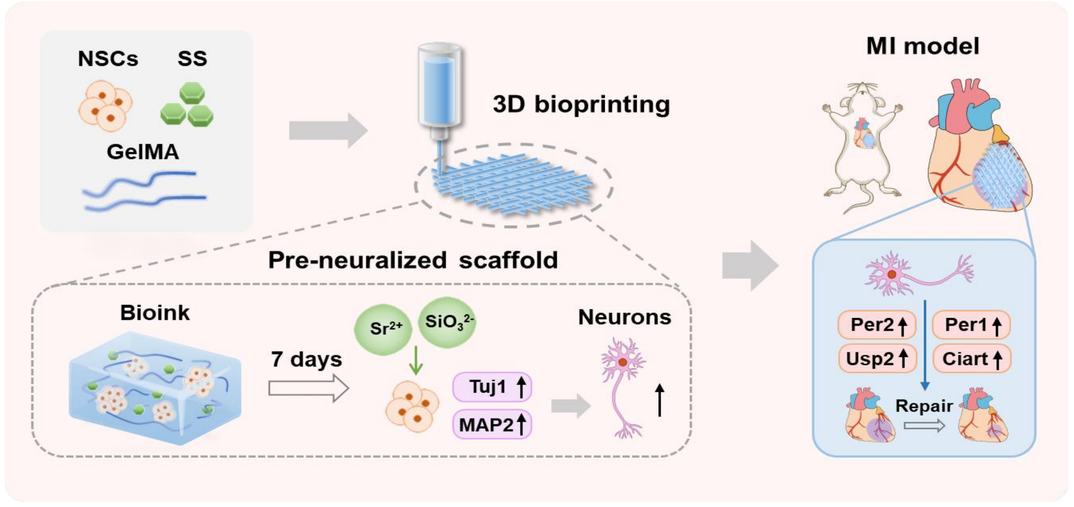
Inorganic Biomaterials Inducing Scaffolds Pre-Neuralization for Infarcted Myocardium Repair

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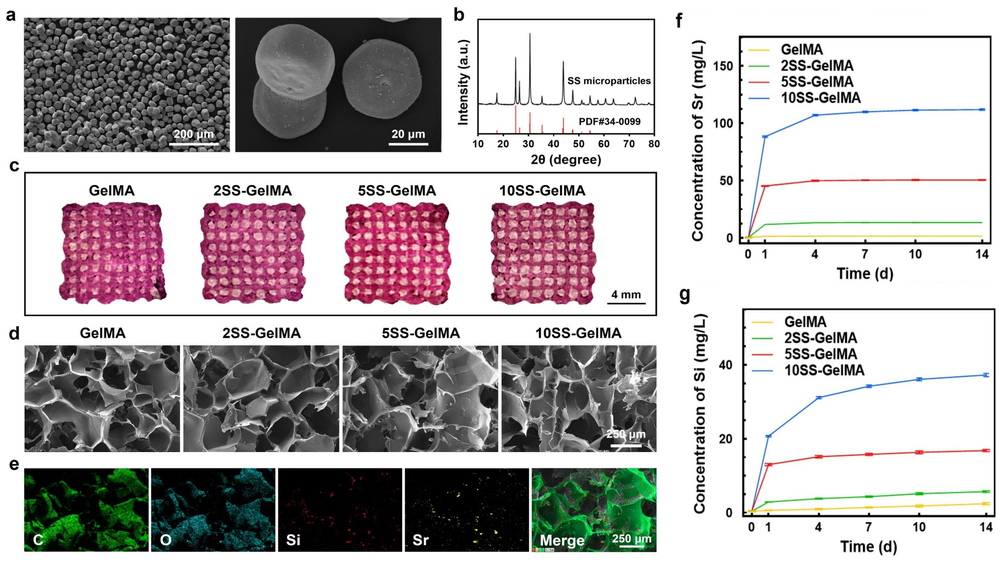
Abstract

In tissue repair, nerves can activate and promote intrinsic tissue regeneration, offering a potential therapeutic strategy for irreversible injuries. Neurons play a positive role in cardiac repair, and neural stem cells (NSCs) are an important cell source due to their neuronal differentiation potential, yet their differentiation uncertainty limits clinical application. Silicate ceramics show significant potential in regulating cell behavior; using them as bioactive factors to guide NSC lineage-specific differentiation is a promising direction. This study constructed a 3D bioprinted NSC scaffold loaded with strontium silicate (SS) microparticles, which effectively promoted NSC differentiation and achieved scaffold pre-neuralization. In vitro and in vivo experiments confirmed that the pre-neuralized scaffold enhanced cardiac repair and improved function by upregulating circadian-related genes expression.



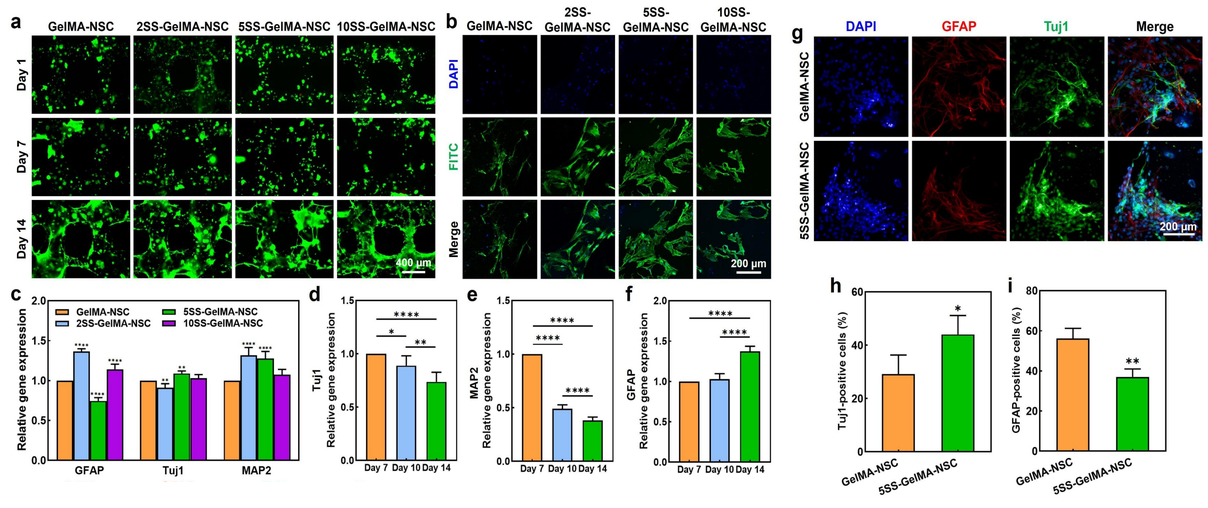
Result

Characterization of the 3D bioprinted scaffold.



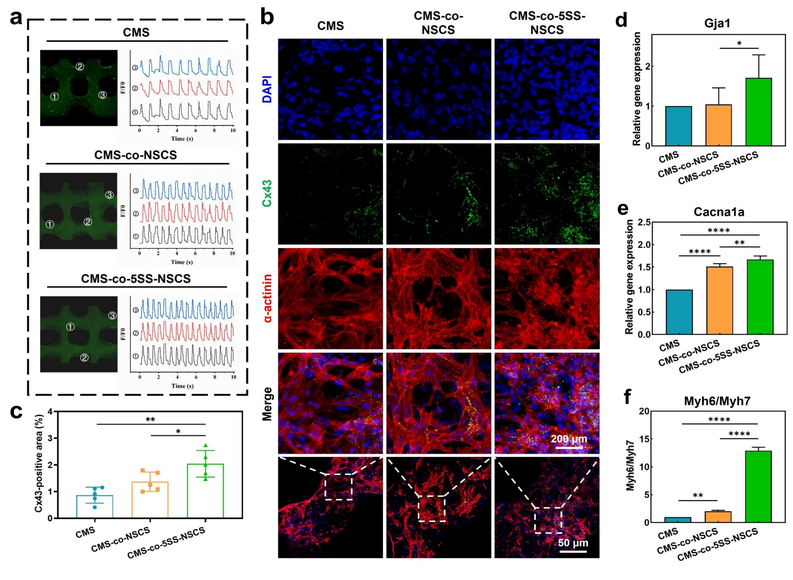
SS microparticles capable of releasing Sr and Si ions were prepared via a hydrothermal method, and a hydrogel scaffold loaded with NSCs and SS was subsequently constructed using 3D bioprinting technology.

Strontium silicate-guided pre-neuralization of NSC-laden scaffolds.



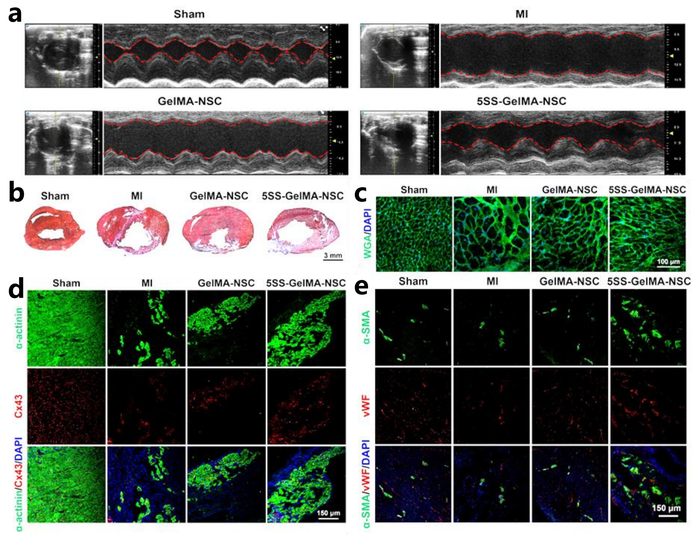
SS-containing bioinks induced the differentiation of NSCs into neurons and promoted their maturation.

Pre-neuralized scaffolds promoted in vitro functionalization of cardiomyocytes.

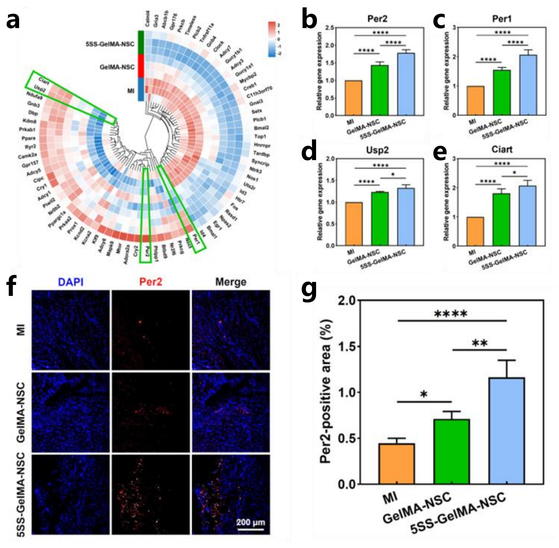


SS-based pre-neuralized scaffolds activated cardiomyocyte maturation and improved contractile function.

Pre-neuralized scaffolds promoted myocardial repair and activated cardioprotective circadian-related genes in rats.



SS-based pre-neuralized scaffolds enhanced rat cardiac contractile function and promoted infarct region repair.



Pre-neuralized scaffolds upregulated the expression of circadian-related genes and proteins associated with cardioprotection.

Conclusion

- SS can regulate the differentiation direction of NSCs by releasing Si and Sr ions, thereby achieving pre-neuralization of NSC-laden scaffolds.
- Pre-neuralized scaffolds were found to promote cardiomyocyte functionalization by activating circadian-related genes in cardiomyocytes. This provides a systematic perspective on the relationship between nerves and myocardial repair.
- In a rat model of myocardial infarction, pre-neuralized scaffolds improved ventricular remodeling and enhanced cardiac function within four weeks, offering a promising new approach for the treatment of myocardial infarction.