ION CONDUCTIVE GUANOSINE-QUADRUPLEX (GQ) HYDROGELS FOR ADVANCING IN VITRO 3D CARDIAC TISSUE MODELS

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1. Introduction

Cardiovascular disease such as myocardial infarction is the primary cause of death[1] among cardiac patients, demanding a significant increase in preventive interventions in the field of regeneration medicine. In this direction, the bio-inspired hydrogel matrices have demonstrated a broad range of applications, from facilitating cell encapsulation in advanced 3D cultures and tissue models to supporting cell-based therapeutics and tissue engineering.

2. Objectives

With this, we aim to develop bio-inspired guanosine-quadruplex (GQ) hydrogel to provide a regenerative microenvironment for cardiac tissue regeneration. G-quadruplexes, four-stranded supramolecular structures have garnered significant attention due to their unique self-assembly, inherent ion-conductive properties and diverse biological functions.[2] During our project we have developed biogenic molecules induced ion-conductive GQ hydrogels to provide a favorable environment for cardiac cells. In this presentation, I will discuss how the unique conductive and hierarchical 3D fibrous network, along with the biocompatibility of GQ hydrogels, pave its way for cardiac cell culture for the development of 3D cardiac tissue models of increasing physiological relevance.

3. Methods

GQ hydrogels were formulated from guanosine analogues in variable concentrations (50-300 mM) combined with diverse biopolymers (chitosan, hyaluronic acid; at 0.1-1 wt%) and calcium ions (0-40 mM). Curing kinetics and mechanical properties were characterized via rheology, morphological characterization was performed via SEM, formation of GQ structures was studied by diverse optical methods (CD and fluorescence spectroscopies), and ion conductivity was measured via electrochemical impedance spectroscopy (EIS). Moreover, hMSCs were cultured on and within GQ hydrogels to test their cytotoxicity as well as ability to support cell culture.

4. Results

GQ hydrogels with stiffness values around G'=10-100 kPa and that remain stable under cell culture conditions for at least one week were successfully formulated. The physically crosslinked 3D hydrogel scaffold via self-assembly dictated the responsive and rapid gelation under physiological conditions. Mechanical stability and ion conductivity of the hydrogel were enhanced upon introduction of calcium ions. The unique conductive and hierarchical 3D fibrous and porous network of GQ hydrogels, proved to support cell culture.

5. Conclusion

GQ hydrogels were successfully formulated as matrices that support the culture of cells. The ionic-crosslinking and hydrogen bonding enable hydrogel scaffolds with faster gelation time, fibrillar microstructure, tunable mechanics, and regulable biological properties, which makes it a promising smart material for engineering tissue models, e.g, cardiac tissue models.

6. References

1. *Townsend, N.; Wilson, L.; Bhatnagar, P.; Wickramasinghe, K.; Rayner, M.; Nichols, M., Cardiovascular disease in Europe: epidemiological update 2016. Eur. Heart J. 2016, 37, 3232–3245.*
2. *Li, X.; Sánchez-Ferrer, A.; Bagnani, M.; Adamcik, J.; Azzari, P.; Hao, J.; Song, A.; Liu, H.; Mezzenga, R., Metal ions confinement defines the architecture of G-quartet, G-quadruplex fibrils and their assembly into nematic tactoids. Proc. Natl. Acad. Sci. 2020, 117, 9832.*