

Hyaluronic Acid - Alginate Hydrogel for the Transdifferentiation of Testis Cells into Erythrocyte and Hepatocyte-like Cells; A Practice Within an Effective Agent Choice

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Abstract : Background: Spermatogonia stem cells (SSCs) exhibit pluripotency, enabling them to undergo differentiation into many cell lineages, including neurons, glia, endothelial cells, and hepatocytes when cultured in vitro. Although the specific mechanisms are not yet fully understood, it has been observed that biopolymer agents, such as hyaluronic acid (HA) and alginate (Alg), have the potential to induce transdifferentiation of SSCs. The current work aimed to examine the process of in vitro spermatogenesis and the conversion of mouse testicular cells into hepatocytes and erythrocyte-like cells utilizing the HA-Alg hydrogel. Method: After being extracted from the testes of a 5-day postpartum mouse (5 DPP), the testicular cells were separated into two enzymatic stages and then put into a composite hydrogel containing 0.5% HA and 1% alginate. On days 14 and 28 of culture, the colonies' growth, the cells' viability, and their histology were assessed. Result: Despite observing significant cell proliferation on day 14 and the development of circular-shaped organoids on day 28, it was noted that the organoids generated in the HA-Alg medium tended to maintain their circular morphology on day 28. Notably, the testicular cells underwent transdifferentiation into cell types resembling erythrocytes and hepatocytes. The hepatocyte-like cells exhibited the presence of glycogen and lipid deposits, indicating their hepatocyte-like characteristics. Interestingly, immunostaining analysis revealed the secretion of albumin and the presence of VEGFR on day 14. However, on day 28, albumin expression was not detected, while the expression of Sox9 (a marker for hepatocytes), Vegf, CD34, and C-kit (markers for erythrocytes) showed increased levels in the gene expression evaluation. Conclusion: The present findings indicated that HA-Alg could be a potent and effective agent for the transdifferentiation of testis cells into erythrocyte and hepatocyte-like cells, as recent studies have confirmed the transformation of SSCs into hepatocyte cells during in vitro culture.

Keywords : 3D culture, mouse testicular cell, hyaluronic acid, liver organoids

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