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SHORT COMMUNICATION

Microfluidic encapsulation of cells in alginate particles via an improved internal gelation approach

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Abstract An improved internal gelation approach is developed to encapsulate single mammalian cells in monodisperse alginate microbeads as small as 26 μm in diameter and at rates of up to 1 kHz with high cell viability. The cell damage resulting from contact with calcium carbonate nanoparticles as gelation reagents is eliminated by employing a co-flow microfluidic device, and the cell exposure to low pH is minimized by a chemically balanced off-chip gelation step. These modifications significantly improve the viability of cells encapsulated in gelled alginate particles. Two different mammalian cell types are encapsulated with viability of over 84 %. The cells are functional and continue to grow inside the microparticles.

Keywords Single cell encapsulation · Alginate · Droplet-based microfluidics

1 Introduction

Cell encapsulation in hydrogel microbeads has promising applications in tissue engineering, regenerative medicine, and cell-based drug delivery (Drury and Mooney 2003; Pierigè et al. 2008; Slaughter et al. 2009; Schmidt et al. 2008; Nicodemus and Bryant 2008; Xu et al. 2009). Encapsulated cells can secrete therapeutic proteins in response to an external stimulus over an extended time period to treat various diseases including renal failure and diabetes (Sun et al. 1996; Prakash and Chang 1996). In cell transplantation therapy for ischemic heart diseases, direct injection of cells results in limited cell survival, while encapsulation in hydrogels improves cell growth and transplantation efficiency (Chachques et al. 2007; Yu et al. 2010). Of all hydrogels, alginate is one of the most suitable biomaterials for cell encapsulation due to its biocompatibility, biodegradability, similarities to the natural extracellular matrix, and ease of gelation (Lee and Mooney 2012). Alginate is a naturally derived polymer, which can physically cross-link with divalent ions to provide an ideal three-dimensional scaffold for cells that allows bidirectional diffusion of nutrients and waste products.

Alginate particles are typically produced by ejecting drops of alginate solution into a bath of divalent ions resulting in millimeter-sized polydisperse beads (Maguire et al. 2006; Hoesli et al. 2011; Mazzitelli et al. 2011). However, for use as carriers of drugs, proteins, or cells, it is desirable to precisely control particle size and monodispersity. Droplet-based microfluidics offers a powerful method to rapidly produce monodisperse alginate microdroplets with diameters of up to a few hundred micrometers (Tan and Takeuchi 2007; Capretto et al. 2008; Workman et al. 2008; Martinez et al. 2012; Teh et al. 2008; Choi et al. 2007). Smaller hydrogel particles (<50 μm in diameter) are

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