NANOTHERMITE-BASED MICROSYSTEM FOR DRUG DELIVERY AND CELL TRANSFECTION

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ABSTRACT

This paper describes a new system for pressure-induced cell transfection. The system generates pressure pulses from a microchip that contains a small quantity of nanothermite material and an electrical igniter. The pressure output from the nanothermite reaction is coupled to the biological target through a PDMS membrane and a tube filled with gelatin. The system generates pressure pulses in the range of 10-40MPa. It has been used to transfect primary cells with 99% transfection rate and cell survival. It has also been used to transfect cell lines (Hela, HL-60, and HT-29). In all cases survival was >99%, and transfection rate in Hela, HL60 and HT-29 was up to 37 60 and 30% respectively. In addition, the system has been shown to transfect intact spinal cords and arteries from chicken (St 30) with no noticeable damage.

1. INTRODUCTION

One of the major obstacles in the development of gene therapy is the effective delivery of the genetic material into the target cells. (Orive et al. 2003) There are many existing techniques, which include physical, chemical, bacterial, and viral.(Baldi et al. 2007; Bergen et al. 2007; Cemazar et al. 2006; Chan et al. 2005; Gao et al. 2007; McCaffrey; Kay 2002; Plank et al. 2003; Racz; Hamar 2008; Recillas-Targa 2006; Rettig; Rice 2007; Simoes et al. 2005; White et al. 2007) However, what is lacking is a system that allows the maximal transfection rates (ideal >99%) with minimal damage (<1%) and high survivability rates (>99%).

One promising method is the use of pressure pulse to permeabilize cells. (Frairia et al. 2003; Kendall 2002; Kodama et al. 2000; Kodama et al. 2002, 2003; Koshiyama et al. 2006; Lee et al. 2000) The majority of research on shock-induced cell permeabilization has been conducted using energy sources based on either laser-ablation or gas-driven shock-tubes. Due to system limitations this research has resulted in low transfection rates of dyes.

An alternative approach to generating pressure waves, which has not been fully explored for drug delivery, is the energy profile generated by the reaction of energetic materials. This is mainly due to the narrow categories of conventional energetic materials (e.g. propellants or high explosives) and the limited ranges of performance tunability. The tunability of energetic output is essential to optimize delivery and minimize cell/tissue damage.

A relatively new finding is that certain types of nanothermite materials are capable of producing a unique pressure pulse when they are ignited.(Apperson et al. 2007) For example, the composition consisting of copper oxide (CuO) nanorods and aluminum (Al) nanoparticles has been shown to have combustion velocities in the same range as the heavy-metal azides, including metallic azides and fulminates but produce pressure levels much lower than those predicted by CJ theory.(Apperson et al. 2007; Bowden; Williams 1951; Shende et al. 2006a) In addition, these materials exhibit levels of performance tunability not seen within any conventional class of energetic materials.(Shende et al. 2006a; Shende et al. 2006b)

In this work, we present a micropyrotechnic-based system in which a nanothermite energy source is coupled to a biological target for gene transfer and drug delivery. Characterization of the pressure waves generated by the system is discussed, and the results of delivering plasmid into primary cells, cell lines, and tissues are presented.

2. EXPERIMENTAL

2.1 Nanothermite Preparation

Nanothermite mixtures consisting of Bi_2O_3 nanoparticles and Al nanoparticles were used for the transfection experiments reported herein. The Bi_2O_3