

## **FLUID MECHANICS CONSIDERATIONS OF GENE AND DRUG DELIVERY TO SKIN AND IMMUNE RESPONSES IN THE BODY**

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Despite its broad utility, with billions of administrations each year, drug delivery with the needle and syringe has many limitations. Perhaps most importantly, is the inability to deliver genes and drugs to immunologically-sensitive antigen presenting cells—called Langerhans cells—resident just below the skin surface (e.g.  $< 50 \mu\text{m}$ ) in very high numbers. This targeting shortcoming limits the effectiveness of a range of DNA targeting strategies in the vaccination and immunotherapy of key diseases.

In this paper, we examine the fluid mechanics of a needle-free method configured for delivering genes and drugs to these skin cells. The concept, called *biolistics*, applies the principle of supersonic rocket nozzle flow to drug delivery. Pharmaceuticals in particle form are accelerated in a hand-held supersonic injection system to a momentum sufficient to penetrate the outer layer of the human skin to target epidermal cells. The fluid mechanics of prototype devices is presented, with a focus on the supersonic gas-particle dynamics of particle acceleration—quantifying an “input” to the skin surface. We then examine the induced physiological “response” in the skin. This begins with an analysis of the effectiveness of targeting DNA to Langerhans cells. Then, we discuss what is known of the subsequent trafficking of Langerhans cells via the lymphatic system to resident lymph nodes—with a focus on current fluid mechanics approaches and challenges.