NOVEL PULSATILE-RELEASE MICROPARTICLES FOR SINGLE-INJECTION VACCINATION

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Many controlled release devices are designed to achieve near zero-order release kinetics, however for some applications, such as vaccination, non-continuous or pulsatile release is desired. Such pulsatile release systems may enable the creation of single-injection vaccines that eliminate the need for subsequent booster immunizations by spontaneously releasing antigen at time points that correspond to normal vaccination regimens. This would be especially important in the developing world where a lack of consistent access to healthcare contributes to approximately 1.5 million vaccine-preventable deaths each year.1 Here we present the fabrication and characterization of biodegradable core-shell microparticles that exhibit pulsatile release kinetics due to their unique structure. These particles are produced using a novel fabrication process that combines soft lithography, picoliter dispensing, optical alignment, and a gentle heat-based sintering step to generate microparticles with a biodegradable polymeric shell surrounding an antigen-filled core. By altering the composition (e.g. copolymer ratio or molecular weight) of the poly(lactic-co-glycolic acid) shell, particles can be tuned to release discrete pulses of a model antigen at times ranging from four days to two months. This fabrication method is also compatible with sensitive biologics, such as the inactivated polio virus, which retains >80% of its antigenicity after encapsulation. Further, because the shell of the particle is physically separated from the core, these particles can be filled with any aqueous vaccine solution without affecting release kinetics and be easily scaled via massively parallel fabrication. As a result, these particles have exciting potential as single-injection vaccines that fully mimic the antigen presentation profile of traditional bolus injections administered over the course of months or years.


Figure 1 - Microfabricated particles exhibit delayed burst release kinetics. A) Diagram depicting particle sealing by heat and pressure-assisted sintering of PLGA bases and caps. B) One particle base prior to filling and sealing. C) Particle array after sealing. D) Diagram of multiple particles being injected with varying composition and therefore release timing. E) Representative in vivo release of fluorescently-labeled dextran from microfabricated particles. F) In vivo release kinetics (n = 6-9)