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Rational design of a fully synthetic nanoparticle-based vaccine

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Vaccines for the prophylaxis of infectious diseases have been one of the most effective interventions for improving human health. Recent advances in immunology and vaccine technology have opened the door to novel vaccine-based therapies for the therapeutic treatment of chronic diseases, such as cancer, chronic infections, allergies, and autoimmune diseases. Here we describe the rational design of SEL-068, an entirely synthetic, self-assembling nanoparticle-based vaccine against nicotine, for smoking cessation. SEL-068 is comprised of four main components: 1) a biodegradable and biocompatible polymer matrix; 2) a synthetic TLR agonist; 3) an encapsulated peptide that serves as universal antigen (Ag) for eliciting T helper cells; and 4) a B cell antigen, nicotine, that is covalently conjugated to the nanoparticle surface. The nanoparticles self-assemble from basic synthetic building blocks, enabling cost-efficient manufacturing. The nanoparticles are designed to flow freely to the lymph nodes enabling direct and concomitant delivery of all required components to the responsive cells of the immune system. Encapsulation and controlled release of the TLR agonist in the nanoparticle minimizes the generation of systemic inflammatory cytokines, improving the overall safety profile and enabling the use of novel adjuvants. The novel universal T cell helper peptide elicits T cell recall responses in PBMC from a broad panel of human donors. No dose-limiting systemic toxicities were observed in a repeat-dose GLP safety and efficacy study in cynomolgus monkeys. A robust and dose dependent induction of high titer anti-nicotine antibodies was demonstrated. SEL-068 is currently being evaluated in Phase 1 clinical trials.

Biography

Dr. Kishimoto is the Chief Scientific Officer of Selecta Biosciences, a biotechnology company developing synthetic vaccines based on a novel self-assembling nanoparticle technology. Prior to joining Selecta, he was Vice President of Research at Momenta Pharmaceuticals where he led a multidisciplinary team in advancing both novel and complex generic products. Previously he held leadership positions at Millennium Pharmaceuticals and Boehringer Ingelheim. Dr. Kishimoto has published over 50 peer-reviewed articles, including articles in Nature, Science, Cell, and the New England Journal of Medicine. Dr. Kishimoto received his doctoral degree in Immunology from Harvard University and his post-doctoral training at Stanford University.

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