An influenza subcomponent vaccine with Th1 polarization using the TLR3-specific adjuvant, ARNAX.

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The purpose of this application is to submit ARNAX, a non-inflammatory, non-toxic adjuvant, for approval and to provide it for human influenza HA vaccine. ARNAX is a DNA/RNA hybrid nucleic acid adjuvant that targets only TLR3 of human antigen-presenting dendritic cells (XCR1+ DC). Subcutaneous administration in animals has been shown to activate cross-antigen presentation and T/B lymphocyte activation without inducing adverse reactions such as cytokinemia. In other words, ARNAX has led to the knowledge that immunity is independently established from inflammation. This and the fact that ARNAX is degraded to natural nucleic acids and barely detected in the bloodstream in animal models, make the invention of this adjuvant a safe method of immunopotentiation that goes beyond conventional concepts.

Alum has been used in many vaccines to prevent infectious diseases; TLR adjuvants have not been approved, but TLR4, 7, and 9 have been repeatedly tested. They are not expressed on human XCR1+ DC and are all linked to an inflammation-inducing adaptor called MyD88. Thus, systemic cytokinemia cannot be avoided and safety is compromised. There is a need to develop an adjuvant that is more effective and safer than Alum or MyD88 adjuvant, and that can be used universally for vaccines against infectious diseases.

In contrast, only TLR3 exceptionally employs TICAM-1 as the adaptor instead of MyD88. TLR3 is highly expressed on antigen-presenting dendritic cells. Thus, ARNAX creates a favorable environment for Th1-biased CTL induction. We have established a chemical synthesis method for nucleic acid adjuvants that fulfills this purpose, and have demonstrated in preclinical studies that vaccines against cancer and infectious diseases can be created without adverse events. We will obtain a preclinical POC for a HA antigen + ARNAX vaccine, and look forward to a Ph1 study. HA vaccines are safe but induce only a transient increase in antibodies, and fail to trigger memory and durable immunity.

During this study period, we will demonstrate the preclinical POC and safety of ARNAX + HA antigen, consider GMP manufacturing of ARNAX, establish a standard API, working with HA antigen providers.

The timing and antigens of a pandemic are unpredictable, and the countermeasures tend to be uneconomical. If safe adjuvants are always available, it is possible to provide safe and effective vaccines against any infectious diseases in a short period of time by adjusting mutant antigens and specific antigens as necessary, confirming the quality of the antigen for vaccine.