A.I.R® Vaccines – A Powerful RNA-Based Platform Against Infectious Diseases

The Platform

Past and recent epidemic viral outbreaks have taught that emerging viruses can quickly cause a global calamity. Conventional vaccines, which are usually based on inactivated or engineered viruses, cannot be produced fast enough to stop newly emerging viral threats. As globalization also reaches remote locations, new vaccine approaches are urgently needed to respond quickly to emerging diseases that may become epidemic threats (Figure 1). To meet this challenge, we are developing an innovative self-amplifying RNA-based Ribological® RNA Amplicon vaccine platform against Infectious Diseases (A.I.R® - Amplified Immune Response) that will allow provision of up to millions of doses of prophylactic vaccines for a given viral threat within the shortest time possible. We are using our knowledge and extensive experience with mRNA vaccines in clinical trials for cancer immunotherapy for the development of the A.I.R® vaccines. Our goal is not only to establish RNA-based vaccines for human use but also to stop outbreaks before they spread globally as a pandemic.

A.I.R® vaccines are characterized by:

- Fast adaptation to rapidly evolving viral strains using synthetic genomic technology
- Favorable safety characteristics of synthetic RNAs
- Short manufacturing times and low costs
- Strong immune-stimulatory potency due to an intrinsic adjuvant activity
- Scalability of cell-free GMP-grade production with a turn around of less than three weeks
- Versatility to improve immune responses by combination of various vaccine targets

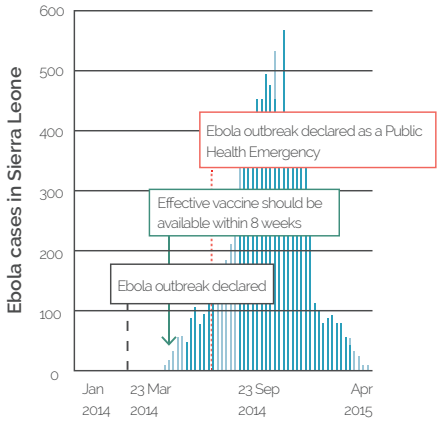

Figure 1: The concept of just-in-time vaccines based on the weekly reported Ebola cases in Sierra Leone of the outbreak that started in 2014 (Patient Database Source: World Health Organization). Our aim is to produce A.I.R® vaccines genetically matched to the respective outbreak viral strain at the latest eight weeks after declaration of an outbreak and before it is declared out of control.

The Technology

A.I.R® vaccines are based on pharmacologically optimized in vitro transcribed, self-amplifying RNA derived from an alphaviral genome. Compared to non-amplifying RNA, self-amplification and subgenomic transcription of self-amplifying RNA results in higher antigen expression (Figure 2); since innate immunity effectively prevents persistent replication, the self-amplifying RNA is considered comparable to non-amplifying mRNA in terms of safety.

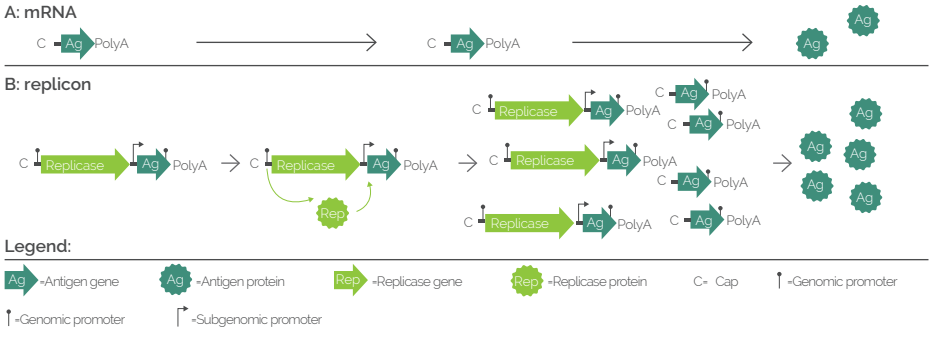

Figure 2: From delivery to expression. A: in vitro transcribed mRNA is translated immediately upon cytoplasmic delivery. B: in vitro transcribed self-amplifying RNA first translates replicase immediately upon cytoplasmic delivery which mediates self-amplification and subgenomic transcription resulting in intracellular amplification of antigen RNA. Subgenomic transcripts are then translated to high amount of the antigen of interest.

The mode of action of A.I.R® vaccines is comparable to our RNA-based anti-cancer vaccines. Upon delivery of mRNA into a patient's target cell, the encoded protein is produced as a pharmacologically active product that induces protective neutralizing antibody and cytotoxic T-cell responses (humoral and cellular immune response). Due to an intrinsic adjuvant activity of the A.I.R® vaccines, no additional adjuvant is required to drive an effective immune response.

Our Vision

... is to use A.I.R® for the development of infectious disease vaccines.
... is to make A.I.R® a standard tool for rapid response vaccine strategies against viral threats.
... is to apply the A.I.R® vaccine platform to many emerging viral infectious diseases by either a warehouse approach comprising pre-characterized (and pre-manufactured) "off-the-shelf" vaccines or on-demand sequence tailoring and fast de novo production of self-amplifying RNA vaccines.

Our Evidence

We have proven the potency and efficacy of the A.I.R® vaccine approach in a preclinical influenza model and have shown robust protective immunity (Figure 3).

- A.I.R® vaccines induce strong T cell and neutralizing antibody response.
- A.I.R® vaccines protect mice against live viral challenge.
- Protection is achieved with a single intramuscular vaccination (prime only).
- Protection is achieved at extremely low doses (submicrogram).
- Formulation of A.I.R® vaccines enhances anti-infective capacity.

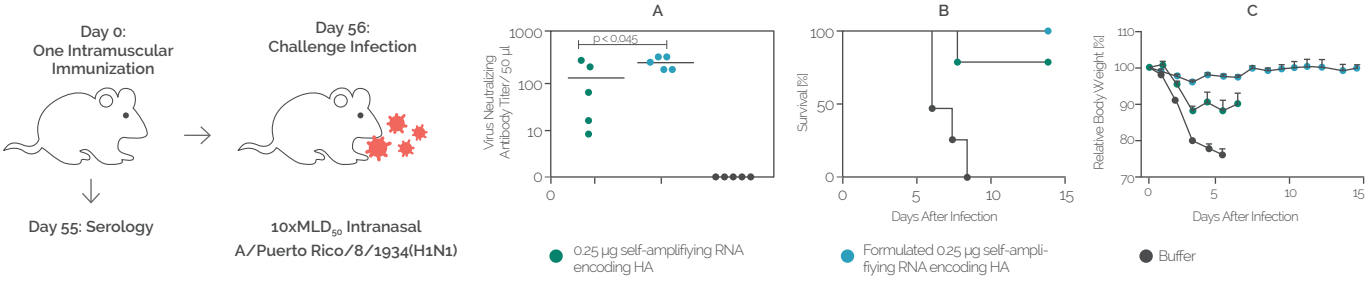

Figure 3: Strong efficacy of BioNTech's A.I.R® influenza vaccine using low doses. Mice were immunized once with 0.25µg self-amplifying RNA encoding hemagglutinin (HA) or with 0.25µg formulated self-amplifying RNA encoding HA. Vaccinated mice developed an antibody response with a significant increase of antibody titer by formulation (A). All mice immunized with the formulated vaccine survived a following lethal challenge infection with influenza virus (B) and showed no weight loss over time (C).

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