Attivare Therapeutics
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Localizing immune reactions to unlock major markets for infectious disease vaccines

Attivare Therapeutics is developing vaccines that offer an amplified humoral and cellular immune response to target infectious diseases with a single-shot option.

Attivare Therapeutics is positioned to transform the management of infectious diseases that affect more than one billion people every year[1,2]. By localizing immune responses, the biotech's vaccines trigger amplified, multicellular reactions, unlocking opportunities that are inaccessible to conventional technologies and make single-shot, long-term protection a reality.

Using established vaccine technologies, the antigen disperses, is recognized throughout the body, and primarily triggers antibody producing cells. Such traditional vaccines cause transient local inflammation and limited durability of response. Attivare's technology, which was developed at the Wyss Institute at Harvard University, Boston, Massachusetts, United States, focuses the immune reaction to change the intensity and type of response.

Vaccines developed using the technology feature one or more antigens associated with a silica-based solid material, plus an immune modulator to enhance the initial response. Associating the antigens with the biomaterial scaffold and immune agonists nucleates the immune reaction at one site. At that site, the scaffold recruits and exposes a variety of immune cells, not just antibody producing cells, to an inflammatory microenvironment (Fig. 1).

The approach provides durable humoral and cellular immune responses that make single-shot, long-term protection possible. Other advantages include dose sparing (because less antigen is needed to trigger an effective immune response) and the ability to manufacture multivalent products in a simple process.

Attivare has validated the technology with various vaccine materials in multiple preclinical experiments in mice and other animals. Internally, the biotech is applying the technology to cancer but the tests also suggest significant opportunities in infectious diseases that it wants to pursue with partners.

The biotech sees three main infectious disease partnering opportunities: a urinary tract infection (UTI) vaccine; a universal influenza vaccine; and improving response to novel, but poorly immunogenic, antigens.

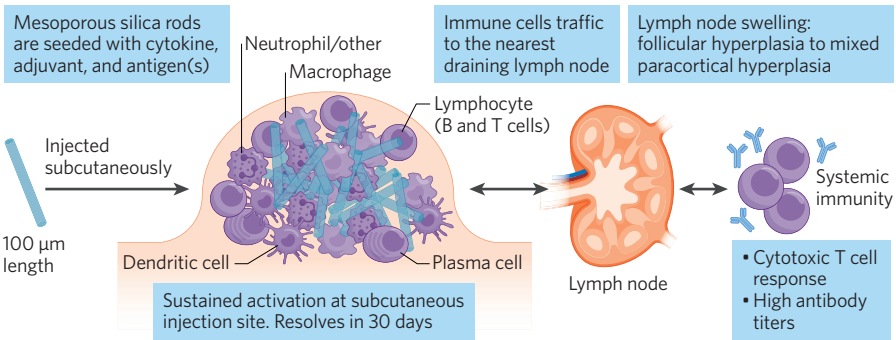

Fig. 1 | The AttImmune technology platform. The biomaterial scaffold recruits, reprograms, and releases target immune cells in an inflammatory microenvironment, and focuses on both poorly immunogenic tumors and infectious diseases.

UTI vaccine

Many women have at least one UTI during their lifetime and, while antibiotics can clear the initial infection, 27% of people have a recurrence within six months[3]. Eighty percent of cases are caused by a specific bacterium, uropathogenic *Escherichia coli* (UPEC), that needs surface adhesion proteins for its virulence.

Adhesion proteins enable the pathogen to bind to bladder epithelial cells and avoid clearance by antibiotics. As such, the proteins are a key driver of the recurrent infections that necessitate repeat treatments with antibiotics. Repeat treatment is a burden on patients and raises the risk of drug resistance.

The role that adhesion proteins play in recurrent UTIs creates an opportunity to vaccinate against the pathogen, but the immune responses triggered by conventional technologies are unable to clear UPEC from the bladder epithelium or stop the pathogen from penetrating cells in the first place. The limitations of conventional technologies stem from their reliance on transient exposure of immune cells to antigens, which results in a transient humoral response.

While systemic antibodies alone are largely ineffective in the bladder epithelium, other types of antibodies and immune cells can clear bacteria from that part of the body. Research shows a multicellular response is needed to clear bacteria from the bladder epithelium, suggesting that Attivare's vaccine technology is ideally suited to the indication.

Universal influenza vaccine

There is also strong, early evidence that the technology is a good fit for the development of a universal influenza (flu) vaccine. Currently, vaccines are changed each year based on a forecast of which influenza strains will be dominant during the flu season. The need to make predictions many months before the start of the flu season means forecasts can be inaccurate. When that happens, flu vaccines provide little protection.

The presence of influenza epitopes that are conserved as the virus mutates suggests it could be possible to develop a vaccine that is effective against all strains. However, conventional technologies are yet to deliver a universal flu vaccine. The technologies have so far proven unable to trigger the strong, focused responses to conserved influenza epitopes that are needed to protect people against the virus.

By triggering an amplified, multicellular immune response, Attivare's vaccine technology could provide strong, durable activity against conserved epitopes and fundamentally change how we protect people from the influenza virus.

Novel, but poorly immunogenic, antigens

The amplified immune response is key to Attivare's third partnering opportunity. Vaccine development efforts can be hampered when target antigens are poorly immunogenic. Focusing the immune response on the scaffold allows Attivare to trigger a stronger response and expand the pool of antigens that can support effective vaccines.

Attivare's preclinical tests suggest it has developed a transformational technology for infectious disease vaccines. With the biotech focusing its internal resources on cancer applications, there are opportunities for partners to use the platform to address major unmet medical needs.

1. Yang, X. et al. *Front. Public Health* **10**, 888205 (2022).
2. The Number of Flu Cases Worldwide: A Global Perspective. https://www.familiesfightingflu.org/number-of-flu-cases-worldwide/ (2022).
3. Medina, M. & Castillo-Pino, E. *Ther. Adv. Urol.* **11**, 1756287219832172 (2019).

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