ImmunityBio, LLC
www.immunitybio.com

Fighting a war on two fronts: ImmunityBio targets cancer and COVID-19

ImmunityBio is applying its second-generation human adenovirus 5 vaccine platform, used as part of its orchestrated multi-modal treatment approach to advanced cancer, to prevent COVID-19.

The SARS-CoV-2 pandemic crisis and COVID-19 disease has brought into sharp focus a critical observation about viral diseases and cancer: both display high infectivity—metastasis in cancer—and an ability to subvert the host immune response to create a microenvironment favorable to their own survival.

ImmunityBio, Inc. is a privately held immunotherapy company dedicated to effectively activating the immune system to seek out, attack and destroy cancer cells or viral particles and has one of the broadest portfolios of biological molecules spanning albumin-linked chemotherapeutics, peptides, fusion proteins, cytokines, monoclonal antibodies and both adenovirus and yeast vaccine therapies. ImmunityBio, a part of the NANT ecosystem of companies, has advanced a comprehensive immunological approach to cancer that centers on the use of vaccines and is now extending this expertise to COVID-19.

ImmunityBio's vaccine approach is distinguished by its use of a human second-generation adenovirus 5 (hAd5) [E1−, E2b−, E3−] platform. Current first-generation Ad5 platforms have a number of disadvantages: they are ineffective if the individual receiving the vaccine has pre-existing immunity to Ad5; if they do not, they can readily develop immunity to the vaccine vector (Ad), which negates their utility for future vaccination. Non-human adenoviruses have been used as vectors to avoid pre-existing immunity, but may still elicit a vector-directed immune response, which again makes them ineffective for repeated use.

The hAd5 platform overcomes these limitations by deletion of the genes encoding the E1, E2b and E3 Ad5 proteins, which enables the generation of vaccines that are effective even in the presence of pre-existing Ad5 immunity. The deletions have the further benefit of leaving additional 'cargo space' which, in the case of the ImmunityBio hAd5-S-Fusion + N-ETSD vaccine, can be used to allow expression of two antigens to increase vaccine efficacy.

Applications in cancer

ImmunityBio has already used the hAd5 [E1−, E2b−, E3−] platform to produce anti-cancer vaccines targeted at a number of antigens, including carcinoembryonic antigen, brachyury, HER2 and MUC1. These vaccines are currently undergoing clinical evaluation by NantKwest, a clinical-stage immunotherapy company harnessing the power of innate immunity to fight cancer and viral infections that is also part of the NANT family. In phase 1 and 2 studies, ImmunityBio's vaccines have demonstrated safety in immunocompromised patients as components of orchestrated combination therapies for advanced cancer that include biologics such as high-affinity natural killer cells, chemotherapy including nanoparticle albumin-bound paclitaxel and/or aldoxorubicin, checkpoint inhibitors such as anti-PD-1 and PD-L1 and N-803, an immune-activating interleukin-15 superagonist also developed by ImmunityBio.

The therapeutic promise of this vaccine approach is now being leveraged by ImmunityBio to advance a 'personalized' approach to cancer therapy that uses neoantigens unique to the individual patient's tumor as the basis for the vaccine. In recent pre-clinical studies performed by ImmunityBio and partners at the National Cancer Institute, administration of hAd5 neoantigens resulted in total tumor remission in models bearing tumors expressing the neoantigen.

ImmunityBio has extensive experience with vaccines against infectious diseases and has published several peer-reviewed articles of studies showing that the second-generation hAd5 platform can achieve both humoral and cell-mediated immunity against H1N1 influenza, HIV, SIV, Lassa fever, Chikungunya and Zika virus. With the outbreak of the COVID-19 pandemic, ImmunityBio rapidly directed its energy to creating a vaccine against this novel coronavirus and has now generated two hAd5-SARS-CoV-2 vaccine constructs.

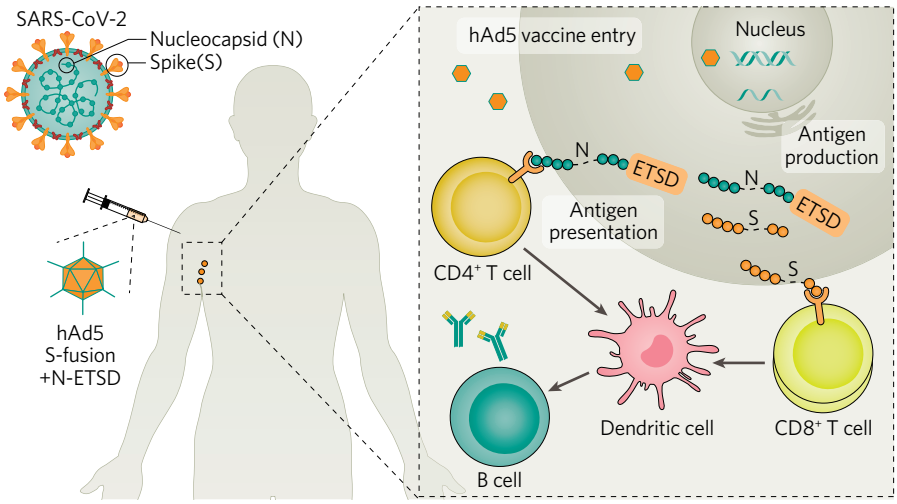

Fig. 1 | ImmunityBio's hAd5-S-Fusion + N-ETSD vaccine. This is comprised of both the viral spike (S) protein and the nucleocapsid (N) protein with an enhanced T cell stimulation domain (ETSD).

Targeting COVID-19

ImmunityBio's first vaccine construct, hAd5-S-Fusion, comprises the spike (S) viral surface protein that the virus uses to gain entry to host cells via the membrane-spanning angiotensin converting enzyme 2 (ACE2) with a fusion linker. S is highly antigenic, and will likely result in an effective immune response. The second construct, hAd5-S-Fusion + N-ETSD, contains both S and the viral nucleocapsid (N) protein, which is also highly conserved and antigenic (Fig. 1). ImmunityBio has added a proprietary signal sequence to the N protein that directs it to the appropriate subcellular compartment so that it elicits a vigorous immune response. These vaccines are expected to induce both humoral antibody-based and cell-mediated including innate antiviral responses that are both safe and durable. ImmunityBio has manufactured finished dosage forms of both vaccines at small scale in its current good manufacturing practice (cGMP) facilities, and has submitted an investigational new drug (IND) application to the US Food and Drug Administration to test them in a phase 1 trial anticipated to begin in June 2020.

ImmunityBio is seeking partnerships with clinical investigators, clinical trial sites and investors to accelerate development of the hAd5-SARS-CoV-2 vaccines and to build large-scale cGMP facilities to manufacture potentially billions of doses. ImmunityBio is also open to collaborations with other pharma companies around its therapeutic molecules.

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