HUMAN VACCINES PROJECT

COVID REPORT

Monoclonal Antibodies – A Hope for Fast and Safe Prevention of COVID-19

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Monoclonal antibodies (mAbs) might be particularly helpful in slowing down the spread of COVID-19 in advance of the development of an effective vaccine. Here are the steps that should be taken to accelerate their development.

Virus-neutralizing mAbs could play an important role in battling the coronavirus pandemic by bridging the gap until an effective vaccine is developed. In general, mAbs can be used therapeutically or prophylactically. Given the limited therapeutic effectiveness against various other respiratory viruses their greatest application in the current pandemic might be centered around disease prevention, in particular for critical populations.

Monoclonal antibodies are derived from B-cells isolated from a human or animal that has developed effective immunity via infection (or in some cases vaccination). Using various methods, protective B-cells are cloned under an industrial process to produce a single monoclonal antibody at scale. MAbs can be delivered via various methods from intravenously to intramuscularly, and offer a rapid shortcut to immunological protection known as passive immunity.

The Many Advantages of Monoclonal Antibodies

MAbs offer numerous advantages in the context of a pandemic, namely that development will likely be faster than for vaccines. MAbs are highly specific, binding only to a certain viral epitope and not to human self-antigens thus limiting off-target toxicities. Working by passive immunity, monoclonal antibodies do not require induction of specific immune responses in the recipient. This makes MAbs particularly helpful in preventing disease in populations where vaccine responses are usually poor such as with the immunocompromised, the very young and aging adults.

While mAb protection is likely to be of much shorter duration than that provided by a vaccine (months versus years), and protective immunity following mAb administration is immediate. One could envision administration of a virus-neutralizing mAb to first responders and health care workers, thereby enabling them to carry out their critical work without delay. Finally, clinical studies of mAbs can provide vaccine developers with insights into one possible mechanism of protection, or alternatively, highlight things that should be avoided.

The First Companies Move into Clinical Testing

A number of companies with profound expertise in the development of mAb therapeutics have announced candidates which will quickly move into clinical testing, among them Regeneron, Vir Biotechnology (in collaboration with Biogen and GSK), and Astra Zeneca. While it may be possible for researchers to find better mAbs (i.e., with greater potency or fewer development liabilities), time is critical and the search for an "ideal" mAb should not prevent development of good drug candidates currently at hand. If SARS-CoV-2 follows the same pattern as other coronaviruses that circulate in the human population, we can expect a second wave of the pandemic this fall.

Preliminary safety studies in humans in late spring and summer 2020 could pave the way for efficacy studies during the second wave, answering the question of whether SARS-CoV-2-neutralizing mAbs can protect humans against COVID-19.

How We Can Accelerate the Development

The fact that tremendous progress has been made in developing candidate mAbs in such a short time is a testament to the ingenuity and determination of researchers engaged in this work. However, drug candidate discovery is often not the most difficult part of the development process. Progressing through safety and efficacy studies and ultimately to licensure is expensive and fraught with complications that can derail, or at least significantly delay drug approval. Given what's at stake, it is more important than ever for companies to work together with regulatory agencies to ensure that everything possible is done to streamline the drug development process without compromising data quality. For example, given that most mAb candidates will be made in Chinese hamster ovary cells (CHO), and that there is a long history of CHO manufacture of mAbs for clinical use, perhaps companies could be permitted to make clinical trial materials using cell pools instead of purified clones, thereby shaving months off development timelines.

If the goal is to get into efficacy studies in the coming fall or winter, this is a meaningful time-saver. Likewise, there should be an openness to novel clinical trial design perhaps emulating some strategies utilized in other therapeutic areas (e.g. oncology) making it possible to quickly and seamlessly progress from early safety evaluation to efficacy. A very conservative approach is usually and appropriately taken in the development of mAbs intended for use in healthy people to prevent disease. However, the threat of an ongoing pandemic should warrant at least some more risk-taking.

We Must Begin Planning for Success

Dose selection will pose a challenge and will likely require efficacy studies to be large enough to accommodate testing of different mAb dose levels. Given that only about 1/100[th] the quantity of mAb in circulation makes it into a healthy lung, it might be prudent to test the highest feasible dose that can be safely administered intravenously while also testing lower dosages administered by intramuscular or subcutaneous injection. The less drug each adult requires to be protected from disease and the more convenient the route of administration, the more widespread the use of an efficacious mAb will be. In this regard, assuming one or more mAb candidates make it through clinical trials to licensure in a relatively short time span, the demand for those drugs is likely to be enormous and may quickly overwhelm manufacturing capacities. Thus, it is important to begin planning for success now – before efficacy studies even are initiated – to outline the steps that could and should be taken to increase capacity in the face of clinical and regulatory success.

MAbs can be part of the solution to the ongoing coronavirus pandemic but this will require resourcefullness and agility. Established processes and procedures can help prevent re-inventing the wheel, while slavish adherence to routine ways of work should be avoided. The circumstances in which we find ourselves are far from usual. There is no time to spare, and certainly no time to waste.

Register Now for the Global COVID Lab Meeting

First Global COVID Lab Meeting With James Crowe Tomorrow at 10 am EST

This Thursday (May 7, the Human Vaccines Project is launching the Global COVID Lab Meeting. In this bi-weekly webinar, leading scientists will present the latest research pertaining to COVID-19 therapeutic and vaccine development. Our goal is to identify the most critical research efforts and the most promising projects to facilitate global information exchange and data transparency.

If you haven't registered for the webinar yet, you can still do so using the link below. The Global COVID Lab Meeting is open to everybody who is interested in the research:

REGISTER FOR THE WEBINAR HERE

First Session: Tomorrow (May 7) at 10 am EST

Dr. James E. Crowe Jr., Director of the Vanderbilt Vaccine Center, will present an overview of his efforts to accelerate human monoclonal antibody therapeutics for SARS-CoV-2. Dr. Crowe's lab is one of the leading groups globally working on antibody identification, and is targeting starting clinical studies early this summer for SARS-CoV-2 therapeutics.

Must Read

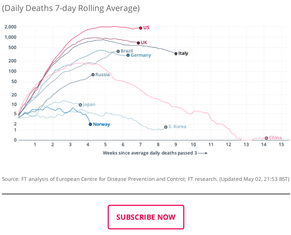
The following articles cover important research around COVID-19 and the development of antibody therapies.

- In a pre-print review article, Huang et al. summarize research on antibody immunity to coronaviruses including 1) antibody kinetics, 2) correlates of protection, 3) immunopathogenesis, 4) antigenic diversity and cross-reactivity, and 5) population seroprevalence.
- Korber et al. have developed an analysis pipeline to facilitate real-time mutation tracking in SARS-CoV-2, focusing initially on the Spike (S) protein. Their findings have important implications for SARS-CoV-2 transmission, pathogenesis and immune interventions.
- Hachim et al. in a pre-published article look beyond the spike to consider new viral targets of antibody responses in COVID-19 patients.
- On the topic of antibodies, biologists have advanced new research on miniature antibodies derived from llamas and other species that could have advantages in speed, cost and pathogen binding when compared to human or mouse antibodies, opening new avenues to combat future pandemics.
- Padron-Regalado looks for lessons learned from vaccine development for other coronavirus strains, including MERS-CoV and SARS-CoV-1.

COVID-19 in Numbers

Global Snapshot of New Cases

(Daily Deaths 7-day Rolling Average)



Source: FT analysis of European Centre for Disease Prevention and Control; FT research. (Updated May 02, 21:53 BST)

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