**COVID19/CoV-2 Research in Pharmaceutical Sciences**

**Project Title:** Accelerating pipelines toward COVID-19 therapies and vaccines using high-throughput single-cell functional screening

**Name of PI** (or names if collaborating).
Weian Zhao

**General Focus/Target of Research**.
COVID-19 therapeutics and vaccines

**Health-related Goal**.

To develop a platform technology that can accelerate development of prophylactic and treatment vaccines and antivirus therapeutic antibodies against COVID-19.

**Keywords/phrases** (5 maximum).
Coronavirus, prophylaxis, neutralizing antibody, vaccine, therapeutic discovery

**World Health Organization Research priority area(s**)

- Candidate vaccines R&D

**Technical Abstract of Research** (150±50 words).

This project aims to develop and validate a single-cell technology specifically for discovering super-neutralizing antibodies against COVID-19, including **a)** a new single-cell functional assay that can simultaneously interrogate antibody cross-reactivities to multiple virus variants, and **b)** technological validation and optimization to robustly and efficiently screen a large number of B cells to identify desirable candidate clones. Our technology represents a paradigm shift from conventional, low-throughput, antibody binding-based methods to high-throughput, single-cell-based functional screening (i.e., broad neutralization of viral infections), thereby significantly reducing the time required for therapeutic discovery and development. Upon completing these goals, the platform will be ready to be rapidly and broadly deployed to pharmaceutical and biotech companies as well as academic centers to accelerate pipelines toward COVID-19 therapies and vaccines.

**Non-technical Abstract** (150±50 words).

The COVID-19 pandemic has infected over 585,000 people and claimed over 26,800 lives worldwide (and counting). Without treatment, the new coronavirus can infect up to half of the population and eventually kill more than 2 million people in the U.S. alone. Currently, no approved vaccine or treatment is available. Therefore, there is an urgent need to develop effective vaccines and therapeutics to fight this devastating disease.

A practical source of antiviral medicine is the broadly neutralizing antibodies derived from recovered patients whose immune system has mounted effective responses to clear the virus. However, these functional antibodies typically exist at low abundance from a large, diverse B cell repertoire in patients and cannot be efficiently discovered with current screening approaches.

We propose to develop a high throughput, single-cell technology that can interrogate the functions of tens of millions of individual B cells in a single experiment to identify the rare cells that produce antibodies with

virus-blocking properties. Once identified, these antibodies can be administered as therapeutics or immuno-prophylactic vaccine in the form of synthetic RNAs or engineered AAV vectors. With unprecedented acceleration of discoveries, the proposed technology holds tremendous potential to enable development of vaccines and therapeutics against COVID-19 in the short term. Therefore, this project can potentially make an immediate, significant, and broad societal impact by helping to save millions of lives and trillions of dollars for our already overwhelmed healthcare system.