Novel, Complementary Alternative to PCR Testing for SARS-CoV-2 Antigen, Using ELISA Platforms & Novel, stable CPN + 'Plastic Antibody' to Increase Mass Testing Capacity

Summary Briefing Document:

The Need:
Substantial increase in antigen mass testing capacity to meet population testing targets.
A complementary alternative to PCR to meet the need.

The Problem:
There is a finite supply PCR equipment in the UK, units of this expensive complex equipment are limited and there is an exceptional world-wide increase in demand from PCR equipment manufactures which will further limit supply. ELISA can deliver the same result in terms of confirmation of infection (yes/no) but relies on a different technique using monoclonal antibodies (mAbs), which have not yet been developed or validated against the Covd-19 virus and is some way off.

Development of conventional ELISA antigen diagnostic high throughput screening (HTS):

1. Relies on developing monoclonal antibodies directly against the virus which are difficult and time consuming to develop taking several months.
2. The process relies on an immune response and raising the antibodies in a controlled cell line.
3. It's done on a batch-by-batch basis, and batches can vary in quality and quantity depending on the manufacturer and the cell lines used.
4. Use of organic fluorophores, which suffer from photobleaching and require special handling.
5. Sensitivity using conventional fluorophores can be an issue as a result of weak brightness (signal strength), particularly in the presence of weak infections potentially giving a false negative result

A new alternative view and approach to conventional ELISA is desperately needed to solve the development issues, and an approach that can be easily adapted to other diseases or variants of covid-19 / SARs in a matter of weeks and not several months.

Background:
Stream Bio Ltd, with a novel technology recently spun out from Kings College London, an exceptionally bright, (sensitive) fluorescent conjugated polymer nanoparticle (CPN™) for cell labelling, imaging and diagnostics, has entered into a Joint Venture, with MIP Diagnostics Ltd, a developer of a stable antibody equivalent (nanoMiP), in order to develop a unique stable SARS-CoV-2 reagent for a range of assays, including ELISA.

The Solution:
A cost-effective, room temperature stable, mass-producible HTS assay, using two novel complementary technologies, conjugated polymer nanoparticles (CPNs) and molecular imprinted polymers (NanoMIPs), in an established 96 well plate ELISA format, for

identification of SARS-Cov-2 by labelling a unique surface protein (S-Protein). Adoption of this assay could effectively double testing capability.

Stream Bio Ltd has a novel intensely fluorescent nanoparticle label with unique properties and advantages over conventional biological labels, such as exceptionally stability to temperature and pH, and significantly increased brightness and sensitivity. CPNs™ do not photobleach and can be functionalised with a range of targeting molecules. As a result of the unique brightness, preliminary measurements indicate, detection limits can be achieved of CPNs down to less than 100 nanoparticles/ml, allowing ultrasensitive detection of SARS-CoV-2 antigen, significantly reducing the possibility of 'false negatives'. MIP Diagnostics Ltd manufacture nanoMiPs, which are novel synthetic targeting molecules ('plastic antibodies') with high stability. Manufacture takes approximately 4 to 5 weeks instead of months for mAbs, and involves immobilisation, mapping and synthesis of nanoscale polymers in the presence of the epitope, in this case the 'spike' protein of the virus, creating a unique imprint with an extremely high affinity. From this imprint, large-scale production volumes of nanoMiPs can be derived. CPNs+nanoMIPs can be linked via standard conjugation methods and incorporated within a variety of assays for antigen testing, including ELISA. Both technologies are robust to temperature and light making the assay easy to handle in the lab and compatible with a wide range of test sample preparation techniques.

This new approach to ELISA development in both the type of fluorescent label and alternative targeting molecule (plastic antibody) will identify and confirm infections as a PCR would in 1-2hrs, compared with 3-12hrs for PCR, utilising plate readers found in almost every lab in the country

The Current Issues & Solutions in red.

1. Relies on developing monoclonal antibodies directly against the virus which are difficult and time consuming to develop taking several months. nanoMips can be made under normal conditions in 6 weeks. In a national emergency with resources, this can be done in 4-5 weeks.
1. The process relies on an immune response and raising the antibodies in a controlled cell line. - Our process does not.
2. It's done on a batch-by-batch basis, and batches can vary in quality and quantity depending on the manufacturer and the cell lines used. - A cast of the 'binding site' is unique and consistent, and so are the mass produced 'plastic antibodies'
3. Uses organic fluorophores, which suffer from photobleaching and require special handling. – CPN's do not fade, are intensely bright and along with nanoMiP's both technologies are robustly stable, which makes for an easy to handle assay.
4. Sensitivity using conventional fluorophores can be an issue as a result of weak brightness (signal strength), particularly in the presence of weak infections potentially giving a false negative result - Preliminary measurements indicate, detection limits of CPNs down to <100 nanoparticles/ml can be achieved, allowing ultrasensitive detection of SARS-CoV-2 antigen, significantly reducing the possibility of 'false negatives'

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Images:

Fig 1. CPN™ Range and CPN 510 (Green)

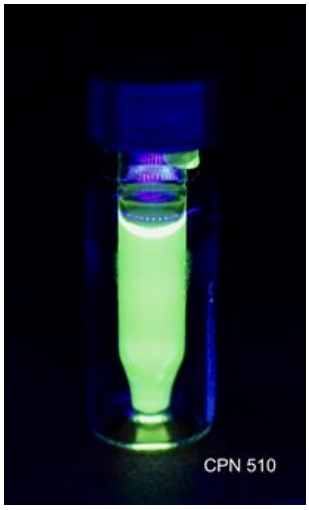
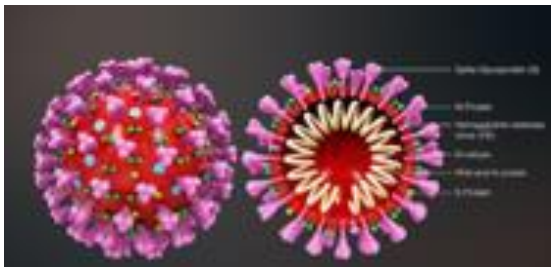


Fig 2. SARS-COV-2



S-protein COVID-19
(SARS-Cov-2) Structure
Source: Wrapp
et al, 2020

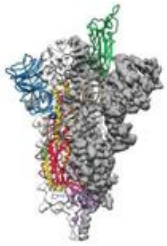


Fig 3: CPN

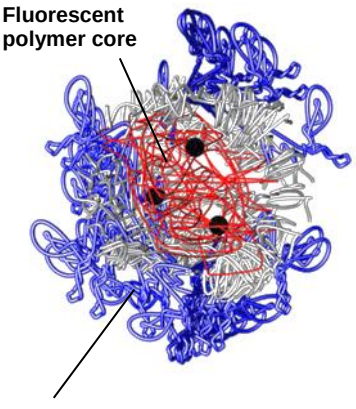
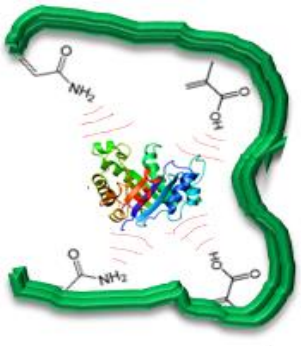


Fig 4: NanoMip



nanoMIPs consist of specific monomers polymerized around a target of interest to create unique binding reagents