SARS-CoV-2 assay development in a bioanalysis laboratory

EBF open symposium November 2020

Else Marie Agger
November 2020
Private contributors during Covid-19 crisis

Antibody testing
Non-clinical and Clinical Assay Sciences (NCAS)

- Bioanalysis
- Biomarkers
- Immunogenicity Assessment

Support non-clinical studies
- Support clinical trials

Develop and validate state-of-the-art assays
Sample analyse
Correlate data to non-clinical and clinical findings
Public-private partnership

- How many develop antibodies?
- Are asymptomatic antibody positives?
- Which antigens to use?
- Can we discriminate to other Coronavirus? (other Corona virus)
- How good are commercial tests?
- Can we get hold on commercial tests?
- Etc.....
Building a robot for Statens Serum Institut
Timelines for the antibody analysis

**MARCH**
- MAR 11, 2020
  Denmark reports its first COVID-19 death

**APRIL**
- MAR 18, 2020
  NCAS discuss the possibility of developing a COVID-19 antibody assay
- MAR 26, 2020
  Mgt ask if an antibody assay can be developed
- APR 8, 2020
  Corona-lab established
  Prototype assay ready and first patient samples analysed

**MAY**
- APR 17, 2020
  Novo produced assay antigens ready

**JUNE**
- APR - JUN, 2020
  Assay optimization and validation
- JUN 10, 2020
  Assay validation done
Antibody assay development
(>16,000 samples)

**Detection reagents**
- Several HRP conjugates
- Sulfo-TAG conjugate

**Buffers**
- Several coating buffers
- Several dilution buffers
- Several blocking buffers
- Several stopping reagents

**Sample matrix**
- Serum
- Plasma
- Sample dilution

**Plate type**
- ELISA (96 and 384)
- MSD (96)

**General testing**
- Concentrations
- Incubation times
- Incubation temperatures

**Detection molecule**
- Anti-IgG
- Anti-IgA
- Anti-IgM
- Mix of anti-IgG/A/M
- RBD

**Control antibody**
- Several monoclonal antibodies
- Several polyclonal antibodies

**Coating antigen**
- Spike protein
- RBD
- Nucleocapsid
- Mix of above
- Non-sense

**Sample types**
- Serum
- Plasma
- Sample dilution
Generation of assay reagents
Analysis of national validation cohort

**NN screening assay**

- **Sensitivity**
- **Specificity**

**ROC curve**

- Sensitivity = 97.3%
- Specificity = 99.0%

Cut point 6.95:

- Sensitivity = 97.3%
- Specificity = 99.0%

Hansen CB et al, JI 2020
Harritshoej LH et al, submitted 2020
How good is the assay?

RBD antibody assay
Correlation of symptoms to antibody titre

Many commercial assays are only validated on severe/critical patients.

Many commercial assays don't detect low titre antibodies in mild/asymptomatic patients.

Danish state continues to use Livzon Point-of-care test and Wantai ELISA.

Hansen CB et al, JI 2020
Research project

“Dynamic characteristics of the antibody response towards SARS-CoV-2 in a company-based population”

• **Aim**: To investigate the antibody incidence and dynamic development towards SARS-CoV-2 in a large population-based cohort and in their adult household members.

• **Study population**: Employees located in Denmark of Novo Nordisk A/S, Novozymes A/S, Novo Holdings A/S and the Novo Nordisk Foundation and their adult household members.
  
  • No fee is paid for participation in the project
  
  • Expected number of participants: approx. 16,000
  
  • Funded by Novo Nordisk Foundation by special grant
Some learnings

• High quality antibody tests can detect individuals without symptoms or with mild symptoms
• “Dark numbers” on no. of infected where not that high
• Measurement of antibodies less informative wrt. long-term immunogenicity
• Antibody analysis is valuable for epidemiological surveillance

• Public-private-partnerships can work very efficiently
• Agile is not only a way-of-working for it projects
• Corona can also generate fun & joy
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And many others.............

Thank you for your attention