Building COVID-19 Testing Capacity from Scratch

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January 25, 2021
The situation in Denmark before Covid-19

- Most testing for infectious agents had been decentralized to regional public hospitals
- The central government laboratory (SSI) is only testing for some rare infectious diseases
- SSI still propose new testing methods to the regional public hospitals
Close-down of Denmark in Marts 2020

• Marts 11:
  • The prime minister close-down the country
  • Novo Nordisk close-down the research laboratories
  • Change of testing strategy

• Marts 21, Novo Nordisk is asked by the PM to help the hospitals with RT-PCR testing for Covid-19

• Marts 29, Novo Nordisk foundation invites for meeting to start an alternative testing track (Test Center Denmark)
The task given by Rigshospitalet

- Use the same RT-PCR package as Rigshospitalet
- Primer-probe mixes for:
  - 2019-nCoV_N1: targets viral nucleoprotein gene
  - 2019-nCoV_N2: targets viral nucleoprotein gene
  - RP: targets human RNase P gene

- Avoid competing with any of the Danish hospitals for reagents, kits or plasticware
- ABI 9600 for RT-PCR
- Biomek i5 and i7 robots for liquid handling including nucleic acid purification

- Validate assay by testing difficult sample sets from Rigshospitalet to demonstrate comparability before first diagnostic use and after any subsequent change of method
The strategy we followed from day 1

1. Start testing real patient samples from the hospital as fast as possible

2. Change to multiplex RT-PCR both for simplicity and for increased capacity

3. Move towards sourcing reagents and plasticware in Denmark. Scandinavia or EU as possible alternatives

4. Could we possibly push a method back to the hospitals where we could guarantee the supply of reagents?
Criticality of simultaneous diagnostic testing and method development

• One week after being contacted by the PM, we were running 400 diagnostic samples/day
• Copy number controls included on all plates for:
  • Viral RNA
  • Viral DNA
  • Cell copy number
• Two partially overlapping teams established for method development and for diagnostic testing
• Transfer to Biomek robots i5 and i7 increased the testing capacity to 2000 diagnostic samples/day two weeks later
Change to multiplex RT-PCR both for simplicity and for increased capacity

- 2,000 diagnostic samples per day corresponds to approximately 7,000 RT-PCR reactions including controls
- The number of ABI 9600s had become the bottleneck
- An opportunity to reduce reagents and plasticware
- April 24, we could run 6,000 diagnostic samples/day using multiplex RT-PCR without compromising sensitivity or robustness
How to avoid stock-out?

- Internally targeting 10,000 samples/day and a total of 2 million tests
- Ordered 1200 kg GuSCN in China (lysis buffer and RNA purification)
- Started own production of silica-coated magnetic beads but ended up sourcing at The Technical University in Oslo, Norway
- Initiated production of DNA polymerase and Reverse Transcriptase
- The flexibility of the Biomek robots allowed the use of different plates
- Developed method for reuse of pipette tips
- Constantly developing and sourcing for 1-2 backup methods
Could we possibly push a method back to the hospitals where we could guarantee the supply of reagents?

- July 1, 2020, we transferred the method, and by that a testing capacity of 10,000 samples/day for the Danish hospitals to the Technical University of Denmark

- PentaBase is on a commercial basis offering testing in Denmark, and have made a business out of exporting kits with the method developed

- Only 3 hospitals in Denmark have implemented the method, and only for a subset of their testing capacity
Three key parameters that I forgot to control

• Standardized tubes with lysis buffer and barcodes at the hospitals

• Supply of swab sticks to the hospitals

• Physical location of equipment
Thank you!
RT-PCR positive/day

Dead with covid-19/day