Belangrijke onderwerpen COVID 19

Lijn 1 Diagnostiek en behandeling

Alternative testing methods:

1. Improved PCR independent diagnostics for Corona SARS CoV2

Testing whether someone is infected with the coronavirus is labor-intensive, requiring specific kits and reagents. To enable more elaborate testing, a consortium with The Hubrecht Institute, RIVM, TNO, Wagening Bioveterinary Research and the Leiden University develops alternative, PCR independent methods for detection of the virus. VWS actively supports the development of this method ([redacted (10)(2e)]) and the method has been presented and discussed with the 'Landelijke coördinatie Testcapaciteit COVID-19'. By this method a short term scale up of 15 000 tests per day seems to be feasible with a further potential of 50 000 tests per day if needed.

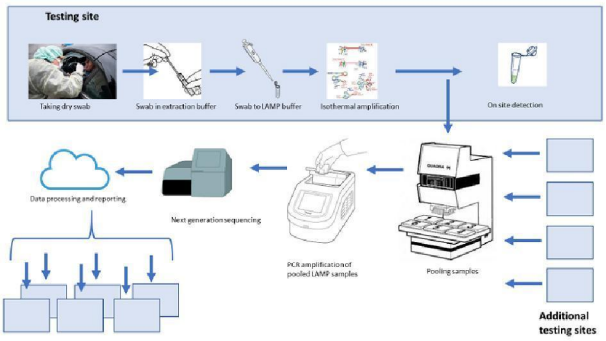
The testing method specifically aims at individuals working in vital jobs and at more frequent testing of individuals that through work or care have regular contact with vulnerable members in society. The method also does not compete with medical protocols for reagents and other requirements and tests are optimized for efficiency: minimizing testing requirements while maintaining maximum of security in the population.

The proposed project has four critical components:

1. Simplified approach for sample handling and pre-processing (paper/cellulose based)
2. PCR independent molecular test protocol for SARS CoV-2 isothermal molecular loop amplification (rt-LAMP) with direct, on site detection (PoC).
3. The implementation of sequence based readout (LAMP-Seq) for enhanced throughput and increased sensitivity and specificity.
4. Combination of scalability and regional/decentralized availability[1].

The first steps on this path have been conducted and were quite successful.

The project foresees in a stakeholder committee that includes among others TUdelft, DSM, Genmab and the University medical Centre Utrecht. Involvement of the GGD is being discussed.



[11] In more detail: we will develop a paper/cellulose based method for integrated sample collection (swabbing), virus inactivation and preservation and purification of nucleic acids for subsequent molecular detection. By chemically treated / derivatization of filter paper, a matrix can be obtained that ensures efficient lysis of virus particles upon contact and allows for direct capturing of nucleic acids. Following wash steps, nucleic acids can be sufficiently purified for analysis. Such strategies have been demonstrated to be useful for the analysis of Zika, and the HIV virus. Using available protocols, we aim to optimize cellulose treatment and derivatization for use in the analysis of SARS CoV-2 and optimal alignment with the molecular detection. To detect viral RNA, isothermal molecular loop amplification (rt-LAMP) will be used. LAMP is a single tube isothermal process, that does not require a complex technical infrastructure. Another advantage of LAMP is its tolerance towards impurities in the RNA sample, thereby optimally aligning with the simple paper based extraction. LAMP allows for factorial amplification of nucleic acids, yielding high levels of DNA, and enabling direct visualization. When combined with next generation sequencing, high throughput and increased sensitivity and specificity can be achieved. Following the development of a protocol, validation will be performed in clinical samples, benchmarking the simplified method against the current rt-PCR dependent standard protocol. While this protocol will be translated into a kit suitable for service laboratories for (experimental) diagnostic purpose. To enable rapid scale up and availability, we will collaborate with implement automated sample handling for LAMP-Seq and work with local supplier of enzymes and biomolecules and collaborate with Netherlands-based paper industry. Importantly, protocols will be developed for multiple enzymes, ensuring backup sources for critical enzymes.