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Brief report A mobile DNA laboratory for forensic science adapted to coronavirusSARS-CoV-2 diagnosis

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Abstract

The Forensic Science Institute of the French "Gendarmerie Nationale" (IRCGN[™]) developed in 2015 an ISO 17025 certified mobile DNA laboratory for genetic analyses. This Mobil'DNA laboratory is a fully autonomous and adaptable mobile laboratory toperform genetic analyses in the context of crime scenes, terrorism attacks or disasters. To support the hospital taskforce inParis during the peak of the COVID-19 epidemic, we adapted this mobile genetic laboratory to perform high-throughput molecular screening for coronavirus SARS-CoV-2 by real-time PCR. We describe the adaptation of this Mobil'DNA lab to assist in

Coronavirus SARS-CoV-2 diagnosis.

Introduction

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On March 11, 2020, the World Health Organization (WHO) classified the outbreak due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as a public health emergency. This epidemic has indeed taken on the proportions of a pandemic (WHO, March 2020) [1]. The viral pathology linked to this Coronavirus was described in China for the first time in December 2019 and named COVID-19 (coronavirus disease 2019) [2]. Quickly, this disease fuelled a massive and legitimate interest, especially in terms of specific molecular diagnosis capabilities. The clinical consequences are multiple and variable but most importantly feature an acute respiratory

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Département Médical Universitaire de Biologie-Génétique-Pharmacie, AP-HP, Université Paris Saclay, 78 rue du Général Leclerc, 94270 Le Kremlin-Bicêtre, France distress syndrome (ARDS), which can be associated with multi-organ failure with myocardial, renal, enteric and hepatic lesions, possibly leading to death, particularly in elderly patients with comorbidities [3]. SARS-CoV-2 transmission has affected more than 2.85 million people and caused more than 196,000 deaths worldwide as of April 27, 2020, including more than 22,500 in France (www.who.int). For these reasons, monitoring COVID-19 is important and strategic [4].

An ISO 17025 certified lab: the Mobil'DNA

In 2015, the French "Gendarmerie Nationale" patented (FR3050945B1) a Mobil'DNA lab for genetic forensic analysis which allows magistrates and investigators to quickly obtain genetic results. This mobile laboratory is transportable as close as possible to scenes of disasters, complex crime scenes or to places where people in police custody are gathered [5]. It has already been used for the identification of the victims of the GermanWings (2015) air crash and the 2016 Nice terror attack [6] where it carried out several hundred analyses per day.

This Mobil'DNA lab makes it possible to implement an analytical process for determining genetic profiles from a biological sample with a configuration which makes it possible to respect the principle of "forward movement" of the processing of a sample described as:

- A sampling area, to manage and analyse the sample
- A PRE-PCR zone, in which the technical operations for the purification of nucleic acids and the preparation of nucleic acids for amplification by PCR or RT-PCR are carried out [7]
- A POST PCR area, in which both gene amplifications by PCR and RT-PCR are carried out and genotyping by capillary electrophoresis of nucleic acids [7]

COVID-19 diagnosis: SARS-CoV-2 detection

Since March 2020, French public health authorities stressed the need to rapidly expand the diagnostic capabilities for COVID-19. This global health crisis shows the need to mobilize a diagnostic force quickly at national and

Fig. 1 The Mobil'DNA lab, the adaptation for genetic diagnosis (inside view)

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The creation of a mixed unit composed of IRCGN and the Microbiology Department of Hospital Raymond Poincaré (GHU Paris Saclay, Assistance Publique-Hôpitaux de Paris) allowed the rapid adaptation IRCGN mobile DNA analysis laboratory in order to guarantee optimal conditions for operator safety, sample traceability and analysis sensitivity in order to detect the presence of COVID-19 by viral RNA analysis [9, 10]. This rapid adaptation is greatly facilitated by the convergence of analytical methods and ISO 17025/ISO 15189 normative requirements between the analysis of a human biological sample for DNA analysis and the analysis of this same biological sample for detecting a pathogen by targeting the RNA Coronavirus (see Fig. 1) [8]. This partnership was authorized by the ordinance of the French government on 5 April 2020 [11] giving the possibility to ISO 17025 certified laboratories to perform



international level. These solutions must interface with clinical diagnostic laboratories to meet the quality standards for medical biology (ISO 15189) [8] and should be mobile to best address the needs. The French National Gendarmerie, as an interior security force serving the protection of the French people, has taken the initiative to adapt the forensic Mobil'DNA. The objective is to propose an autonomous mobile biomolecular laboratory for rapid tests at high-throughput level for the endemic pathogen SARS Cov-2, in support of local hospitals and health systems, in rural or confined areas and overseas.

To be efficient for this mobile force for microbiological diagnosis, the IRCGN combined its expertise in mobile and high-speedanalysis ofbiological samples with the expertise of a French medical biology structure in the diagnosis of endemic pathogens. biomedical testing by RT-PCR in order to detect COVID-19 infection.

Material and strategy

Validation process, sample processing and highthroughput COVID-19 detection by RT PCR

Regarding this outbreak context, the Mobil'DNA lab of the French gendarmerie was adapted as a true extension of the fixed hospital laboratory by validating and following an analytical process.

The validation of the analytical process of the Mobil'DNA lab was carried out over a period of 10 days

through comparative studies between the reference analytical technique used by the hospital and the analytical process performed by the Eur J Clin Microbiol Infect Dis

IRCGN [2]. To this end, the analytical parameters of the processwerecleared with verification f sensitivity, of repeatability and of reproducibility, carried out on more than 100 prospective clinical samples. The lack of cross-contamination was verified at all stages with the assays of high concentration RNA extracts.

The analytical process is performed in 5 steps:

- Taking samples and recording them for traceability on the basis of the unique barcode identifier. All is done using a computerized system LIMS, which is connected to the hospital unit in order to transfer automatically the results of the essays. It provides a complete overview and control of analytical data to the microbiologists.
- 2. Sampling a fraction of the biological sample to be analysed. This operation is carried out under a type 2 microbiological safety cabinet (MSC).
- 3. Extraction of the RNA contained in the sample by lysis of the virus using the hospital's procedures [10].
- 4. Quantification of purified DNA by real-time PCR (RTPCR) system.
- 5. Result interpretation and generation of reports, using GendLink® an original gendarmerie software adapted to generate a report on the results of COVID analyses.

In order to ensure operator safety against COVID-19, each operatoriswearing a singleusepersonalprotective equipment including an integral Tyvek type suit, a double pair of gloves (external pair changed between each sample), a surgical mask or an FFP2 type mask for steps 1 and 2, a hood and protective goggles.

The analyses are done on an Applied[™] 7500 real-time PCR system (software v2.3) according to the hospital procedure, using RNA extraction negative control, internal quality control (ICQ) composed by quantified virus RNA from patients diagnosed as COVID-19 infected, nontemplate control for RT-PCR and positive control from the GeneFirst® RUO COVID-19 Detection kit. In this configuration, the Mobil'DNA can provide a maximum of 1000 results per day involving five technical persons from IRCGN and 3 clinical microbiologists from the hospital to validate the results

Results

Since the validation of the technical procedure, on the 14April 2020 at Garches Hospital, around 4000 samples were analysed in 14 days with throughput between 100 and 700 samples per day depending on the delivery of samples. After reception of the samples, the results are given in less than 24 h. The Mobil'DNA lab and the forensic science laboratory of the French gendarmerie in the context of the COVID-19 pandemic can provide three short-term issues with a direct impact on this crisis:

- The possibility within a short time of setting up an additional testing capacity to deal with a massive influx of individuals to be tested on a hospital site
- 2. To respond to a demand for test capacity in rural areas or overseas, for citizens distant from the test centres
- 3. To validate a global and efficient concept of mobile lab unit for rapid molecular diagnostic tests, easily transposable and deployable anywhere in the world during such outbreak scenario

Conclusion

Using this mixed concept mobile laboratory between the French National Gendarmerie and hospital centres has demonstrated the ability to pool skills and resources to cope with the current outbreak period by creating a single autonomous mobile solution, deployable in a very short time. This concept will provide an effective solution in the following cases:

- Mobile rapid diagnostic unit to be deployed on a remote site, isolated or contained contaminated areas, point of entry into the territory of a source of propagation of a pandemic (port, airport, border).
- Extension of diagnostic test capacities to other pathogens (viruses such as Ebola and dengue or bacteria such as cholera and the tuberculosis bacillus). IRCGN is at the cutting edge of technology, as are collaborating medical microbiologists. This will make it possible to deploy the most efficient technologies depending on the situations in areas that cannot be equipped in such a short time.
- The possibilities to extend the concept to other means of deployment (train, plane, etc.).

It shows that forensic police forces can collaborate with medical capabilities using the same technologies for the same purpose: health security and diagnostic assistance. Acknowledgements The authors would like to thank Mr. Christophe Castaner, Minister of the Interior and General Christian RODRIGUEZ, Director General of the National Gendarmerie, who made it possible for the Gendarmerie Scientifique to work quickly with the AP-HP microbiologists to improve the detection capacity of COVID-19. We are also grateful to the Pr Philippe Berta, geneticis at Nîmes University and John Watson, expert for the European Commission, for their excellent technical assistance and reviewing.

Compliance with ethical standards

Conflict of interest

Hubac S. is the owner of the patent of Mobil'DNA.

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