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# Horizon Scanning: Rise of Planetary Health Genomics and Digital Twins for Pandemic Preparedness

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## Abstract

The Covid-19 pandemic accelerated research and development not only in infectious diseases but also in digital technologies to improve monitoring, forecasting, and intervening on planetary and ecological risks. In the European Commission, the Destination Earth (DestinE) is a current major initiative to develop a digital model of the Earth (a “digital twin”) with high precision. Moreover, omics systems science is undergoing digital transformation impacting nearly all dimensions of the field, including real-time phenotype capture to data analytics using machine learning and artificial intelligence, to name but a few emerging frontiers. We discuss the ways in which the current ongoing digital transformation in omics offers synergies with digital twins/DestinE. Importantly, we note here the rise of a new field of scholarship, planetary health genomics. We conclude that digital transformation in public and private sectors, digital twins/DestinE, and their convergence with omics systems science are poised to build robust capacities for pandemic preparedness and resilient societies in the 21st century.

**Keywords:** digital transformation, digital twins, public health genomics, SARS-CoV-2 sequencing, pandemic preparedness, genomic surveillance

## Introduction

**O**VER THE PAST DECADE, digital transformation in public health have evolved into a broader, planetary scale, scope, and relevance. The COVID-19 pandemic has further catapulted digital transformation around the world that is now taking off in a variety of large scale planetary health

initiatives. In the European Commission, the Destination Earth (DestinE) is a current and major initiative to develop a digital model of the Earth (a “digital twin”) with a very high precision (<https://digital-strategy.ec.europa.eu/en/library/destination-earth>) (Fig. 1).

DestinE is part of a broader vision and growing awareness that the COVID-19 pandemic is a kind reminder for future

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**FIG. 1.** DestinE milestones—the road to digital twins of the Earth. Source of information: European Commission, 2021. DestinE, Destination Earth.

planetary health crises looming on the horizon. Omics systems science offers veritable prospects for genomic surveillance of emerging pathogens, including new zoonosis threats. Omics is itself undergoing digital transformation impacting nearly all dimensions of the field, including real-time phenotype capture to data analytics using machine learning and artificial intelligence, to name but a few emerging frontiers.

We discuss the digital transformation in omics and the ways in which this offers synergies with digital twins. In addition, the present article introduces and highlights the rise of a new field of scholarship, planetary health genomics.

### Digital Transformation in Omics from Phenomics to Data-to-Knowledge Trajectory

The Covid-19 pandemic is the most important public health crisis in the last century and one of the three major infectious outbreaks in the first decades of this century (World Health Organization, 2021a). An important characteristic of the Covid-19 pandemic was the early and widespread use of digital health technologies such as telemedicine platforms, contact tracing apps, wearables, genome sequencing, artificial intelligence and machine learning, genomic data sharing platforms, data dashboards, real-time and real-world data from mobile devices (including global positioning systems), electronic health records, disease and vaccination registries, e-prescriptions, and Internet of Things. These developments, in part, built on earlier efforts to incorporate digital technologies in public health (Evangelatos et al., 2020a).

Digital health technologies and extensive use of data have been incorporated into several layers of the health systems: implementation of public health measures for containment and mitigation, planning and tracking of the severe acute

respiratory syndrome coronavirus 2 (SARS-CoV-2) variants, clinical management, and political and administrative decision. The implementation of digital health technologies was different from one country to another, “countries that have quickly deployed digital technologies to facilitate planning, surveillance, testing, contact tracing, quarantine, and clinical management have remained front-runners in managing disease burden” (Van Spall et al., 2020).

During the Covid-19 pandemic, the access to digital technologies has emerged as a fundamental determinant of access to health and care (Evangelatos et al., 2020b). Across the Globe, health systems and societies are in different stages of digital transformation, and those health systems already advanced in terms of digital health technologies implementation have had a prompt and efficient response. The risk of digital divide in the context of Covid-19 should be discussed even more in relationship to omics and other emerging technologies (digital twins, machine learning).

Omics is impacting nearly all dimensions of the response to the Covid-19 pandemic, including single-cell multiomics analysis of the immune response in COVID-19 (Stephenson et al., 2021), large-scale multiomics analysis of COVID-19 severity, and multiomics approach in the identification of potential therapeutic biomolecule for COVID-19 (Singh et al., 2021).

From the public health perspective, the most important benefits of the omics systems science are related to the implementation of genomic surveillance of the SARS-CoV-2 aiming to early identify potential variants of interest or variants of concern of the virus. From the medical practice perspective, one of the most challenging but promising applications of the omics sciences is the real-time phenotype capture by Internet of Things followed by data analytics using machine learning and artificial intelligence.

The measurement of the phenotype for Covid-19 by multilevel proteomics analysis reveals the perturbations produced in the human body through the interaction of SARS-CoV-2 proteins and the host proteome, profiling the interactome of the virus as well as the influence of the SARS-CoV-2 on the transcriptome, proteome, ubiquitinome and phosphoproteome of a lung-derived human cell line (Stukalov et al., 2021).

Assessment of the proteome (a measure of phenome, the interaction between the human genome and the environment, including the viral proteins) of the Covid-19 patients and the use of machine learning led to the identification of disease progression and prognostic biomarkers and risk-adapted treatment strategies, as well as a map linking clinical parameters usually used for diagnostic to proteome and their dynamics in an infectious disease (Demichev et al., 2021).

Real-world data are meant to capture in real-time different sets of characteristics of an individual (phenotypes). Traditionally, the real-world data included registries, electronic medical records, and self-reported individual data, but the current understanding of the real-world data incorporate more real-time objective measurement provided by wearable devices and other Internet of Things as well. The challenge is to transform the real-world real-time data in real-world real-time evidence and knowledge.

Digital transformation in omics began with the exponential development of next-generation sequencing and other emerging technologies, which will increasingly be incorporated into Internet of Things (IoT) devices, allowing real-time and precise monitoring of parameters that currently can be measured rather in hospitals and specialized clinics.

“Digital transformation is impacting every facet of science and society, not least because there is a growing need for digital services and products with the COVID-19 pandemic.” (Lin and Wu, 2021).

Digital transformation in omics has the potential to transform the doctor-patient relationship and to increase the inequalities. The response to the Covid-19 pandemic was and is still different from continent to continent, from country to country, and sometimes within the same country. Lack of a common response and the limited use of innovative tool such as omics and digital technologies contributed to the poor control of the pandemic around the globe. Digital determinants of health has emerged over the past 2 years in particular as important pillars of preparedness for current and future ecological threats (Moon and Kickbusch, 2021; Özdemir, 2021).

### Planetary Health in the Age of Pandemic

Planetary health is a concept focused on the interconnections and interdependence of human health, animal health, and environment (Haines, 2016). Planetary health has a marked emphasis on ecological determinants of health (Seltnerich, 2018).

Climate change is a trademark of the 21st century. For infectious diseases, climate change is a threat multiplier (Chan, 2017). Climate change expands the distribution of the existing infectious disease pathogens and creates the conditions for other pathogens to emerge. Disruption of forests, rapid urbanization, and population growth are driving zoonotic

events simply by increasing close contact between people and animals (Waugh et al., 2020).

At least 30 new infectious agents affecting human population have emerged over the last 40 years, with 44% involving RNA viruses (Nii-Trebi, 2017). Between 631,000 and 827,000 unknown viruses might be zoonotic and thus have the potential to infect humans after spillover from host animal populations (Jonas and Seifman, 2019). Most of this new pathogens are zoonotic, significantly correlated to socioeconomic, environmental, and ecological factors. Some of this new pathogens, apart from the current SARS-CoV-2 virus causing Covid-19 pandemic, have demonstrated in the last 20 years the capacity to spread, infect large populations, overwhelm health systems, create economic difficulties, and increase morbidity and mortality.

In 2003, SARS (the coronavirus causing acute respiratory syndrome) emerged in China, spread to around 30 countries, and caused more than 8000 cases and around 774 deaths, with an economic impact of more than 40 billion dollars worldwide in only 6 months (Council on Foreign Relations, 2020). In 2012, Middle East respiratory syndrome coronavirus (MERS-CoV) (the virus causing Middle East Respiratory Syndrome) emerged in Saudi Arabia and spread to 27 countries in the region, caused 2519 cases and 866 deaths, with a very high mortality rate (33%) (National Institute of Allergy and Infectious Diseases, 2020).

Data suggested that both SARS-CoV and MERS-CoV originated in bats. SARS-CoV then spread from civets to people, while MERS-CoV spread from dromedary camels to humans.

Research indicated for many years that bats host a significantly higher proportion of dangerous viruses than other mammals (Olival et al., 2017). This scientific data should have already led to the development of extensive viral surveillance programs of bats populations in the hotspot areas with the objective to contribute to the development of predictive models and to prevent future emergence of the virus. Established before the emergence of Covid-19 pandemic, the initiatives in biodiversity genomics as Bioscan, Earth Biogenome Project, and Global Virome Project had a limited role for Covid-19 prediction but could reach the potential of genomic and data-driven surveillance to prevent future pandemics.

### Pandemic Preparedness

Established in 2005 by the World Health Organization, the International Health Regulations (IHR) provide the legal framework that defines the countries' rights and obligations in the context of public health emergencies such as pandemics. The IHR are an instrument of international law in the field of health. One hundred ninety-six countries, including 194 WHO Member States, are part of the IHR. WHO has the coordinating role in the implementation of IHR and help countries to build capacities to have the adequate response if a public health crisis arrives. States are responsible for implementing the IHR at national level. The IHR has required all the countries to build the capacities able to detect (surveillance systems), assess, report, and respond in a timely matter to any public health emergency of international concern. The goal of country implementation of IHR is to limit the spread of health risks to other countries and to prevent travel and trade restrictions.

WHO recommended that all Member States update their pandemic preparedness plans based on the lessons learnt from 2009 pandemic (H1N1), new evidence on the effectiveness of public health measures that has become available in the meantime, and an ongoing risk assessment (World Health Organization, 2019a). At the beginning of Covid-19 pandemic, only 15 out of 53 countries from the European Region of WHO have published revised national pandemic plans. None of the 15 revised national pandemic plans refers to the role of genomics in public health surveillance. The only “omic” mentioned in some pandemic plans was “economic.” (World Health Organization, 2019b).

Published jointly by WHO and European Centre for Disease Prevention and Control (ECDC), the document “Key changes to pandemic plans by Member States of the WHO European Region based on lessons learnt from the 2009 pandemic” include no reference to the genomics or other omics as a potential tool to be used in the pandemics control.

The IHR Review Committee declared in 2011: “The world is ill-prepared to respond to a severe influenza pandemic or to any similarly global, sustained and threatening public-health emergency.” According to World Health Organization, “pandemic preparedness is a continuous process of planning, exercising, revising, and translating into action national and subnational pandemic preparedness and response plans. A pandemic plan is thus a living document, which is reviewed regularly and revised if necessary, for example, based on the lessons learnt from outbreaks or a pandemic, or from a simulation exercise.” (World Health Organisation, 2019a).

The “Interim progress report of the Review Committee on the functioning of the IHR (2005) during the COVID-19 response” recognize that “the COVID-19 pandemic has revealed significant gaps in pandemic preparedness in countries across the world, including in the areas of: surveillance, health systems, equipment and training, essential public health functions, and the role of national IHR focal points, emergency legislation, risk communication, and coordination.” (World Health Organization, 2021b).

The Interim Progress report recognize the role of the genomics for pandemic response and public health surveillance: “In order to engage the global scientific community in these response efforts, it is critical that pathogens, their genomic sequence, and relevant clinical samples be rapidly made available to the global medical research community.” (World Health Organization [2021a]).

### **The Use of Genomics to Control the Infectious Diseases Outbreaks**

SARS-CoV-2 represent the third emergence of a coronavirus outbreak in the last 20 years, after SARS-CoV and MERS-CoV, both have been known to cause lung disease in humans. To control the previous pandemics and to prevent future outbreaks with SARS-CoV and MERS, WHO provided recommendations on the surveillance systems both for animal and human health.

In 2018, the Interim Guidance of WHO on MERS-CoV specifics: “Specimens testing positive for MERS-CoV should be genetically sequenced, and the data uploaded to publicly accessible databases. If the laboratory doing the initial test does not have the capacity for genetic sequencing, an aliquot of the specimen should be forwarded

to a reference centre. Such centres should attempt to isolate viruses from all cases so that whole genome sequencing can be performed, either in the national or international reference laboratory.” (World Health Organization, 2018).

Genomic sequencing is used to determine if the dromedary camels from North Africa and the Middle East, who are the natural reservoirs of MERS-CoV, are infected with the virus and enable a more precise approach on understanding the epidemiology and the viral dynamics (Kandeil et al., 2019). The use of genomic data could help to have a better understanding of the transmission history, of the hosts (animals and humans), natural reservoirs, and viral transmission enabling effective public health interventions, and prevention of future outbreaks.

Africa has to face a complicated landscape when it comes to infectious diseases (World Health Organization, 2020). Over the past decade, Africa experienced two Ebola virus epidemics (Delamou et al., 2017), and overall more than 140 infectious diseases outbreaks are reported every year (WHO, 2018). In this context, in some African countries, genomic surveillance systems for Lassa fever (Nigeria—Siddle et al., 2018) or Ebola virus (Democratic Republic of Congo—Mbala-Kingebeni et al., 2019) were implemented. For the implementation of the genomic surveillance of the HIV and subsequent data-driven strategies, the Phylogenetic and Networks for Generalized Epidemics in Africa (PANGEA—Abeler-Dörner et al., 2019) aiming to “guide targeted prevention efforts through characterizing transmission dynamics and identifying unrecognized clusters and untreated individuals who are probable drivers of HIV transmission” (Inzaule et al., 2021) was built.

### **The Role of Genomics in the Covid-19 Pandemic**

According to the European Centre for Disease Prevention and Control, “sequencing of (partial) genes and whole genomes (WGS) has been proven as a powerful method to investigate viral pathogen genomes, understand outbreak transmission dynamics and spill-over events and screen for mutations that potentially have an impact on transmissibility, pathogenicity, and/or countermeasures (e.g., diagnostics, antiviral drugs and vaccines). The results are key to informing outbreak control decisions in public health” (European Center for Disease Control, 2021).

In the Covid-19 pandemics, genomics has been used so far for rapid identification and initial characterization of the virus, for the development of diagnostic tests and the development of the vaccines (Table 1). The genomic surveillance leads also to the identification of new concerning strains of SARS-CoV-2 such as B.1.1.7, B.1.351, or P.1. Within a year of the initial identification of SARS-CoV-2, more than 450,000 full genome sequences have been shared through public database GISAID (van Noorden, 2021). The world leader in the area of genomic surveillance of SARS-CoV-2 is United Kingdom with a total of more than 350,000 samples sequenced (COG Consortium UK).

### **The Use of Genomic Information to Inform Public Health Decisions at EU Level**

Published in 2012 as part of the Public Health Genomics Network Europe II Project (Brand, 2012). The *European Best*

TABLE 1. EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL—OBJECTIVES OF SARS-CoV-2 GENOMIC SEQUENCING

Main objectives	Early detection and characterization of emerging variant viruses to define if they are of particular concern; Assessing the impact of genetic and antigenic variant viruses for the pandemic and monitoring them over time to guide public health action.
Specific objectives	Investigating virus transmission dynamics and introductions of novel genetic variants; Modeling the antigenic properties of the virus to assess the risk of vaccine escape; Selecting viruses for vaccine composition; Assessing the impact of mutations on the performance of molecular diagnostic, antigen characterization and serological methods; Investigating the relationship between clades/lineages and epidemiological data such as transmissibility and disease severity or risk groups; Understanding the impact of response measures on the virus population; Assessing relatedness of viral strains within epidemiological clusters and supporting contact tracing and other public health interventions; Assessing and confirming reinfections; Monitoring emerging lineages within wild/domestic/farmed animal populations that may impact human health; Prompting further basic research investigation to confirm the relevance of observed mutations in the pathogenesis of the disease (e.g., infectivity, receptors binding); Assessing the impact of mutations on the performance of antiviral drugs; Assessing the potential incidence of vaccine-derived virus infections and transmissions should live SARS-CoV-2 vaccines become available.

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

*Practice Guidelines for Quality Assurance, Provision, and Use of Genome-based Information and Technologies (GBIT)* provided concrete recommendations to the European Commission and Member States for the best use of Genome-Based Information and Technologies (Table 2).

Despite this conceptual framework, the use of genomics in the Covid-19 pandemic differs from one Member State to another, with Denmark as European leader. Most of the EU Member States did not implement genomic surveillance systems for infectious diseases. Denmark increased the surveillance and analytics capacity to sequence all the samples at the beginning of 2021 when the new variant B.117 threatened to become dominant.

As a consequence, both in Denmark and in United Kingdom, the genomic data informed in real-time the public health interventions implemented by the Governments to control the outbreak at the beginning of 2021.

To control the Covid-19 pandemic, European Union must be ready and prepared for the possibility of future variants being more or fully resistant to existing vaccines. European Commission announced the launch of “HERA Incubator: Anticipating together the threat of COVID-19 variants,” “a new bio-defence preparedness plan, to access and mobilize all means and resources necessary to prevent, mitigate, and respond to the potential impact of variants.” HERA Incubator “will serve as the vanguard for the European Health Emergency Preparedness and Response Authority. HERA Incubator will work closely with the European Centre for Disease Prevention and Control (ECDC) to ensure that Member States have sufficient sequencing capacities and access to sequencing support services. HERA Incubator and ECDC will standardize sequencing procedures so that the data are comparable.” (European Commission, 2021a).

SARS-CoV-2 genome sequencing, data sharing, and analytics should become a priority for public health policies at EU level and beyond. The free movement of citizens in the

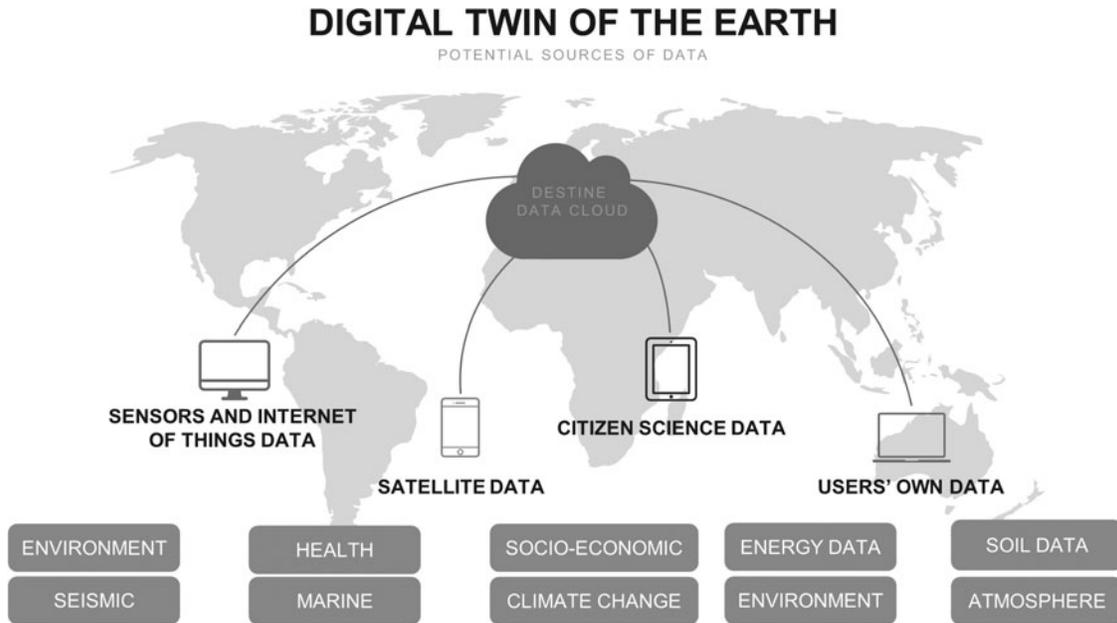
European Union is followed by the free movement of different variants of SARS-CoV-2. In this context, a common approach of all EU Member States on the genomic surveillance of SARS-CoV-2 could contribute to a better control and finally to a shortening of the Covid-19 pandemic.

The European Health Data Space, one of the top priorities of the European Commission for 2019-2025, should include a *Centre for SARS-CoV-2 Genomics Data and Analytics* to collect, standardize and analyze sequencing data from all the EU Member States and to provide regular public health reports aiming to inform the decision-makers on the evolution of the Covid-19 pandemic. This pan-EU data-driven public health initiative will pave the way to more precise and coordinated public health interventions and could shorten the course of the Covid-19 pandemic. In addition to the sequencing of the samples collected from the Covid-19 patients, the regular surveillance of waste water could also add value.

TABLE 2. THE EUROPEAN BEST PRACTICE GUIDELINES FOR QUALITY ASSURANCE, PROVISION, AND USE OF GENOME-BASED INFORMATION AND TECHNOLOGIES (PART OF THE RECOMMENDATIONS)

Develop new strategies for the use of GBIT within the public domain.
Identify and assess new GBIT for proactive and timely decision-making.
Maintain an infrastructure for the sharing of GBIT data in public health settings.
Improve the implementation of promising GBIT under conditions that safeguard the wellbeing of citizens
Support health policies related to GBIT based on good governance and trust.
Integrate GBIT into the professional training and life-long learning curricula of health professionals

GBIT, Genome-based Information and Technologies.



**FIG. 2.** Digital twin of the Earth—potential sources of data. Source of information: European Commission, 2021.

Public health genomics, as we move forward for pandemic preparedness, will likely expand toward planetary health genomics, signaling a broadening in scope of public health genomics from public to planetary health, and emphasis on ecological determinants of health.

### Digital Twin of the Earth to Prevent Future Pandemics

DestinE will be launched in 2021 by the European Commission in the context of Green Deal and Digital Strategy aiming to “unlock the potential of digital modeling of the Earth’s physical resources and related phenomena such as climate change, water/marine environments, polar areas and the cryosphere, etc. on a global scale to speed up the green transition and help plan for major environmental degradation and disasters.

At the heart of Destination Earth will be a federated cloud-based modeling and simulation platform, providing access to data, advanced computing infrastructure (including high-performance computing), software, AI applications, and analytics. It will integrate digital twins—digital replicas of various aspects of the Earth system, such as weather forecasting and climate change, food and water security, global ocean circulation and the biogeochemistry of the oceans, and more—giving users access to thematic information, services, models, scenarios, simulations, forecasts, and visualizations. The platform will enable application development and the integration of users’ own data” (European Commission, 2021b).

A high-precision digital model of the Earth is aimed to be developed by the DestinE to monitor and simulate natural and human activity. A digital twin is a digital replica of a living or nonliving physical entity. Digital twins use multiple data sources and rely on the integration of continuous observation, modeling and high-performance simulation, resulting in highly accurate predictions of future developments (Fig. 2).

“The digital twins created in DestinE will give expert and non-expert users tailored access to high-quality information,

services, models, scenarios, forecasts and visualisations. This includes models of the climate, weather forecasting, hurricane evolution and more. Digital twins rely on the integration of continuous observation, modelling and high performance simulation, resulting in highly accurate predictions of future developments.” (European Commission, 2021b).

From the planetary health, pandemic preparedness, and omics perspective, a planetary digital twin based on omics data generated through the continuous monitoring of high-risk animals (e.g., bats) and human populations, and also other types of real-world real-time data, could enable the prediction of future events, early warnings, and precision planetary health interventions. Big data in both the public domain and the health care industry are growing rapidly, for example, with broad availability of next-generation sequencing and large-scale phenomics datasets on patient-reported outcomes (Tanwar et al., 2021).

### Conclusions and Outlook

The Covid-19 pandemic is a planetary health issue and requires a global action based on data and new and efficient technologies. Planetary health needs to adopt a “one health” type approach that moves beyond an anthropocentric framework and considers the interdependencies among human, animal, and plant health. Genomic surveillance of the SARS-CoV-2 should become a key part of the pandemic response and planetary health genomics allowing the tracking of the new variants and implementation of precision planetary health interventions. For the future, the planetary digital twin could increase the resolution of the pandemic preparedness process and the capacity to predict and react to the next pandemics.

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#### Abbreviations Used

DestinE = Destination Earth

FHML = Faculty of Health, Medicine, and Life Sciences

GBIT = Genome-based Information and Technologies

IHR = International Health Regulations

MAHE = Manipal Academy of Higher Education

SARS- = severe acute respiratory syndrome

CoV-2 = coronavirus 2

SPARC = Scheme for Promotion of Academic and Research Collaboration

UNU- = United Nations University—Maastricht

MERIT = Economic and Social Research Institute on Innovation and Technology