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Science & Society

Joining European Scientific Forces to Face Pandemics

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Despite the international guidelines on the containment of the coronavirus disease 2019 (COVID-19) pandemic, the European scientific community was not sufficiently prepared to coordinate scientific efforts. To improve preparedness for future pandemics, we have initiated a network of nine European-funded Cooperation in Science and Technology (COST) Actions that can help facilitate inter-, multi-, and trans-disciplinary communication and collaboration.

COVID-19 emerged at the end of 2019 as a novel zoonotic disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The World Health Organization (WHO) declared this disease a pandemic on the March 11 2020 [1]. As of the beginning of October 2020, this emergent new virus has infected more than 34 million people and caused more than 1 million deaths worldwide (https://coronavirus.jhu.edu/map.html). Other infectious diseases are also responsible for many deaths. For example, seasonal flu causes 290 000 to 650 000 respiratory deaths every year [https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal)]. This has triggered little reaction other than recommending vaccination, indicating that the supposedly common thread that should link every action, from prevention to therapy, still has several gaps, despite our thorough knowledge of this disease. Established international guidelines have been published for both seasonal flu (https://www.who.int/influenza/preparedness/pandemic/en/) and COVID-19 (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/maintaining-essential-health-services-and-systems; https://www.covid19treatmentguidelines.nih.gov/; https://www.ecdc.europa.eu/en/publications-data/guidance-health-system-contingency-planning-during-widespread-transmission-sars). However, no country has been sufficiently prepared to tackle the COVID-19 pandemic, despite this support.

The world has witnessed several pandemics in the last 100 years: the 1918 pandemic (H1N1 virus), the 1957–1958 pandemic (H2N2 virus), the 1968 pandemic (H3N2 virus), and the 2009 H1N1 pandemic (H1N1pdm09 virus). Other emergent diseases have caused serious epidemics, such as SARS in 2003, Middle East respiratory syndrome (MERS) in 2012, and Ebola in 2014 (https://www.cdc.gov/flu/pandemic-resources/basics/past-pandemics.html). Sufficient time has passed and both science and technology have significantly evolved. So why were we not better prepared? Why did we not have a better coordination of scientific efforts to control, prevent, and treat COVID-19?

The first peak of the COVID-19 pandemic has seen unprecedented efforts by the scientific community. However, the international scientific community needs to be better prepared for the ongoing second wave of COVID-19 and for future pandemics.

In our opinion, four pieces of evidence showing the lack of coordinated action among scientists have emerged during the COVID-19 pandemic.

First, the whole world in general, and Europe in particular, has suffered from a severe lack of accessible and comprehensive multinational platforms to facilitate interdisciplinary discussion and collaboration. Although national-level initiatives have provided a good starting point for collaborative platforms in several countries, as far as we know, these national platforms did not join international interdisciplinary networks. In our opinion, the lack of international and interdisciplinary networks has slowed down Europe's capacity to react quickly and control the disease effectively.

Second, reliable scientific information has been scattered. With the pandemic underway, the amount of scientific information

has been overwhelming and sometimes widely dispersed among articles that have reported conflicting data.

Third, there has been a lack of coordination between research laboratories with complementary expertise and resources.

Fourth, in most cases, communication between scientists, governments, and national and international organizations [such as the WHO, National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), and European Centre for Disease Prevention and Control (ECDC)], has been guarded rather than being open, contributing to the lack of timeliness in public-health response. This guardedness was not due to negligence, but was simply because the limited information on COVID-19, that single research institutions and hospitals started to collect in Europe, has not been effectively shared. Neither the ongoing nor future pandemics will be solved by a solution provided by a single research discipline. Multilayered solutions will be required, which means that scientists from different areas of research must join forces, communicate better across and within their own disciplines, and share resources (e.g., samples from biological banks, data repositories, instrumentation, and expertise).

Organizing an inclusive platform to allow inter- and trans-disciplinary networking on emerging infectious diseases is an urgent need in Europe. Ideally, this platform could contribute towards international collaboration between scientists. It could work closely with pre-existing national platforms, become an active partner for future trans-national initiatives, or liaise with international organizations and decision makers. By accelerating the exchange of scientific information and expertise and by proposing international plans to act immediately at diagnostic and research level, the platform would produce reciprocal benefits for

scientists and stakeholders against future waves of COVID-19.

European Cooperation in Science and Technology (COST) is an organization that promotes bottom-up ideas across multiple disciplines and creates networks (i.e., COST Actions, funded by EU research and innovation framework programs). COST Actions include scientists, principally from European countries, working on specific topics in disciplines such as social sciences and humanities, physical sciences and engineering, or life sciences. These networks promote the rapid exchange of knowledge, expertise, and research, by funding meetings, training schools, and short-term tenures at the institutions of members involved in COST Actions. Unlike other EU-funded consortia that are fixed from the moment they are established, COST Actions are flexible, as they accept new members, including academic and public institutions, private companies, non-governmental organizations, and European and international organizations, at any point in time after inception.

Given this flexibility of COST Actions, we believe that the previously mentioned collaborative scientific anti-pandemic approaches can be coordinated in Europe by a novel Trans-COST Actions initiative. With this aim, in April 2020, we initiated an informal Trans-COST Action network on COVID-19, gathering scientists from nine COST Actions with different expertise (Figure 1) (https://www.cost.eu/news/cost-actions-unite-efforts-in-the-fight-against-covid-19/).

In the last 3 months, 64 Actions have collaborated, with the aim of initiating another mega-network supported by COST Association, including disciplines from 11 core scientific fields (https://www.cost.eu/wp-content/uploads/2020/06/COST_CovidBooklet_V10.pdf). Other European networks have also been established

during the course of the pandemic: the Dariah-EU, to assess the societal and human impacts of COVID-19 (https://www.dariah.eu/2020/05/18/launch-of-world-pandemic-research-network-to-assess-the-societal-and-human-impacts-of-covid-19/), the European Clinical Research Infrastructure Network (https://ecrin.org/), the Confederation of Laboratories for Artificial Intelligence Research in Europe (https://claire-ai.org/), The Institute Pasteur International Network Collective Effort, involving member institutes from Europe, Asia, and Africa (https://www.pasteur.fr/en/covid-19-pandemic-institut-pasteur-international-network-collective-effort), the Network Medicine Alliance and Institute (https://www.network-medicine.org/), and the EU-CardioRNA Task Force, which launched a 'call to action for the cardiovascular side of COVID-19' [2]. Moreover, other initiatives around the world have emerged, such as the 'Covid-19 action initiative' promoted by the American Lung Association (https://www.lung.org/research/about-our-research/covid19-action-initiative) and the 'Global Health Platform' (https://pti-saludglobal-covid19.corp.csic.es/en/). Even though the Trans-COST Actions network mostly fosters internal collaborations, we will interact with these other emerging networks.

At present, the Trans-COST Action network (Table 1) provides an unprecedented platform to promote interaction between scientists with complementary expertise and skills, as it gathers critical mass from diverse disciplines, including virology, epidemiology, sociology, clinical disciplines involved in the treatment of COVID-19 (e.g., intensive care, pneumology, cardiology, neurology, nephrology), bioinformatics, medicinal chemistry, pharmacology, and cell biology. This cross-disciplinarity speeds up scientific collaborations and achievements. For instance, the know-how of a virologist on SARS-CoV-2 may help cell biologists to select the best *in vitro* tools to understand the pathogenesis of COVID-
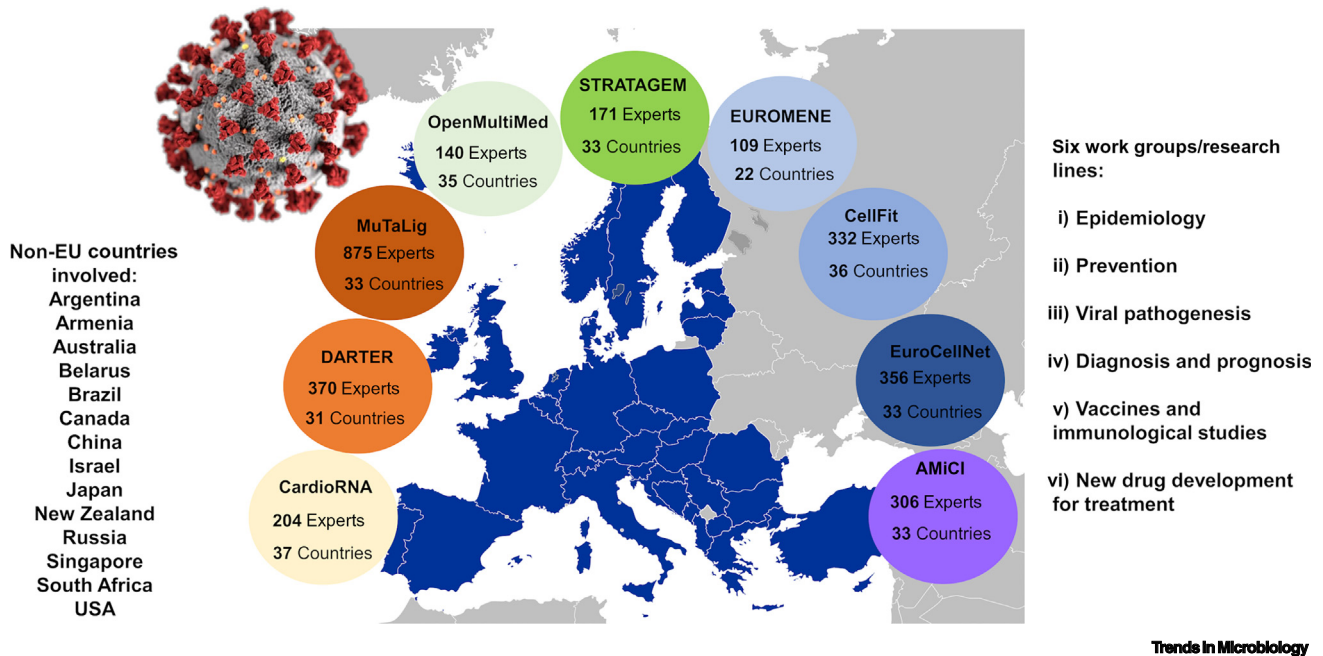
Figure 1. Trans-Cooperation in Science and Technology (COST) Action Network at a Glance. Representation of the Trans-COST Action network. Colored circles represent the nine participating COST Actions; the contents of the circles indicate the number of experts participating in each Action and the number of countries involved. Other non-EU countries that are members of those Actions have been also listed. The Trans-COST Action network has been organized into six work groups or research lines: epidemiology, prevention, viral pathogenesis, diagnosis and prognosis, vaccines and immunological studies, and new drug development for the treatment of coronavirus disease 2019 (COVID-19).

19, medicinal chemists and pharmacologists to design putative antiviral agents, and clinicians to treat patients infected with SARS-CoV-2.

Even though the coordination of such a large network will be difficult, as the main organizers of this currently informal platform, we will work towards obtaining formal recognition by COST, including the necessary funding for the improved coordination of scientific effort when facing pandemic situations. In fact, although COST networks are always very large, COST has had many success stories that prove its effective approach in managing and coordinating networks. One example is the AMiCI ePlatform (https://sub.samk.fi/projects/amici-eplatform/), which is a part of the COST network that was born from a previous COST Action and is supported by Horizon 2020 (the biggest EU-funded research and innovation program for the period 2014–2020). The

AMiCI ePlatform aims to define a 'test bed' tool for antimicrobial coating solutions in health care.

The Trans-COST Action network has been discussing the key steps that need to be undertaken, from both scientific and public-health perspectives, while tackling COVID-19, since these two areas are interconnected during a pandemic. For example, the screening of European Medicines Agency- and FDA-approved drugs for cardiovascular or inflammatory diseases using virtual screening, followed by biological validation assays, could be effectively translated into methods to rationally select drugs for testing in infected patients. Another example is the ongoing research into improving the chemical properties of antimicrobial coatings and disinfectants, which could be readily exploited to recommend specific cleaning guidelines for public places where the risk of transmission is higher.

As soon as it was created, the Trans-COST Action COVID-19 network set goals, research lines, and means of cooperation via remote calls. To enable collaborations, the platform immediately facilitated rapid contact with suitable and complementary experts via a simple survey to identify each member's expertise and, also, the expertise that they require. The sharing of basic research expertise (e.g., cellular models to simulate SARS-CoV-2 adhesion and replication, techniques to monitor viral proliferation and cell damage, tools for drug synthesis and drug-target prediction, platforms for drug screening, computational modeling, and artificial intelligence-based algorithms) and translational information (e.g., clinical databases reporting information of diagnosis and follow-up of COVID-19 patients, biological samples such as blood and exhaled breath condensate) has favored the complementation of skills and the development of collaborations.

CellPress

Table 1. Areas of Expertise of the Trans-COST Action Network to Face Current and Future Pandemics

COST Action acronym	Name of COST Action	Possible contributions to studying current and future pandemics	Refs
EUROMENE CA15111	European Network on Myalgic Encephalomyelitis/-Chronic Fatigue Syndrome	Multidisciplinary expertise, including epidemiologists, clinicians, virologists, molecular biologists, biochemists, public-health specialists. By using SARS-CoV-2 virus in culture and established infection models, researchers have already started investigating different conditions related to COVID-19 morbidity and SARS-CoV-2 infection, focusing on the interaction between virus and host organism, the immunological response (especially on T cell response), the development of novel antiviral agents and immunomodulator drugs, and the surveillance of post-SARS-CoV-2 chronic fatigue syndrome.	[3,7]
EuroCellNet CA15214	An Integrative Action for Multidisciplinary Studies on Cellular Structural Networks	The researchers of the Action are experts in analyzing host–pathogen interactions, entry and proliferative mechanisms, and drug–protein and protein–protein interactions, using cellular and animal models of inflammation and drug screening with infection-mimetic models studied in connection with multidisciplinary platforms working on COVID-19 (https://www.csic.es/en/research/interdisciplinary-thematic-platform) and biobanks (https://www.bbmri-eric.eu/covid-19). Top expertise, including ultra-high resolution imaging technologies, is available at the institutions of the Action (https://eurocellnet.eu/database-of-available-techniques) and the EuroBioImaging network (https://www.eurobioimaging.eu/data).	[8,9]
AMiCI CA15114; AMiCI ePlatform CIG 15114	Anti-Microbial Coating Innovations to prevent infectious diseases; ePlatform for a 'test bed' tool across the EU for antimicrobial coating solutions in health care entering to the market	Expertise in designing AMCs and methods that test their efficacy. The Action has established guidelines for cleaning practices using AMCs, regulations, and risk-benefit analyses for public health. AMCs have potential not only in health-care settings, but also in other environments, such as public places and transportation.	[10]
EU-CardioRNA CA17129	Catalyzing transcriptomics research in cardiovascular disease	Multidisciplinary expertise, including clinicians, molecular biologists, biochemists, bioinformaticians, systems biologists, and experts in artificial intelligence and science communication. These researchers apply the knowledge gained in cardiovascular diseases to COVID-19. They also have access to multiple cohorts of patients, clinical data, and biological samples to develop novel RNA-based tools to monitor the progress of the patients after the onset of infection and identify therapeutic targets.	[11]
EU-OpenMultiMed CA15120	Open Multiscale Systems Medicine	Expertise in network and systems medicine, mathematical modeling, agent-based multiscale simulators, bioinformatics, and drug repurposing. Some researchers in the Action are already actively working on several approaches toward COVID-19 network-based drug repurposing.	[6]
EU-CellFit CA16119	In Vitro 3-D total cell guidance and fitness	Expertise in building in vitro platforms that recreate mechanical cues and 3D architecture of the in vivo environment, allowing cell homing in a controllable and reproducible manner. The 3D cell culture models can be used as tools to explore how tissues interact with SARS-CoV-2, as well as to provide useful knowledge for possible future Coronaviridae infection waves. This modeling approach ensures safety and by-passes the problem inherent in the manipulation of the real pathogen, which inevitably reduces manpower because the number of infrastructures qualified to work with SARS-CoV-2 is currently very limited, representing a bottle-neck in COVID-19 research. The choice of new in vitro models that mimic infection by SARS-CoV-2 without the need to work with the real pathogen will speed up our understanding of the infection mechanisms, consequently enabling the screening of different antiviral compounds.	[12]
EU-STRATAGEM CA17104	New diagnostic and therapeutic tools against multidrug-resistant tumors	Expertise in pharmacogenomics, bioinformatics, data mining, identification of drug targets, drug repurposing, drug development and delivery, toxicology, drug resistance, and pharmacovigilance. The researchers will translate their expertise in the field of tumor drug resistance to the study of resistance mechanisms of SARS-CoV-2 towards currently used antiviral agents, taking advantage of the multiple and complementary expertise present in the Action.	[4,13]
MuTaLig CA15135	Multitarget paradigm for innovative ligand identification in the drug discovery process	Expertise in medicinal chemistry, including synthetic and natural products, biophysical and theoretical chemistry, molecular modeling, and biological screening. The multitarget issue is specifically relevant in the case of COVID-19, because of the presence of multiple (defined) macromolecules, which can be targeted in the structure of the virus.	[5]
EU-DARTER CA17103	Delivery of Antisense RNA Therapeutics	Expertise, including pharmaceutical chemistry, drug-delivery systems, and disease models for a wide array of targets, from rare diseases to cancer and cardiovascular diseases. Participants include academics, clinicians, big and small pharmaceutical companies, and pharmaceutical regulators. Participants have previous networking experience that has led to the development of advanced therapies for a wide range of disorders.	[14,15]

In addition to published studies [3–5], the first successes were the development of the COVEX software (https://exbio.wzw.tum.de/covex/) to study the SARS-CoV-2 and SARS-CoV-1/host interactome [6] and the generation of the Drug Repositioning And Cooperation Database (DRACD; https://dracdb.mohrkeg.co.at/dracdb). DRACD will allow the upload of information on FDA-approved drugs or novel substances that our medicinal chemists may have synthesized. Following upload, DRACD queries databases on known substance–target interactions. Finally, contact information is stored to allow rapid contact with users that own a particular substance, thus facilitating collaborations between groups that work on the same molecule. These tools are all freely accessible and integrated with the latest tools for drug repurposing (https://arvix.org/abs/2004.07229). An additional initial success in terms of public health activities was the involvement of one of the network's Actions in the preparation of the guidelines on 'Clinical, biochemical, immunogenetic paradigms of COVID-19 infection and their correlation with socio-demographic, etiological, pathogenetic, diagnostic, therapeutically and prognostically relevant factors', which is part of the Latvian 'COVID-19 MITIGATION program. This involvement will be supported by the network's wide range of expertise.

We intend to empower COVID-19 research by avoiding its confinement to a restricted number of high-security laboratories that can work with the pathogen. The existence of an inclusive and multidisciplinary group of experts will help, in a step-by-step manner, our understanding of infection mechanisms and expedite drug screening and repurposing and the development of vaccination strategies. This is necessary to speed up the screening of treatment options and of exploratory research lines that are set up in laboratories that work with surrogate models of SARS-CoV-2. After such screening, only the most promising research lines will be subsequently validated by the few available high-security virology laboratories working with the real pathogen.

Even though the network was initiated very recently, the platform has already gathered 2863 researchers from 49 countries. To become operational, we have organized our network into six working groups (Figure 1) that are gathering critical mass to move in four directions. First, we are drafting a roadmap for each of the aforementioned disciplines (Table 1) to facilitate faster responses to emergencies. Second, we are creating a network of laboratories that are equipped to quickly work on the diagnosis, treatment, and prevention of SARS-CoV-2 infection. Third, we are building a core set of trans-disciplinary research tools that would be available to the scientific community to aid research into COVID-19 and future pandemics. Finally, we are exploiting the tools and resources present in the network, to gather available clinical and epidemiological data, and to work on new pharmacological strategies to treat COVID-19 and develop new antimicrobial solutions to prevent infection.

Concluding Remarks

Coordinating scientific effort in Europe, and beyond, and integrating our activities with other similar networks in non-European countries will contribute to the development of faster and more effective ways to prevent, control, and treat pandemics, with obvious health and social benefits. What we learn from the ongoing COVID-19 pandemic will help us to establish strategies to combat future pandemics. In this sense, the current pandemic may become a paradigmatic 'opportunity' for future pandemic mitigation strategies.

Author Contributions

All authors contributed to this manuscript. The first and last authors were responsible for drafting original drafts and revising the final version. All authors edited the manuscript and approved the final version for publication.

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