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Wastewater Biomarker CoV-2—Wastewater-based Epidemiology Using SARS-CoV-2 as an Example Biomarker to Assess COVID-19 Infections at a Population Scale

Risk Management of Emerging Compounds and Pathogens in the Water Cycle (RiSKWa)

Scientists the world over are looking for new methods to detect coronavirus infections rapidly and reliably. One important approach here is wastewater-based epidemiology, in other words analyzing wastewater samples to acquire information about the health of the people living in a specific geographical area. Using PCR tests, it is also possible to identify the coronavirus pathogen SARS-CoV-2 in wastewater. The joint Wastewater Biomarker CoV-2 project uses the virus as a biomarker in wastewater analyses in order to detect a change in the infection pattern at an early stage, and to shed light on the unreported Covid-19 cases in the population. The novel SARS-CoV-2 biomarker concept is intended to support the authorities by serving as an early warning system in the fight against the pandemic.

Optimizing Detection of the Virus

Wastewater-based epidemiology is becoming an increasingly popular diagnostic method for estimating the development of local coronavirus infections. Following a recommendation by the European Commission in March 2021, the German Government is currently evaluating the nationwide application of SARS-CoV-2 wastewater monitoring in Germany.

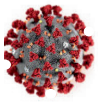
For accurate wastewater monitoring, the amount of virus in wastewater (transmitted through the fecal waste of infected individuals) must be reliably analyzed and detected. The detection of SARS-CoV-2 is based on different PCR analyses of previously prepared wastewater samples. To date, however, no standardized methods of detection designed specifically for wastewater have been available for enveloped viruses such as SARS-CoV-2. There is also a need for more research on sample preparation.

This is where the joint Wastewater Biomarker CoV-2 project comes in. The researchers involved in the project seek to optimize methods enabling reliable monitoring of coronavirus infections and prediction of local outbreaks at an early stage. The results of this wastewater monitoring will automatically be made available to the relevant health authorities and crisis management teams, who will be able to consult the results directly to estimate the spread of infection. This will support them in their decision-making regarding Covid-19 response measures.

Dashboard for Easier Access to Data

The Wastewater Biomarker CoV-2 project has been tested in several cities and municipalities in Bavaria and Baden-Württemberg. The wastewater in these areas has already been sampled regularly since mid-2020. Here, different SARS-CoV-2 genes serve as biomarkers and, based on the prevalence of these biomarkers in the samples, conclusions can be drawn regarding the local infection incidence. The project researchers are working on the development of a detection method that is sufficiently sensitive to provide a positive result even in the case of low incidence and virus concentrations. Numerous factors are considered here, including population density, the size and coverage of the sewage system, the volume of wastewater generated, precipitation volume, excretion rates per infected individual, and the fate and transport of SARS-CoV-2 in the sewage system.

With the dashboard, the municipal authorities in Berchtesgadener Land have a clear overview of wastewater monitoring data



Biomarker

NaWaM RiSKWa

In the municipality of Berchtesgadener Land in southeast Germany, for example, high-resolution wastewater monitoring has been underway since November 2020, in close cooperation with the local crisis management team and Joint Medical Service of the German Armed Forces. The virus concentrations recorded in the wastewater here are compared with the community-specific case numbers. The municipal authorities receive the data with minimal delay via a specially developed wastewater dashboard, which clearly displays the information in figures, diagrams, and maps. This dashboard—which is unlike anything developed in Germany to date—is the cornerstone of the wastewater monitoring system and enables efficient information management and short decision-making paths. The dashboard is supported by a sampling data collection app as well as a lab input mask for SARS-CoV-2 biomarker findings.

Over the course of the project, the SARS-CoV-2 wastewater dashboard used in Berchtesgadener Land will be developed further with a view to it being transferred to other municipalities and health authorities. The project team will create a set of relevant implementation guidelines. Three municipalities with different local conditions have been selected for the other pilots: the district of Ebersberg (east of Munich), the city of Augsburg, and the district of Augsburg. These model regions also have different digital infrastructures, reflecting the disparities between Germany's local health authorities.

Transferrable and Scalable

Comprehensive, georeferenced wastewater monitoring is an effective way to support decision-makers in local crisis management teams in their efforts to tackle coronavirus. The dashboard developed as part of the joint Wastewater Biomarker CoV-2 project serves as a transferrable tool which is compatible with various different reporting systems, making it suitable for nationwide use. Another advantage is that the analytical methodology can easily be adapted for other pathogenic viruses or for detecting resistance to antibiotics. Wastewater monitoring thus serves as an early warning system for the emergence of new infectious diseases.

Funding Measure
Risk Management of Emerging Compounds and Pathogens in the Water Cycle (RiSKWa)

Project Title
Wastewater-based Epidemiology Using SARS-CoV-2 as an Example Biomarker to Assess COVID-19 Infections at a Population Scale (Wastewater Biomarker CoV-2)

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CoroMoni—Development of a Communication Platform for Wastewater Monitoring to Determine the Level of SARS-CoV-2 Infection Among the Population

Risk Management of Emerging Compounds and Pathogens in the Water Cycle (RiSKWa)

The coronavirus pandemic has been impacting our daily lives for more than a year now. It has been known from the start that the virus is transmitted to our wastewater through human fecal waste. And while the virus in the wastewater is not viable, its genome can already be detected before a new wave of infection breaks out. A number of research projects in Germany and abroad are therefore working on the development of a wastewater-based COVID-19 early warning system. The CoroMoni project brings these research partners together, forming a network which, using synergies and research findings, will create a foundation that will pave the way for a Germany-wide wastewater monitoring system.

National and International Research Network

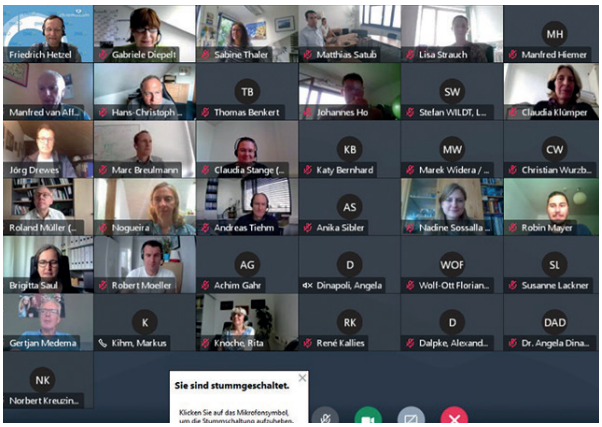
A number of EU member states, including the Netherlands, Finland, and Spain, are already systematically monitoring wastewater for COVID-19. This is important because wastewater provides an indication of the prevalence of COVID-19 infections in an area as well as the dominant variants of the virus. In fact, SARS-CoV-2 fecal shedding occurs in the majority of COVID-19 positive cases, even if the infected individuals are asymptomatic or the symptoms do not manifest themselves till later. For example, traces of the virus are detected in the wastewater seven to ten days before being confirmed with a positive test. The EU Commission has called on EU member states to make full use of this efficient and reliable source of information on the virus including variants and put wastewater monitoring systems in place as quickly as possible. Such systems can help authorities monitor developments and support them in their decision-making for COVID-19 response measures.

Numerous research projects on wastewater monitoring are currently underway in Germany, too. The Federal Ministry of Education and Research (BMBF) is funding three such projects: the “Wastewater Biomarker CoV-2” project which is being conducted by the Technical University of Munich, the Technical University of Darmstadtled project “SARS-GenASeq”, and the “COVIDready” project coordinated by the Research Institute for Water and Waste Management at RWTH Aachen (FiW). These projects are investigating different methods of tracing infection events in wastewater and developing the foundation for the development of a wastewater-based COVID-19 early warning system.

To help push forward this development and create synergies in this area, the CoroMoni project will form a network comprising national and international researchers. One of the key instruments here is a communication platform for the exchange of research findings. The project partners will then translate these findings into a strategy for the development of a wastewater monitoring system that can be implemented relatively easily and at no great cost, including selecting strategically important test locations.

Developing Guidelines and Concepts

The CoroMoni project partners will begin by developing quality standards and drafting guidelines that will apply throughout the entire wastewater monitoring process, from sampling and sample preparation to analysis and evaluation, and the presentation of the research findings.



CoroMoni project participants in a video conference

The project team will also be developing a training concept for the operating staff of the sewage works conducting the sampling.

To start with, COVID-19 wastewater monitoring will be trialed in various different pilot projects. The locations for these trial runs are selected in the EU-funded project ESI-CorA on the basis of various criteria, including the size of the sewage plant and sewage system, sampling system, digital equipment in the plant and crisis management teams as well as options for comparing data on case numbers in a municipality with the results for plant's respective catchment.

CoroMoni will support the ESI-CorA project and will also be involved in pilot project activities. Information on the German locations used for the trial runs will be published in the form of a digital map, providing an overview of the sewage plants participating in the wastewater monitoring project. CoroMoni will also provide information for the operators of wastewater treatment plants in municipalities and businesses that are not involved in the pilot projects. This will pave the way for Germany-wide introduction of the wastewater monitoring system once the model project phase is complete.

The key research topics in the CoroMoni project are developed in four working groups that meet in online video conferences. The groups' reports and research findings are published on a common digital communication platform, through which the teams can also access the minutes of the online meetings, project profiles, and updates on developments at EU level.

Valuable Findings for Future Pandemics

The project partners see the potential for their research results on wastewater monitoring to go beyond the scope of a COVID-19 early warning system, envisaging the results being transferred to a monitoring system that incorporates early warning, variant detection, and moving into all-clear level. Furthermore, current research will not be restricted to COVID-19 but will be instrumental in preparing for future epidemics or pandemics.

Funding Measure
Risk Management of Emerging Compounds and Pathogens in the Water Cycle (RiSKWa)

Project Title
Development of a Communication Platform for "Wastewater Monitoring to Determine the Level of SARS-CoV-2 Infection Among the Population" as a Networking Initiative for Research Actors in Germany (CoroMoni)

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COVIDready—Decentralized SARS-CoV-2 Monitoring in Sewage: Development of a Validated Surveillance Method for Routine Laboratories at Wastewater Treatment Plants

Risk Management of Emerging Compounds and Pathogens in the Water Cycle (RiSKWa)

The European Commission has called on member states to use systematic wastewater monitoring to combat the COVID-19 pandemic. Preparations are being made to trial a national monitoring system at a series of pilot plants in Germany, too. At the moment, however, the specialized labs that can detect genomes of the SARS-CoV-2 pathogen, including different mutations, in wastewater have insufficient capacity to conduct comprehensive analyses. The project partners in the joint COVIDready project will therefore be exploring ways to upgrade existing wastewater labs in sewage plants so that they can conduct this task. To ensure results can be quickly transmitted to the relevant health authorities, the project partners are creating interfaces and communication channels between the wastewater sector and the public health services.

Helping to Fight the Pandemic

We know that human beings carrying the coronavirus shed SARS-CoV-2 genomes through their feces. For this reason, analyzing wastewater for the prevalence of the virus can help provide a more complete picture of the pandemic situation, regardless of the population's willingness to be tested for the virus.

On the recommendation of the European Commission, EU member states have been urged to take steps to introduce national monitoring systems for SARS-CoV-2 and its variants as soon as possible. These monitoring systems will use wastewater samples taken at least twice weekly in every city with a population of 150,000 or larger. In Germany this applies to 56 cities and upwards of 200 sewage plants designed for more than 100,000 residents. The findings from the analyses, which are transferred to the relevant health services within 48 hours, provide valuable information that can assist decision-makers in implementing and communicating COVID-19 restrictions.

Owing to its decentralized wastewater economy, however, Germany is currently lacking the virology lab capacities and established communication channels with the public health services needed to fully implement the Commission's recommendation. To address this, the COVIDready project centers on existing labs in municipal sewage works. The project partners are developing viable, practical methods that enable wastewater labs to use ready-to-use test kits to determine the viral load on the basis of the Virus-RNA and that can also serve as an early warning system for variants of concern.

Decentralized Workflows for Wastewater Treatment Labs

To begin with, a semi-automatic workflow for decentralized use in wastewater labs is validated and trialed at three sewage plants in Germany's Emscher-Lippe region. Parallel to this, the researchers recreate the workflow in a second lab, assessing it for sensitivity, selectivity, workplace safety, usability, staff training requirements, operability, and costs.

Wastewater lab: Samples being prepared for the ready-to-use test kits

COVIDready
Dezentrales SARS-CoV-2 Monitoring im Abwasser

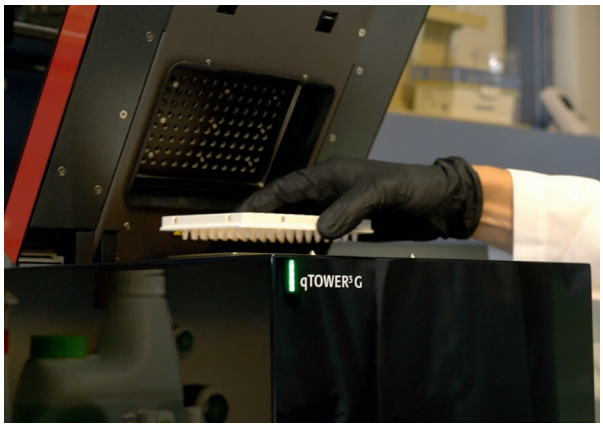
NaWaM RiSKWa

The project team will put together a training video that can be used to transfer the workflows to other laboratories in the wastewater sector. To ensure that virus mutations are reliably detected in wastewater samples, the project researchers use digital PCR (dPCR), a method that makes it possible to test irregular samples for variants of concern more quickly and at lower cost than with genome sequencing. The digital PCR method involves partitioning a positive SARS-CoV-2 sample into multiple individual PCR reactions, each of which can contain genomes of critical (positive-strand) or non-critical (negative-strand) RNA virus mutations. The ratio of positive to negative PCR reactions provides an indication of the prevalence and the spread of variants of concern in the population

Close Collaboration with Public Health Authorities

The project team collaborates with the public health authorities in the respective study area with a view to determining the requirements, needs, and expectations for the prospective chain of reporting. This includes networking workshops with the health authorities, water boards, and municipal water and wastewater utilities.

The joint COVIDready project will help pave the way for the establishment of a national monitoring system for COVID-19 and its variants. In addition to this, the solutions developed open up prospects for biotech companies to use their wastewater-adapted SARS-CoV-2 molecular detection methods and analytical instruments to create new fields of business in wastewater-based epidemiology. Over the medium term, the products developed can also be used to detect other viruses in our wastewater.



Samples are analyzed using PCR tests

Funding Measure
Risk Management of Emerging Compounds and Pathogens in the Water Cycle (RiSKWa)

Project Title
Decentralized SARS-CoV-2 Monitoring in Sewage-Development of a Validated Surveillance Method for Routine Laboratories at Wastewater Treatment Plants (COVIDready)

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SARS-GenASeq—SARS-CoV-2 Genome in Wastewater—Monitoring the Development of the Pandemic Using Sequencing

Risk Management of Emerging Compounds and Pathogens in the Water Cycle (RiSKWa)

With modern diagnostics we can detect almost anything in wastewater that people excrete via their stool and urine. And coronavirus or SARS-CoV-2 is no exception. Particularly because those infected with COVID-19 often do not develop any symptoms, yet still excrete the virus, wastewater analysis combined with individual testing can provide valuable information about the prevalence of local infection and help contain the pandemic. Wastewater analysis has proven especially valuable when it comes to virus mutations and new variants. These can be identified via traces of the relevant genome in wastewater. This hitherto under-researched area is the focus of the joint SARS-GenASeq project. Based on genomic analysis of wastewater samples, the project participants seek to develop concepts which enable reliable tracing of virus mutations and variants.

Tracking Virus Mutations

When it comes to combatting the coronavirus pandemic, mutations of the virus and the spread of new variants play an increasingly important role. Besides quantitative detection of SARS-CoV-2 in wastewater, it is also possible to use wastewater samples as sources of genome information—the genome provides all the genetic information about an organism—and thus identify how mutations spread at an early stage. To date, barely any research has been conducted on the potential use of wastewater samples for this purpose. In light of this, the objective of the joint SARS-GenASeq project is to improve measurement methods and concepts for tracking mutations and virus variants in wastewater. Detection methods have to be adapted to the specific challenges of wastewater. Because of its complex composition and numerous influences in the sewer network, generating robust data from the analysis of wastewater samples has so far proven difficult.

Adapting Methods for Wastewater

One focus of the project is to develop advanced sequencing techniques. Sequencing enables us to decipher the structure of viruses. All sequences that are found are compared to the original SARS-CoV2 genome, also known as the "wild type". This enables researchers to identify mutations. For genome analysis to be successful the genetic information or "Virus-RNA" has to be isolated.

The tools required to do this were originally developed for the clinical field but are now being tested and optimized by researchers within the SARS-GenASeq project for use with wastewater samples. For this purpose, genomic analysis is conducted with two different sequencing platforms. By comparing them, the intention is to show which of the two are better suited for the analysis of wastewater samples. With the help of the Virus-RNA, the scientists can crossreference the information with bioinformatic databases to acquire information about the variants that already exist in the catchment area of the sewage plant.

Virus-RNA from a wastewater sample is placed in the sequencer

The next step is to process the sequencing data such that the relevant health authority can effectively use the findings of the analysis in practice. To this end, the project partners are developing new methods of bioinformatics which condense complex data sets into meaningful results.

To ascertain which locations in the sewage system are best suited for sampling for the purposes of genome analysis, the researchers are investigating various sewage plants in the catchment area around the River Emscher. To do so, they take samples from plant inflows, pumping stations as well as sewer networks.

Corona and Beyond

With wastewater-based monitoring of the genetic material of viruses, valuable—and to date unavailable—epidemiological information on the origins and spread of variants and mutations can be generated with comparatively few samples. In exchange with other working groups and stakeholders, the results of the SARS-GenASeq project are intended to contribute to the development and establishment of a comprehensive nationwide monitoring system in Germany. A system of this type could also be used to analyze other viruses or antibiotic-resistant bacteria, thus helping prevent future pandemics or at least making it possible to get them under control more quickly.

Funding Measure
Risk Management of Emerging Compounds and Pathogens in the Water Cycle (RiSKWa)

Project Title
SARS-CoV-2 Genome in Wastewater—Monitoring the Development of the Pandemic Using Sequencing (SARS-GenASeq)

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