



Deliverable 4.2.3

Workpackage 4

JIP COVRIN

Responsible Partner: WBVR

Contributing partners: ANSES (P1), FLI (P10), APHA (P21), ISS (27), IZSLER (P29), PIWET (P34), INIAV (P35)



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CORONAVIRUS VARIATIONS RELATED TO ECOLOGICAL FACTORS AND INTERVENTIONS

All viruses, including SARS-CoV-2, the virus that causes COVID-19, change over time. Most changes have little to no impact on the virus's properties. However, some changes may affect the virus's properties, such as how easily it spreads, the associated disease severity, or the performance of vaccines, therapeutic medicines, diagnostic tools, or other public health and social measures.

To follow the emergence of SARS-CoV-2 variants, WHO established a Virus Evolution Working Group with a specific focus on SARS-CoV-2 variants, their phenotype and their impact on countermeasures. During the pandemic, within a large number of studies and also within the COVRIN project, SARS-CoV-2 variants have been characterized, mainly in humans but also in different animal species, to prioritize global monitoring and research, and to inform and adjust the COVID-19 response.

While monitoring the circulation of SARS-CoV-2 globally, it also remains essential to monitor their spread in animal populations and chronically infected individuals, which are crucial aspects of the global strategy to reduce the occurrence of mutations that have negative public health implications.

Within the COVRIN project, coronaviruses and SARS-CoV_2 variants have been genetically characterized in an increasing number of animal species. To assess the impact of ecological factors (species interactions, habitat, etc.) and human interventions (vaccination, trading of animals, etc.) on coronaviruses evolution (rates, composition of recombinants, potential contribution of vaccine strains) and spread (transmission chain between breeding facilities, detection of focal points or super spreaders), in the COVRIN project analyses are made of the genetic diversity and the global scale phylodynamic of coronaviruses of domestic animals and wildlife. In addition, virus diversity was also analyzed using the sequences obtained from the environment studies in the project.

Mutations occurring in Coronaviruses may affect the characteristics of the virus – including its ability to spread, cause severe disease or make treatments or vaccines less effective. In many cases, such alterations do not have competitive advantages that help the virus rise. However, they may also result in faster spread and evasions of the immunity induced by vaccination. Contribution of outcomes of several COVRIN research tasks, to better assessments of the risks of SARS-CoV-2 variants can be evaluated:

In the COVRIN subtask 2.4.3 in vivo experiments with SARS-CoV-2 variants (alpha, beta gamma, delta, omicron) were undertaken in hamsters, ferrets and humanized mice respectively, investigating infection parameters, drug efficacy, modes and routes of transmission contact and aerosol, disease pathogenesis, and virus survival on bio-matrix i.e. fur and skin. These studies contribute to our understanding on the threats of novel SARS-CoV-2 variants with regards to infection and transmission. The aim is to continue this kind of analyses for additional variants of SARS-CoV-2 that may be of concern for public health.

In the COVRIN subtask 3.4.5, transmission characteristics of the mink outbreaks are described for the countries where data was available. In the mink outbreak in the Netherlands studies were done to elucidate which factors determined the transmission dynamics. Spatiotemporal outbreak patterns were analyzed as well as virus genetic sequencing data, observed variation in clinical outcome and information on the between-farm contact structure. Analyses of the between-farm contact structure showed a significant correlation between cluster and the frequency distribution of different types of contact. Different AA mutations in the spike protein were identified among these clusters with some specific mutations being dominant in Cluster A2. Infection characteristics such as shedding and clinical presentation were also assessed and compared among clusters. Combining genetic and epidemiological models led to assessing transmission in higher detail.

COVRIN subtask 4.3.1 focused on the coronavirus detections in bat species. The findings in the subtask demonstrate that coronaviruses circulate among the bat population in Europe (in countries that have conducted studies), confirm high host specificity of BtCoVs, and expand the data on the geographical



distribution of coronaviruses. European BtCoVs are highly diverse and comprise two genera, Alpha- and Betacoronavirus, the latter including sarbecoviruses, the SARS-related CoVs that were or are the etiological agents of recent epidemics. Coronaviruses, as zoonotic pathogens with the ability to cross the species barrier, pose a potential risk of virus transmission to animals and humans; however, the spillover mechanism of bat related CoVs is multifactorial and mostly requires adaptation to replication in a new host.

Analyses of coronaviruses and SARS-CoV-2 variants within the COVRIN project, including genetic characterizations in different animal hosts to assess the impact of ecological factors and interventions, contribute to the public health preparedness regarding coronaviruses. The aim will be to continue this type of research in the coming years. Several studies in animal species, that have been initiated in the COVRIN project are continued and additional results should help to improve coronavirus preparedness also after the running period of the COVRIN project.