

Virology: Freedom to Operate?

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Origin of Corona Virus?

Recent information released by the German BND in April 2025 raises the question of how free can research be? In principle – research is free. The question is, whether dangerous research can be free – and more difficult is the question, what kind of research is dangerous? The report by the BND refers to studies performed by the German BND in summer 2020 and had been initiated by the then German Chancellor Angela Merkel. The report was immediately kept secret and is only now mentioned in newspapers. It is not published. The information from newspapers states, that with a probability between 80 to 95% the SARS Corona virus-2, CoV-2, escaped from a laboratory of the Wuhan Institute of Virology (WIV) in Wuhan. Even with my offer to sign a secrecy agreement, the document is unavailable to a virologist like me. I published a paper on “Risky Research” in 2021 [1,2] describing possibilities of laboratory accidents with human pathogens, including examples known from the past, mainly in context with SARS CoV-1. It is most important to learn, whether there is any information in the report about research on viruses what caused the pandemic and in order to learn, how to prevent other pandemics in the future. This

is of important general interest. So far it is kept secret and we cannot learn from it. There is a Freedom of Information Act (FOIA) in the USA, which exists also in Germany. Several organizations have recently released information about how to perform research with viruses, such as the German Society of Virology (GFV), the Leopoldina and the German Science Foundation (DFG) (2022), as well as local Ethics Committees. In all cases it is up to the researcher how to classify his research and whom to consult or include.

Gain-of-Function Studies

A major research approach in virology is based on recombinant DNA technologies. It is based on a natural mechanism how viruses evolve, such as by Horizontal Gene Transfer, the pick-up of genes and their transfer to other cells. Viruses serve as transport vehicles. This has recently been demonstrated with the mRNA vaccine by Biontech, which requires lipid vesicles, like incomplete viruses for packaging, transport and transfer. Horizontal Gene Transfer is an important contribution of viruses to the benefit of mankind, their role as drivers of innovation and evolution [3]. This includes also a risk if the viruses integrate and

disrupt or deregulate genes which might cause cancer. This is not obvious during a world-wide catastrophic viral outbreak. Also, in laboratories it is common to modify viruses for research. Modifications include insertions of foreign genes, often marker genes for easier virus detection, but also mutagenesis for understanding viral mechanisms, including how viruses cause diseases and how to develop drugs or vaccines. These Gain-of-Function technologies are not even difficult and students can learn them quickly. It is easy and even fun to combine for example 10 genes of different viruses and create a new one, which does not exist in Nature! Cell-culture experiments under sterile and high containment conditions or animal studies are more demanding and need to be learnt, they require training. They are also more dangerous for the experimentalists and the public.

Virologists want freedom for their research. However, studies with viruses with potential risk for human or animal health need to be restricted. For that reason there are safety conditions available, defined at 4 levels, biosafety level 1 to 4, BSL1 to BSL4. There exist three high containment laboratories BSL4 in Germany. Almost every laboratory has BSL2 (about 2000 in Germany), a few have BSL3 (about 100, which require among others a safety sterile clean bench and low pressure in the room). During the pandemic SARS CoV-2 research was upgraded and no longer classified as BSL2 but as BSL3 by the Robert Koch Institute. According to unproven information corona viruses were analyzed under BSL2 conditions, also in Germany before the pandemic started. However, it is unknown when and which type of Coronaviruses were analyzed under such conditions. Published photographs on the Wuhan laboratories often show the spectacular outfits of scientists in protecting gears and ventilators in BSL4 laboratories. They are available in the WIV, where they were initially constructed with the help by French virologists

from Lyon, who later left. Whether these rooms were used for Studies on Corona viruses and for what kind of research - animal studies? – is unknown. The pictures showing BSL4 rooms may be misleading.

Safety Measures

The problem is manifest: how to handle a potentially human pathogenic virus in the laboratory for cloning, cell-culture and animal studies? Who decides? We have regulations for recombinant DNA technologies, for Gene technologies (ZKBS), for protection of embryos (ESCHG), and restrictions for animal studies (TSchG), regulations against fire and organic solvents with special safety equipment. They all require training and documentation. However, nothing like this exists for viruses. Passage of viruses for adaptation to certain animal species or cells is not included in the ZKBS regulations. A new publication, more than 80 pages, has just been published by the German Science Council (Wissenschaftsrat) in May 2025, on safety in science - but it deals with five risks about how information can be "stolen", abused, interfered by political or social interference. The BNC was gratefully acknowledged. This is another problem than risky research.

Risks?

The Diagnostics Department at the Institute for Medical Virology, where I was Director in charge, employed more than a dozen technicians all of which were trained, and had certificates about how to handle infectious virus materials. They received regular bonus payments, because of the potential risks involved. Furthermore, there were very demanding audits, controls by official experts about methods, procedures, documentations, including visual inspections etc., which was guaranteed by an expert Head for Diagnostics with an academic

degree and practical experience. It was his responsibility that safety rules were fulfilled. This does not exist for virus research. The researcher can decide himself about potential risks and whether the local Ethics committee or the DFG should be involved or informed. A discussion about "potential risk" of virus research was initiated when it became known that a corona virus isolate from the USA was transferred to Wuhan including financial support. This act was possible because the respective Corona virus was then considered non-pathogenic for humans. However, based on the history with Corona viruses, it was "potentially" pathogenic for humans. Whether it was related to the later pandemic strain, is unknown. This indicates how difficult it is to judge the risk involved in research on viruses. The potential risk is important.

Gain-of-Function

Germany suffers from being overregulated. Especially the gene technology law put German research at a disadvantage. How could safety be implemented without such consequences? Universities could offer to virology students a course with certificate similar to animal studies. Virology Institutes should have a senior scientist responsible for safety as is standard for a diagnostics department on virology such as e.g. at the Zurich University. Viruses should be classified, described, listed and named according to risks such as Influenza, Corona, MERS, HIV and others. The Global Virome Project (GVP) estimated 25 viral families to have substantial risk of infecting people [3]. A potential risk should be sufficient to increase the safety measures and allow certain changes of viral genomes only under safety laboratory conditions. Viral envelopes have been modified in the past by mutagenesis or adapted to human cells with the risk of increased human pathogenicity. Certain modifications should only be allowed if the

virus was crippled or rendered non-pathogenic or replication incompetent. One could construct safe model viruses. Studies have to be restricted to appropriate safety laboratory conditions. Modifications of certain regions of viruses, such as the envelopes with their receptor binding sites, require safety laboratories. A Corona virus in a laboratory in Durham, North Carolina in the USA was first adapted to mice by serial passage and then adapted to a human lung cell-line, which had been modified before to express the ACE-2 receptor, "the best available model for human disease". The corona virus adapted to small animals and cell-culture showed a "gain in pathogenicity" as described by the authors [4]. The project had been approved by the local ethics committee and was performed solely under the "responsibility of the authors". No BSL3 facility was mentioned. This is a high-risk research, which the authors discuss themselves to be at the borderline between gain of knowledge for pandemic preparedness and risk of creating more dangerous pathogens. They ask for studies with non-human primates - and ask whether "these types of chimeric virus studies warrant further investigation versus the inherent risk involved". They mention the US government-mandated pause on gain-of-function studies from 2014 [5]. In the case of Influenza virus, GoF mutations were performed to evaluate the transmission of mutant viruses from ferret to ferret - an accepted animal model for human-to-human transmission. The data were published twice, by groups of Kawaoka and Fouchier. One manuscript got published immediately, the other one was put under a moratorium and the publication delayed. It had to be modified and the method section shortened to reduce the chance of a repeat [6,7]. Since researchers need to build their follow-up research on previous publications, journals could play an important role to restrict or refuse such publications as they did in the case of Influenza.

For publications authors have to always declare "no competing financial interest". This is mandatory. But nobody has to certify, that the study with viruses in animals was approved - by whom?

Summary

Research with certain viruses and certain genes and adaptations of viruses to human cells by serial passages require special safety measures - which are available. Animal studies with virus for vaccine development with challenge experiments, especially using wild-type viruses, are the most dangerous experiments and should be restricted to BSL4.

Clear rules have to be issued.

Virology has become an attractive topic of research. The annual meeting of the German Society of Virology (GFV) in Hamburg in April 2025 was attended by more than a thousand young researchers – many of them young students. They require our special guidance, training, education and warnings by seniors. Our freedom for research is limited by pandemic preparedness, to perform research under sufficient safety conditions. Training courses should become available and certificates mandatory. The risks in virology should be more clearly specified, named and described than at the present time to increase researchers' and public awareness. What went wrong in the WIV? This information, known only to the BND could help to prevent another pandemic.

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