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Using electrons to inactivate viruses More efficient vaccine production

Many vaccines contain viruses that are inactivated to prevent them from harming recipients. This is generally achieved by adding chemicals. Fraunhofer scientists are taking a different approach, using low-energy-electrons to irradiate the pathogens. The advantages of this new method are that it produces no toxic waste and provides a faster and less aggressive way of rendering pathogens inactive.

- **Viruses in many vaccines are inactivated by means of formaldehyde.**
- **Scientists at four Fraunhofer Institutes have developed a new method that makes it easier to inactivate pathogens: low-energy electron irradiation.**
- **The project is funded by the Bill & Melinda Gates Foundation.**

Polio, influenza, hepatitis A: one quick shot, and their pathogens have no chance. Most inoculations are based on inactivated vaccines – in other words, vaccines whose viruses have been killed and whose pathogens can no longer harm recipients. Their immune system nevertheless recognizes them, produces the necessary antibodies, and therefore provides effective protection. Up to now, chemicals – typically formaldehyde – have been used to kill the pathogens. But there are several disadvantages to that method: formaldehyde, just like the other chemicals used for the same purpose, is toxic. To minimize the risks to human health and the environment, these substances are used only when greatly diluted. This means that the pathogens must be exposed to the chemical for a long time in order to be destroyed. For instance, formaldehyde takes around two weeks to inactivate the poliovirus, which triggers poliomyelitis. A process that takes that long represents a disadvantage for industry. Moreover, formaldehyde also modifies the proteins in the viruses against which the immune system produces antibodies. Put another way, formaldehyde alters the viruses, which in turn reduces the effectiveness of the vaccine.

A faster and less aggressive way of rendering pathogens inactive

A promising alternative has been developed by researchers at the Fraunhofer Institutes for Cell Therapy and Immunology IZI, for Interfacial Engineering and Biotechnology IGB, for Organic Electronics, Electron Beam and Plasma Technology FEP, and for Manufacturing Engineering and Automation IPA. “We use low-energy electrons to irradiate the pathogens,” says Dr. Sebastian Ulbert, head of the working group at Fraunhofer IZI.

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Rather than days or even weeks, a few milliseconds are all that is needed to kill off viruses or bacteria. Not only does this significantly shorten vaccine production times, the electrons destroy only the nucleic acids in the viruses and bacteria, leaving their proteins intact. So the elements to which our immune system launches the desired immune response are also still intact after irradiation. A further important benefit is that no toxic chemicals are produced.

While there have long been experiments to use irradiation to eliminate pathogens, the experimental effort required has so far proven virtually unmanageable. For safety reasons, exposure to radioactive irradiation was possible only behind solid walls – certainly not within the production halls of the pharmaceutical industry. “In contrast, low-energy electron irradiation is possible in a normal laboratory,” says Ulbert. At the laboratory scale of 10 to 15 milliliters, researchers have already shown that the technique is error free: viruses are verifiably eliminated, and in initial experiments on animal models, the vaccine proved comprehensive protection.

Eliminating pathogens automatically and in large numbers

In a next step, the scientists want to inactivate viruses also in larger volumes. This is not as easy as it sounds. Since low-energetic electrons penetrate less than a millimeter into the liquid containing the viruses, the liquid must be presented in thin layers if the electrons are to reach every last target. With funding from the Bill & Melinda Gates Foundation, researchers are now developing two suitable prototypes that will inactivate pathogens automatically. The first prototype is almost finished: the solution to be irradiated is filled into bags, which ensures a sufficiently thin layer of liquid. With the second prototype, the scientists achieve a fine layer of liquid by running the solution over rollers. The scientists hope that clinical trials for vaccine production using these methods can start in around five years' time.

The applications of the new technology are not restricted to vaccines, however. “Using electron irradiation, we can also inactivate hazardous material without destroying it,” says Dr. Ulbert. As an example this would allow blood samples taken from people infected with the Ebola virus to be prepared in such a way that they can be examined safely in ordinary laboratories.

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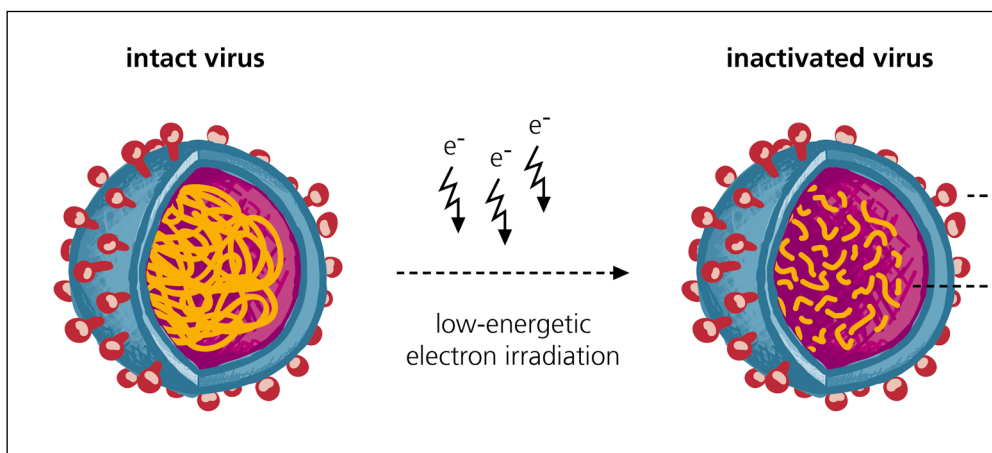
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The role of Fraunhofer Institutes in the project

Four Fraunhofer Institutes have pooled their expertise to work on viral inactivation. Fraunhofer IZI delivered proof of concept, which means it has demonstrated that the technique works as intended. Its researchers also undertook the vaccination studies. Colleagues at Fraunhofer IGB molecularly characterize the effect of irradiation on pathogens. Pathogens were inactivated due to the destruction of their genomes. At the same time, pathogen proteins were preserved enabling their use for efficient vaccination. Fraunhofer FEP is providing the irradiation technology, contributing its expertise in dosimetry, and is involved in building the prototype that is to be housed at Fraunhofer IZI in Leipzig. Fraunhofer IPA is developing a completely new technical procedure to transfer the "laboratory scale inactivation of small volumes" to an industrial scale for vaccine production.

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