Transgenic mice in influenza research – risk assessment and vaccine development

A research team from Freiburg is developing a method for identifying human influenza viruses of animal origin. This could potentially improve measures taken to prevent imminent pandemics. The researchers are working with genetically modified mice. Transgenic mice also play a role in the development of a 'universal' influenza vaccine.

Prof. Dr. Peter Stäheli, leader of a research group at the Institute of Virology at the Freiburg University Medical Centre.

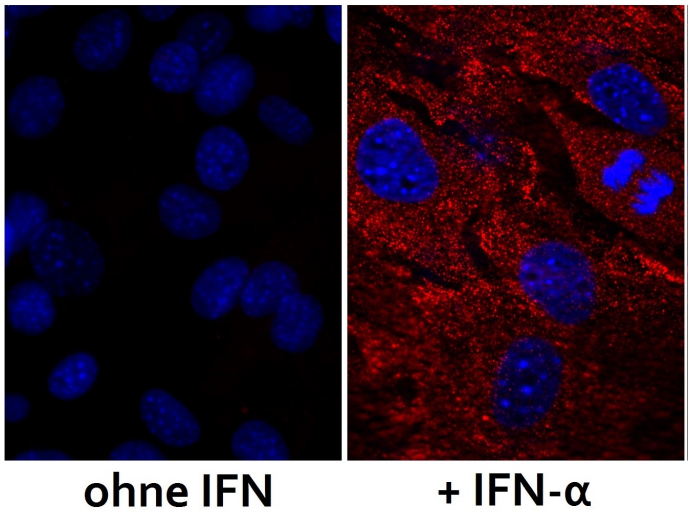
The Institute of Virology at the Freiburg University Medical Centre is both a teaching institute and a research centre that conducts modern diagnostics and competitive basic research. Prof. Dr. Peter Stäheli and his team are active in teaching and research. The virologists are using transgenic mice to investigate how easily new influenza viruses are able to cross the species barrier from birds to humans, potentially causing pandemics. The importance of identifying new influenza viruses in animals at an early stage and reliably assessing their potential hazards for humans dates back to well before the swine flu pandemic in 2009. Stäheli and his group of researchers are working on improving available early detection methods. With current methods, it is impossible to reliably determine whether there is a greater than normal risk of human infection with influenza in the case of strains like these.

A protein called Mx plays a central role in the defence mechanisms of mice against viruses. As humans have a protein, MxA, that is structurally similar to the one in mice, the researchers from Freiburg are using a genetically modified mouse strain with a defective Mx gene. Instead of this gene, this mouse strain carries a large fragment of human chromosome 21, which makes the mice produce human MxA

protein. “We now know that the defence system of this transgenic mouse strain is very similar to that of the human lung as far as the defence against influenza viruses is concerned,” says Stäheli going on to add that for this reason such animals are well suited for investigating the immunological events in the respiratory tract shortly after infection with viruses.

New method to complement existing methods

At present, it is almost impossible to predict whether a certain unknown animal variant of H5 or H7 influenza viruses carries a serious risk to human health. This can only be clarified by an infection test. However, up to now, no suitable animal models have been available for such purposes. The research group leader comments: "The new mouse model can be useful for assessing the disease potential of a newly occurring influenza virus from the animal world." It could complement already existing diagnostic methods and optimise prophylactic measures. "However, there is not yet a specific procedure available,” Stäheli adds. Researchers are therefore still looking for such a method. Current knowledge only enables statements to be made about bird flu viruses. "The 2009 pandemic was caused by a swine influenza virus," says the virologist, "research into the disease potential of swine influenza viruses using our transgenic mice is therefore of great interest."



Fibroblasts of a transgenic MxA mouse under the microscope. These cells were either grown in normal culture medium without IFN (labelled 'ohne IFN') or for 18 hours in medium with interferon (+IFN-α). Interferon treatment led to the synthesis of restriction factor MxA, which was subsequently detectable in the cytoplasm (stained red). The cell nuclei (stained blue) were visualised using a different dye.

Rapid determination of the genome of newly occurring viruses enables the quick prediction of certain biological properties of viruses from gene sequences. “However, genome sequence information does not provide information about the resistance of new viruses against inhibition through the human MxA restriction factor,” says Stähele. “We are able to close this gap with our new mouse strain.” However, at the moment, it is still unclear what health policy measures would be taken should studies with transgenic mice suggest that a new virus strain is dangerous for humans.

Development of a ‘universal’ influenza vaccine is desirable

A major problem with influenza is that effective vaccines cannot be developed fast enough. “Many researchers are therefore of the opinion that a ‘universal’ vaccine effective against a wide range of influenza viruses needs to be developed.” This vaccine would then always be available and not have to be adapted, as is currently the case, to changing situations. Stäheli says that, based on current, state-of-the-art research, it will be years before such a vaccine is available. Different researchers are taking different approaches to achieve this goal. Stäheli is a member of the international UniVacFlu consortium, which aims to develop a vaccine that targets the extracellular part of the M2 protein (M2e) of influenza viruses. “In the UniVacFlu project, we use a broad range of different transgenic mice to find out whether the vaccine can prevent horizontal virus propagation

(contact infection)."

Article

22-Aug-2017
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Further information

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