Contagious Heart Disease:"The Virus Manipulates the Host Cell on Different Levels"

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Prof. Guiscard Seebohm in front of a electrophysiological patch clamp measurement stand; © private

Heart diseases can be triggered by special viruses that affect the cardiac muscle. Preventive drugs could definitely be developed – if the virus does not mutate.

MEDICA.de spoke with Professor Guiscard Seebohm from the University Hospital of Münster, who has closely investigated the responsible Coxsackievirus over the past few years.

MEDICA.de: Professor Seebohm, you were able to discover in your research that Coxsackieviruses can affect the myocardium and cause severe damage. Why was it a surprise at first that these special viruses are able to expand into the cardiac muscle?

Guiscard Seebohm: We have already known for a while that these viruses are able to attack the myocardium. There are certain receptors on the heart surface the viruses bind to. When they do this, they are allowed into the cells and change the characteristics of the infected cells. All of these kinds of viruses do this. The goal is always to prompt the cells to produce new viruses. This always happens under the same basic principle and changes the cell on many different levels. For several years, researchers have worked on finding out which transport vesicles are acting in the cell. This year' s Nobel Prize is being awarded for this. This is also a very modern, new

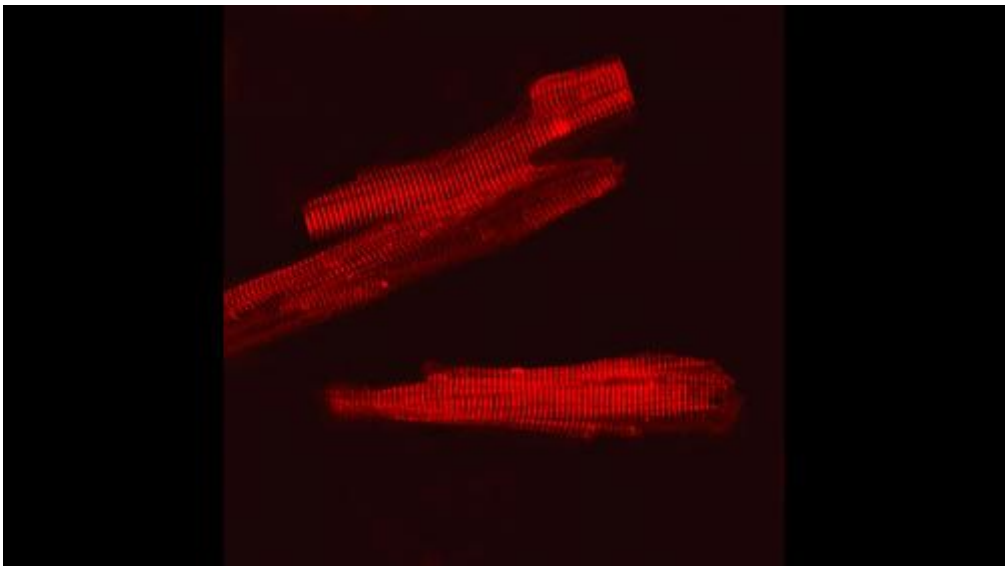
direction in medical science. Scientists investigate how the cell lives and what happens during its life. The studied viruses that attack the myocardium also impair this process. The virus manipulates the host cell on different levels and therefore also hinders vesicle transport. Everything wrapped in vesicles is transported to the wrong locations. In doing so, the cell is virtually being rebuilt. Specific ion channels and presumably also transporters for instance are brought to the wrong locations. When this happens with ion channels, the heart cell no longer works like a healthy heart cells. When this happens at several places, it can work like its own pacemaker. Therefore, you have many tiny potential pacemakers that can trigger heart arrhythmias. However, this is probably just the tip of the iceberg. Naturally, other somatic cells can be attacked by Coxsackieviruses, for instance insulin-producing beta cells. This means, the same type of virus could definitely also play a very big role in type 1 diabetes.

MEDICA.de: How were you able to prove that this virus subtype is responsible for the deadly changes in the heart?

Seebohm: We know this, because this is the only virus type of the entire virus family of Type B Coxsackieviruses that is able to attack these cells. Only they are able to bind to the surface of heart cells. The selectivity comes from the binding to the respective cell.

MEDICA.de: Why was this so surprising?

Seebohm: Actually, we worked on this for seven years. What's so special is that nobody has observed this vesicle transport in this connection before. We did not know that cell electrical characteristics could be changed by individual heart cells. What we knew until then was that such viral infections occur often, and some patients are not able to break down these viruses with their immune system. They get chronic myocarditis. Approximately half a million Germans suffer from chronic myocarditis. The virus that probably causes myocarditis for the most part is the Coxsackievirus B3. We are talking about approximately one hundred thousand patients that suffer from this chronic infection.



Immunostaining of the properly locatlized KCNQ1 channel of the cardiac muscle cell of a house mouse. The correct localization of this channel clearly determines the affinity for developing potentially deadly arrhythmias. This important, clear order is destroyed by the CVB3 virus. The possible result are cardiac arrhythmias; © UK Münster

MEDICA.de: Do patients generally die from this disease?

Seebohm: Chronic myocarditis can definitely reduce life expectancy. In the case of acute myocarditis that we researched, this only happened when people are for instance already prone to arrhythmias due to a rare gene variant. This can bring the electrical balance off-kilter and you can die from it. Normally, the affected person lies down and cures himself/herself. Of course, there are also situations where people pay no attention to their health, and then go and play soccer for example. You occasionally hear about professional soccer players collapsing unconscious on the field and then receive an acute viral myocarditis diagnosis at the hospital.

MEDICA.de: Why does it help you that several people in Asia are immune against this virus?

Seebohm: A gene variant appears in more than 150 million people in Asia and

apparently originated in Japan. This genetic variant of the ion channel presumably causes the heart cell to be far less susceptible to the viral infection. It could be that this virus represents an evolutionary factor, meaning the human genome changes over time. This is why we could try to develop drugs that imitate this genetic variant, if you know for example that a specific ion channel can be uncoupled from viral impacts, which protects against negative viral effects. Then you can try to mimic this with drugs. This has already worked for us in a simple cell system.

MEDICA.de: How long would it take to develop such a drug?

Seebohm: A long time. If you begin drug development now, it is probably going to take about eight years until it can be used – if everything goes according to plan. Of course, there might already be substances that have this effect, but that still need to be tested and further developed. This is probably the case and would reduce development time somewhat.

MEDICA.de: Why is it generally difficult to get viral infections under control with drugs?

Seebohm: Antiviral drugs very often have side effects. Viruses tend to develop mutations quickly. They proliferate very quickly and one virus suddenly turns into a million viruses. It is a form of evolution for those viruses that carry a beneficial mutation to develop very quickly. If I have a drug that inhibits viruses, it can definitely happen that a virus has developed where this drug no longer works. These mutated viruses spread and the drug thus becomes quickly ineffective.