

Healthcare industry BW

Transregional research cooperation

New research consortium to develop new liver cancer treatments

The causes, signs and symptoms of liver cancer are extremely complex. Investigating them requires the collaboration of many experts across university and regional boundaries. A new transregional research group is now studying the complex overall mechanisms at the cellular, genetic and molecular level in order to develop new concepts and drugs for treating liver and bile duct cancers.

Liver cancer can have many causes – cirrhosis (fatty liver) caused by alcoholism is just one of them. For example, severely overweight people have a high risk of developing chronic liver inflammation that can lead to cancer. Hepatitis B and C viruses can be the cause of hepatocellular carcinoma, which is one of the most common types of liver cancer. Chronic infection with these viruses can also lead to chronic liver inflammation, which can subsequently develop into liver cancer. In addition, all types of liver cancer are influenced by genetic and epigenetic factors. While more and more research data on specific aspects become available, an overall network of cancer events that would enable new therapy options to be developed is still missing. Producing such a network requires individual research strands to be much better connected than they have previously been. This is the only way decisive knowledge gaps can be closed and the thicket of old and new research data assembled in a logical context.



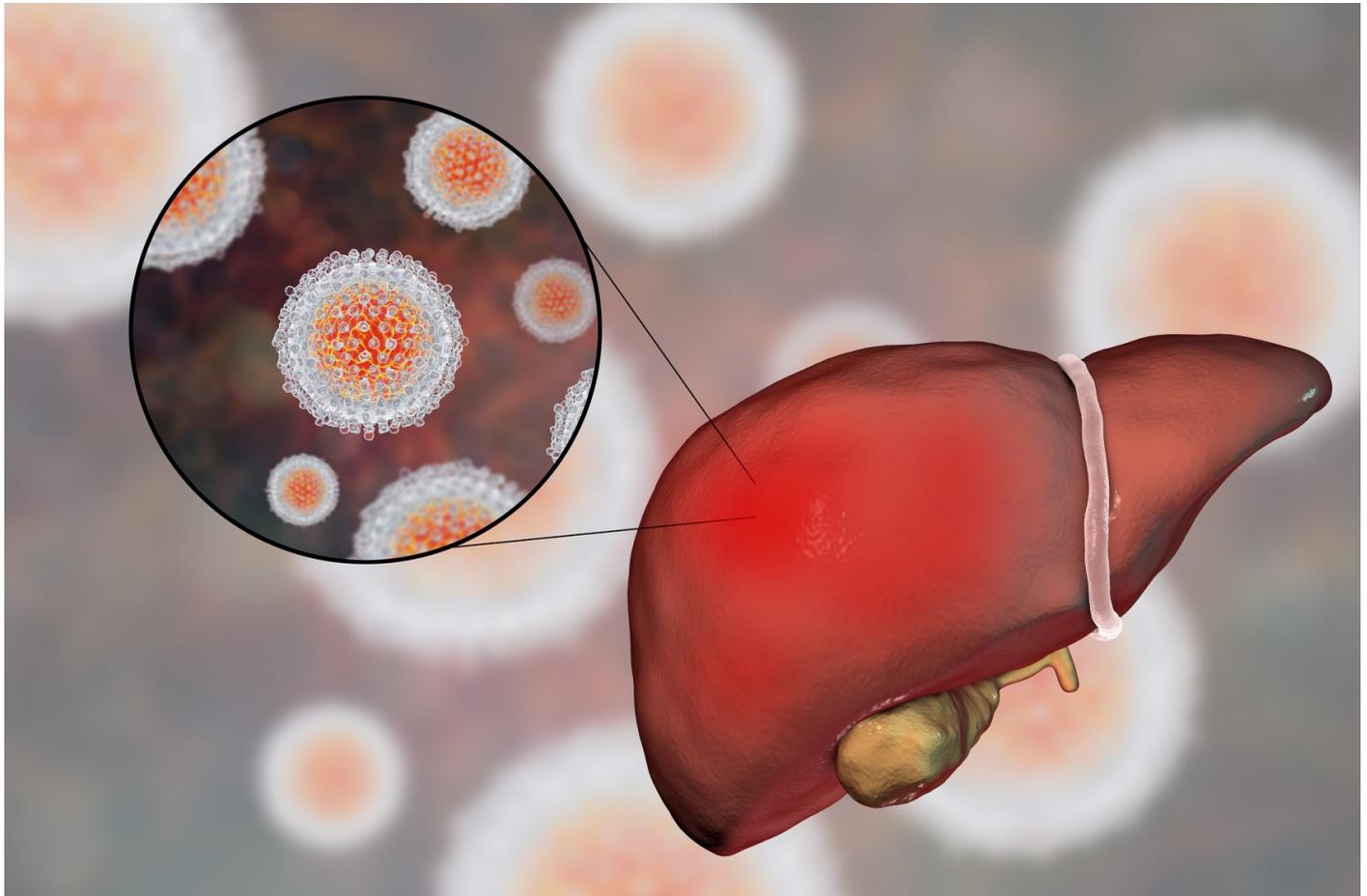
Prof. Dr. Nisar Malek has been director of the Department of Internal Medicine I at Tübingen University Hospital since 2011. His research priority is identifying new active pharmaceutical ingredients for cancer treatment.

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This mammoth task requires the concerted collaboration of many specialised working groups. This is what the new DFG-funded transregional cooperative research centre (CRC/Transregio 209) called "Liver cancer - New mechanistic and therapeutic concepts in a solid tumour model" is seeking to achieve. The funding volume totals eleven million euros and will support research activities at three locations over a four-year period. The project involves teams from the Universities of Heidelberg and Tübingen as well as the Hannover Medical School. Prof. Dr. Peter Schirmacher from the Institute of Pathology at the University Hospital of Heidelberg is the overall project spokesperson. Prof. Dr. Nisar Malek from the Department of Internal Medicine I at the University Hospital of Tübingen is the spokesperson for Tübingen. In keeping with the consortium's research concept, Malek will not be assigning subprojects to specific locations. "We want to resolve a number of different, larger issues that are structured into different blocks but not organised regionally. Work will be distributed across all three universities according to their specific skills," says Malek.

Plea for transregional research cooperation

In this way, the researchers hope to manage the extremely complex research activities. "With our new transregional cooperative research centre, we have a constellation that is unique world-wide in that it brings together three German university institutions that are at the forefront of liver cancer research," says Malek who also takes this as an indication of a general development that he explicitly welcomes. "Very few universities are able to study multiple aspects of such complex topics as liver cancer on their own. I therefore think that there will be a growing tendency for multilateral research networks. Moreover, this will also increase the international visibility of German research. In my view we should be even more flexible in including further research groups from other cities and universities in our research projects." That said, the partners involved in the liver cancer project have some individual priorities: Hannover is specifically focused on research into the immunological mechanisms of liver cancer development and Heidelberg on research into signal transduction pathways that lead to cancer.



Infection with hepatitis C viruses is one of the causes of chronic liver inflammation, which can lead to liver cancer. The new CRC/Transregio 209 will study, amongst other things, the mechanisms of cancer development as a result of viral infection. Some hepatitis C viruses are highlighted in the left of the photo above the liver.

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The Center for Quantitative Biology (QBIC) is establishing a bioinformatics infrastructure for the CRC/Transregio's "omics" approach at Tübingen University in order to pool the proteomics, genomics and metabolomics data that are being compiled at the three universities. The QBIC will administer the data. "The data will be collected in a professional way, stored and made accessible to all partners. The establishment of this infrastructure was a major plus in terms of selection as CRC/Transregio research centre. The project is also investigating viral liver inflammation and the cancers this might cause.

As far as viral liver inflammation is concerned, the project will focus specifically on the comprehensive pathological changes occurring in patients with hepatitis C infections. Effective hepatitis C medication has recently become available, and the infection can now be treated quite well. "We have a large number of people with untreated hepatitis C infections, which will lead to a peak of viral liver cirrhosis in about five years' time, and which can lead to cancer. After that, the disease will become much less frequent due to the new antiviral drugs that have recently become available," Malek predicts. However, some hepatitis infections are either not diagnosed at all or only at a late stage. Therefore, research into pathways that lead to liver cancer needs to remain a long-term priority, also with regard to the basic findings that can be gained from this research.

Tumour environment provides important information for treating cancer

The CRC/Transregio 209 researchers also want to investigate the consequences of non-viral fatty livers and the resulting chronic liver inflammations. They are hoping to obtain insights that are as detailed as possible into the inflammatory mechanisms associated with the disease, and about the metabolic changes and genetic changes that lead or contribute to the development of liver cancer. "Amongst other things, we are interested in which mutations are driver mutations, and which are only secondary ones," says Malek. The project also focuses on epigenetic changes associated with cancer. Amongst other things, the researchers are studying the differences in DNA methylation patterns in healthy and malignant liver cells and their implications, as well as the microenvironment of the tumour cells. How do tumour cells communicate and how do they change the immune system, the connective tissue and blood vessels in their environment? These are all issues that the CRC/Transregio 209 researchers are trying to resolve over the next few years.

Another important goal is the discovery of new target structures for active pharmaceutical ingredients against liver cancer. "As far as we know, hepatocellular carcinomas are not caused by a single mutation. Monocausal therapies do not therefore have any effect. As a long-term goal, we hope that our research will provide us with the base to identify the Achilles' heel of tumours in each individual patient and target those tumours with the appropriate combination therapy," says Malek referring to personalised medicine applications on which, in his role as director of the Centre for Personalised Medicine in Tübingen, he naturally focuses.

