



Fatty liver Nano-/Antibody Therapy - (FAITH)

Berichterstattung

Projektinformationen

FAITH

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Periodic Reporting for period 1 - FAITH (Fatty liver Nano-/Antibody Therapy - (FAITH))

Berichtszeitraum: 2020-08-01 bis 2022-01-31

Zusammenfassung vom Kontext und den Gesamtzielen des Projekts

Making a diseased liver healthy again

Changes in our lifestyle and diet have dramatically increased the incidence of obesity, overweight and metabolic syndrome. Overweight and obesity are not only a problem in the developed countries of the Western world. The World Health Organization has sounded the alarm on obesity, predicting that the

number of obesity-related diseases will double – if not triple – over the next two decades. Amongst those diseases is non-alcoholic fatty liver disease, or NAFLD.

Using anti-platelet therapy, we could successfully reverse non-alcoholic fatty liver disease and, in part, fibrosis. The breakthrough treatment could also be used to prevent liver cancer. Non-alcohol fatty liver disease (NAFLD) is a consequence of chronic overweight.

Subsequently, this chronic, often asymptomatic disease can cause non-alcoholic steatohepatitis (NASH), a pathological fatty liver disease that can lead to liver dysfunction or even liver cancer, neither of which can be efficiently treated.

Consequently, hepatocellular carcinoma, or liver cancer, has one of the highest growth rates of patients in Europe, India and the United States, amongst others.

Unfortunately, the disease lacks the predictive markers needed to identify which NASH patients are at risk of developing liver cancer. Furthermore, efficient therapies for treating NASH, preventing NASH from liver cancer transition, or controlling NASH-induced liver cancer do not exist. Thus, the goal of the EU-funded FAITH project was to develop specific, side-effect-free therapeutic treatments. To do this, our research looked at the underlying mechanisms that trigger this inflammatory liver disease.

Whereas past research has focused on using small molecules to block fibrosis and other forms of liver damage, the FAITH project investigated the link between inflammatory cells, aberrant liver metabolism, and NASH.

The underlying ratio of this approach is (I) NASH is an inflammation-induced, aberrant metabolic disease and, (II) while fibrosis is linked to NASH, it does not cause it.

We applied the following technological approaches: generation of humanized antibodies, screening for binding affinities by applying various biochemical assays and consequently testing for therapeutic activity in a preclinical model that carry upon genetic engineering the humanized of the target molecule and develop NASH and subsequently HCC in response to prolonged feeding with various high caloric diet.

By conducting preclinical trials in mice and human tissue, we found that immune cells are key to initiating and maintaining NASH. The project also demonstrated that platelet count, activation and aggregation all increase in a NASH-diseased liver, with these platelets actively attracting and retaining immune cells to and in the liver. These findings indicate that conventional anti-platelet therapy reverses NASH and, in part, fibrosis in a therapeutic fashion. Based on this work, we proposed a novel approach to treating NASH and NASH-to-liver cancer. The approach uses platelet-specific antibodies or nanobodies to block the pro-inflammatory function of platelets without affecting platelet-haemostasis. The preclinical models definitively show that the use of platelet-specific anti- and therapeutic antibodies can make a fatty, diseased liver healthy again. Thus, we believe our approach can be used to not only treat NASH, but also prevent a fatty liver from developing into liver cancer. FAITH's anti-platelet therapy and treatment have since been reproduced in larger studies for treating liver cancer and fibrosis. To this end, the work lay the groundwork for next-generation treatment and for developing drugs to both treat NASH and prevent its progression to cancer. Thus, it might represent the future of treating chronic liver disease.

Although the project is now over, we continue to work in the fields of NASH, platelets and liver cancer. In addition to preparing for a large screening of their proposed treatment, the team is also working with experts to develop more efficient methods for producing the necessary antibodies.

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