Hepatit virus patogenes och strategier för att undvika immunförsvaret: Nya transgena musmodeller och nya behandlingsformer

A Data Management Plan created using DMPonline

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Project abstract:

We have for almost three decades studied chronic infections caused by the hepatitis B virus (HBV), hepatitis C virus (HCV) and hepatitis D virus (HDV) as these cause severe liver disease and hepatocellular carcinoma (HCC). The past five years have significantly changed the possibility to treat some of these conditions and immunotherapies for HCC are being developed and tested. We here aim at understanding the pathobiology of these infections and to develop new treatment regimens. HCV used to be the major cause for liver transplantation in the Western world, but today >90% of those with chronic HCV can be cured using the new directly acting antivirals (DAAs; [1]). Still, to control and eradicate HCV a vaccine is needed, and those who remain uncured need alternative therapies. For HBV, HDV, and HCC caused by these infections there is a great need for “curative” therapies. Thus, we will use our extensive experience in basic and clinical research to develop new preventive and therapeutic immune therapies. The approach differs for the different diseases. For HCV, we have developed a unique mouse model [2]. In this model we can in detail understand T cell dysfunction induced by HCV replication. We are trough different technologies trying to understand the mechanism behind the immune modulatory effect of the HCV replication itself. This is essential when we explore new concepts for preventive immunotherapies using DNA, RNA and viral vectors through international collaborations. For HBV our major goal is to develop an immunotherapy induce off-therapy control of HBV. When the HBV replication is controlled this reduces the risk of liver disease as well as a reduced infectivity. We have done significant progress in the past year, with a potent immunotherapy candidate ready for clinical testing, and a completely new chimeric antigen receptor (CAR; [3]) technology targeting the liver. HDV is an aggressive satellite virus to HBV for which there are no good therapies. We are generating both T cell therapies and an active immunotherapy. In conclusion, we are building on our previous experience to rapidly develop new immune therapies for these leading causes for liver disease.

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General Information

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Description of data – reuse of existing data and/or production of new data

Data is generated mainly during animal experimentation and analysis of human tissues. Eventually data will be generated in clinical trials.

Data from in vitro experiments are generated through analysis of cells by RNA, DNA and protein analysis. These are stored in KIs ELN. Original pictures are scanned or generated electronically and saved as jpg files.
Data from animal experiments are generated through either analysis of living animals through inspection, weighing, and in vivo imagingsaved as jpg files. These are recorded in the journals of the animal faciliti and also introduced into ELN.
Analysis of immune responses are analyzed and data is stored in xls files. These data are then transferred to programs for analysis. This can be as xls or pzf files.

Documentation and data quality

Stored in ELN and on paper and then transferred to ELN.

All data is stored and all experiments are repeated with all original data points recorded

Storage and backup

ELN is bascked up by KI servers. Data is also stored on multiple personal computers, which are backed up through the KI network and OneDrive.

ELN requiers passwoer access. All paper files are stored in locked offices.

Legal and ethical aspects

All data is according to GDPR. We will not have any data that can identify a person. Any human data is pseudonymised and the key is stored in a locked cabinet with the responsible physician.

All experiments and data handling weill be according to ethical approvals.

Accessibility and long-term storage

Data will be made accessible through publication and in supplemental material. Anyone who ask for data will obtain it. Some data will be accessible thrpugh public web sites for example opencorona/ki.se.

Using the KI ELN and back up systems.

No. All data is accessible through commecial programmes.

Through PUBMED and other public sources

Responsibility and resources

The PI is responsible. after the retirement of the pi it will be ki servers and the ki internal documentation and archive system.

These costs are covered by the KI INDI. Storage on ELN and publication ensures fulfillment of FAIR principles. Also, only commercial programmes are used to generate and interpret data in line with FAIR principles.