DEVELOPMENT AND CHARACTERIZATION OF A HUMAN MONOCLONAL ANTIBODY FOR PREVENTION OF HCV RECURRENCE IN LIVER TRANSPLANT PATIENTS

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Background

- Hepatitis C virus (HCV) infects more than 170 million people worldwide.
- Chronic hepatitis C develops cirrhosis, hepatocellular carcinoma and liver failure.
- Liver transplantation is the only option for patients with HCV-induced end-stage liver diseases.
- A prophylactic vaccine is still not available.
- Infection of the newly grafted liver occurs immediately and universally after transplantation.

Methods

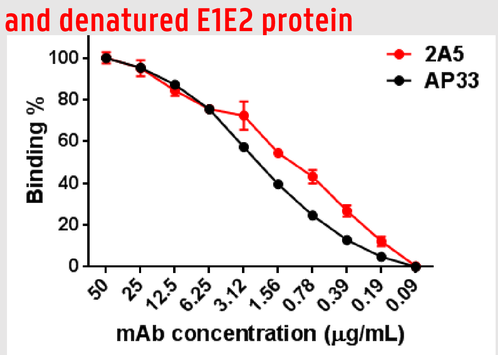
- Isolation of HCV monoclonal antibody, designated 2A5, from an HCV genotype 1b chronic patient.
- Evaluation of this antibody by testing:
  1. The binding activity towards HCV envelope glycoprotein (E1E2) using ELISA.
  2. Epitope mapping using alanine mutants.
  3. The neutralizing activity towards HCV pseudoparticles (HCVpp) and cell culture produced virus (HCVcc).
  4. Prevention of HCV infection in immune-deficient mice of which the liver is repopulated with primary human hepatocytes (humanized mice).

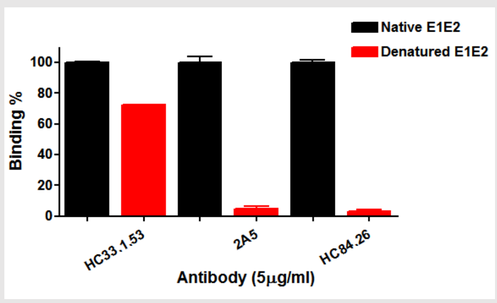
Results

Isolation, cloning and sequencing of mAb 2A5

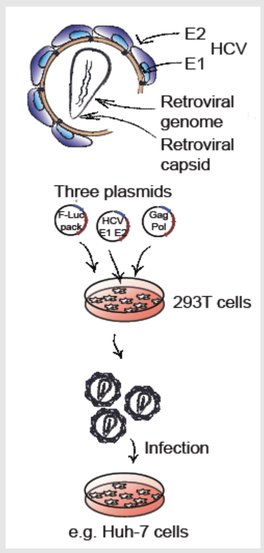
Heavy Chain	V-GENE and allele	Homsap IGHV1-69*14 F
	J-GENE and allele	Homsap IGHJ5*02 F
	D-GENE and allele by IMGT/JunctionAnalysis	Homsap IGHD1-26*01 F
Light Chain	V-GENE and allele	Homsap IGLV2-14*01 F
	J-GENE and allele	Homsap IGLJ1*01 F

Binding activity of mAb 2A5 to native and denatured E1E2 protein

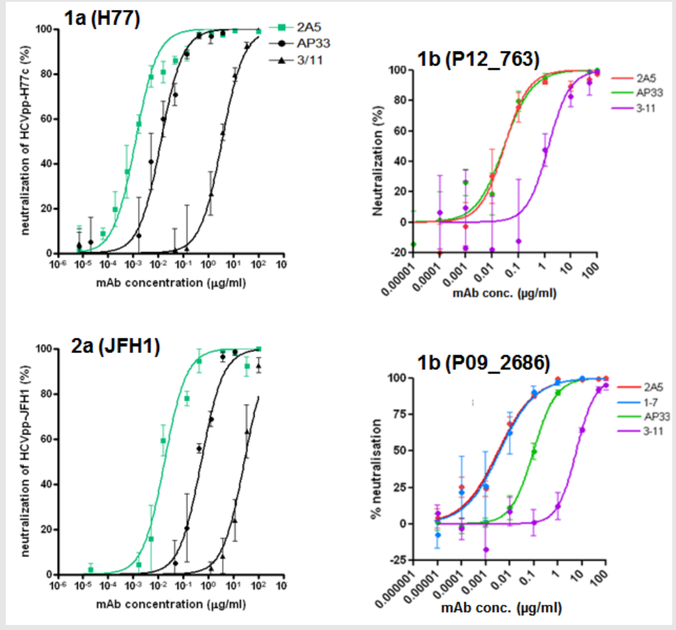




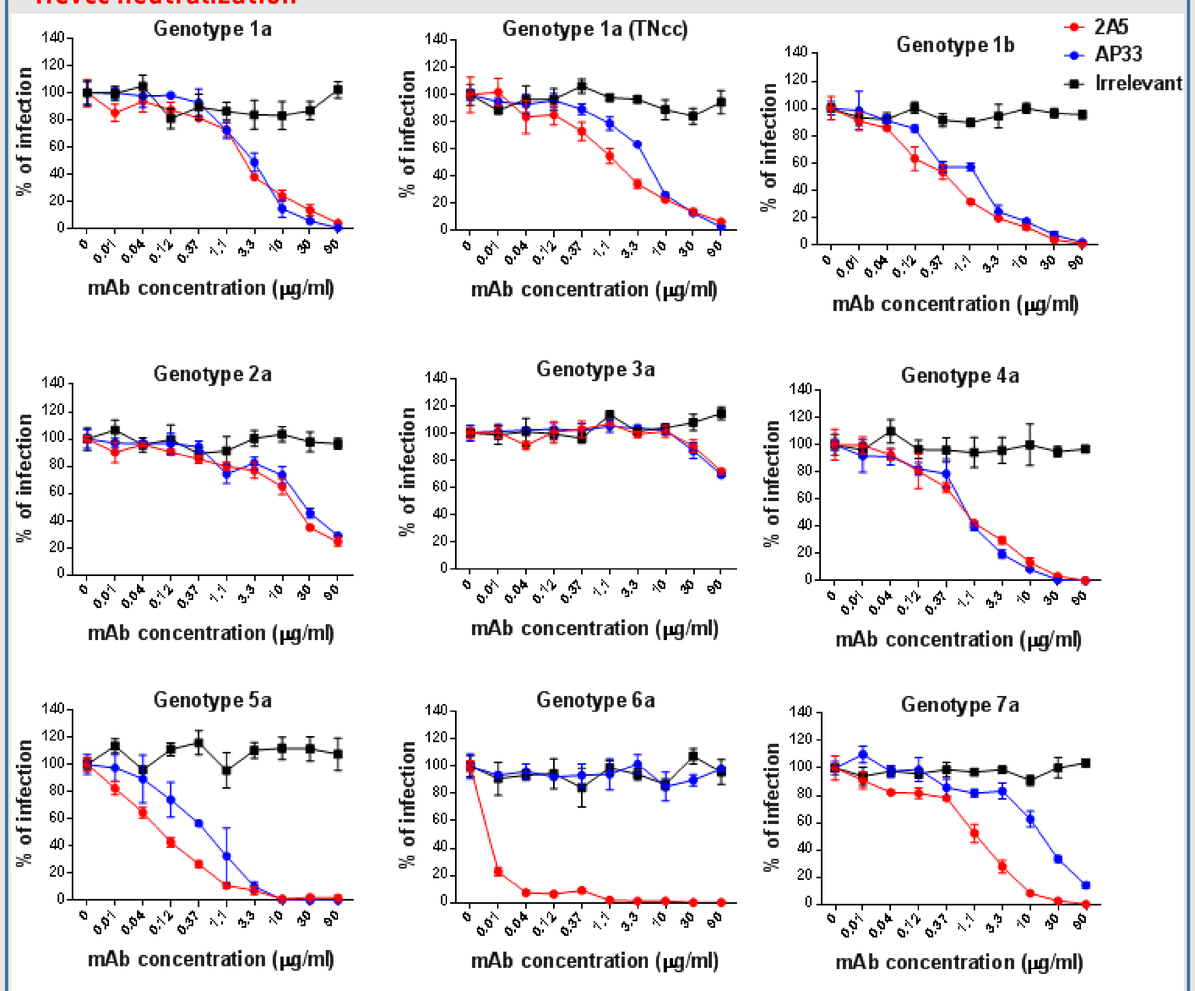
Neutralization of HCV pseudoparticles (HCVpp) by mAbs



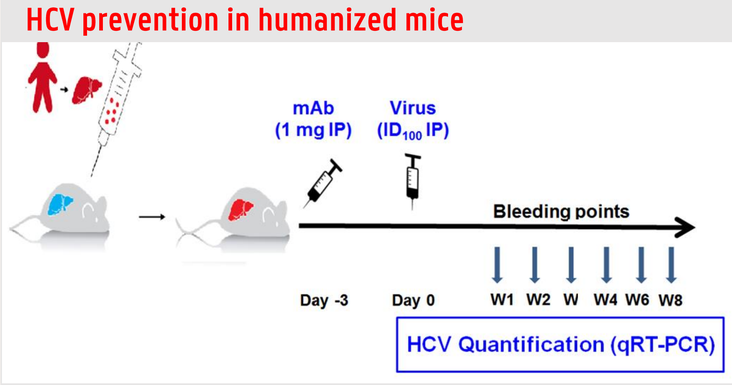
Bartosch *et al.*, JEM 2003

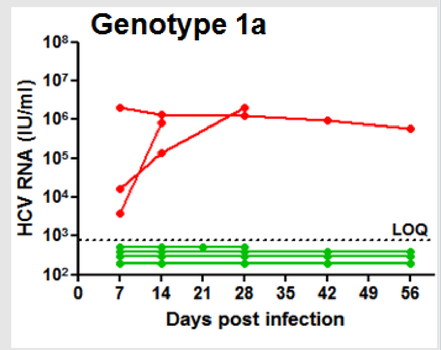


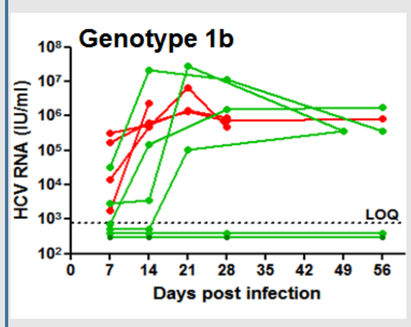
HCVcc neutralization

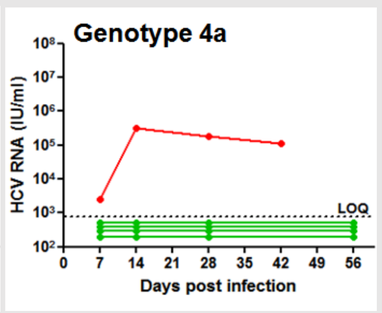


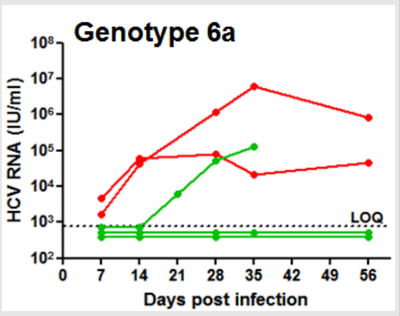
HCV prevention in humanized mice



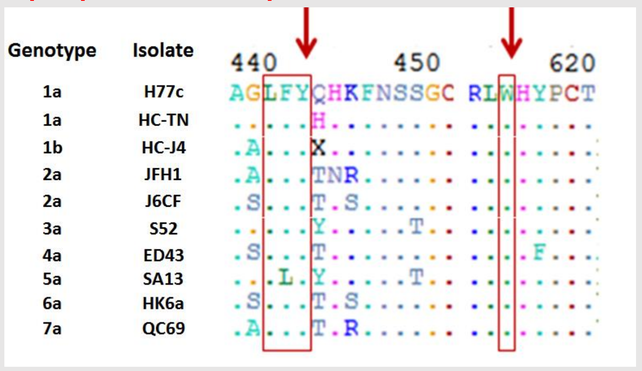


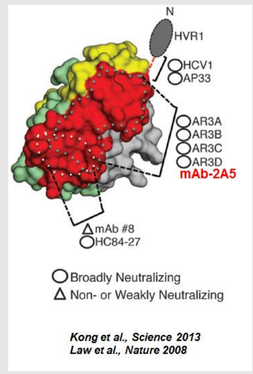






Epitope identified by mAb 2A5





Conclusion

- ❑ mAb-2A5 efficiently neutralizes HCV *in vitro* and in humanized mice.
- ❑ mAb-2A5 could be used to prevent HCV infection after liver transplantation.
- ❑ The broad neutralizing activity of this mAb presents a valuable epitope for the design of HCV vaccine.

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