



# Laboratory methods to guide hepatitis B and C treatment

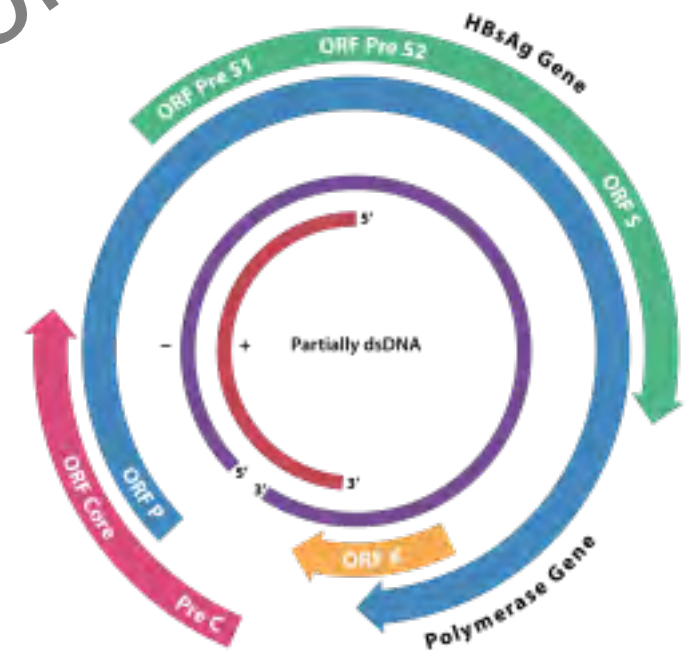
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# Hepatitis B

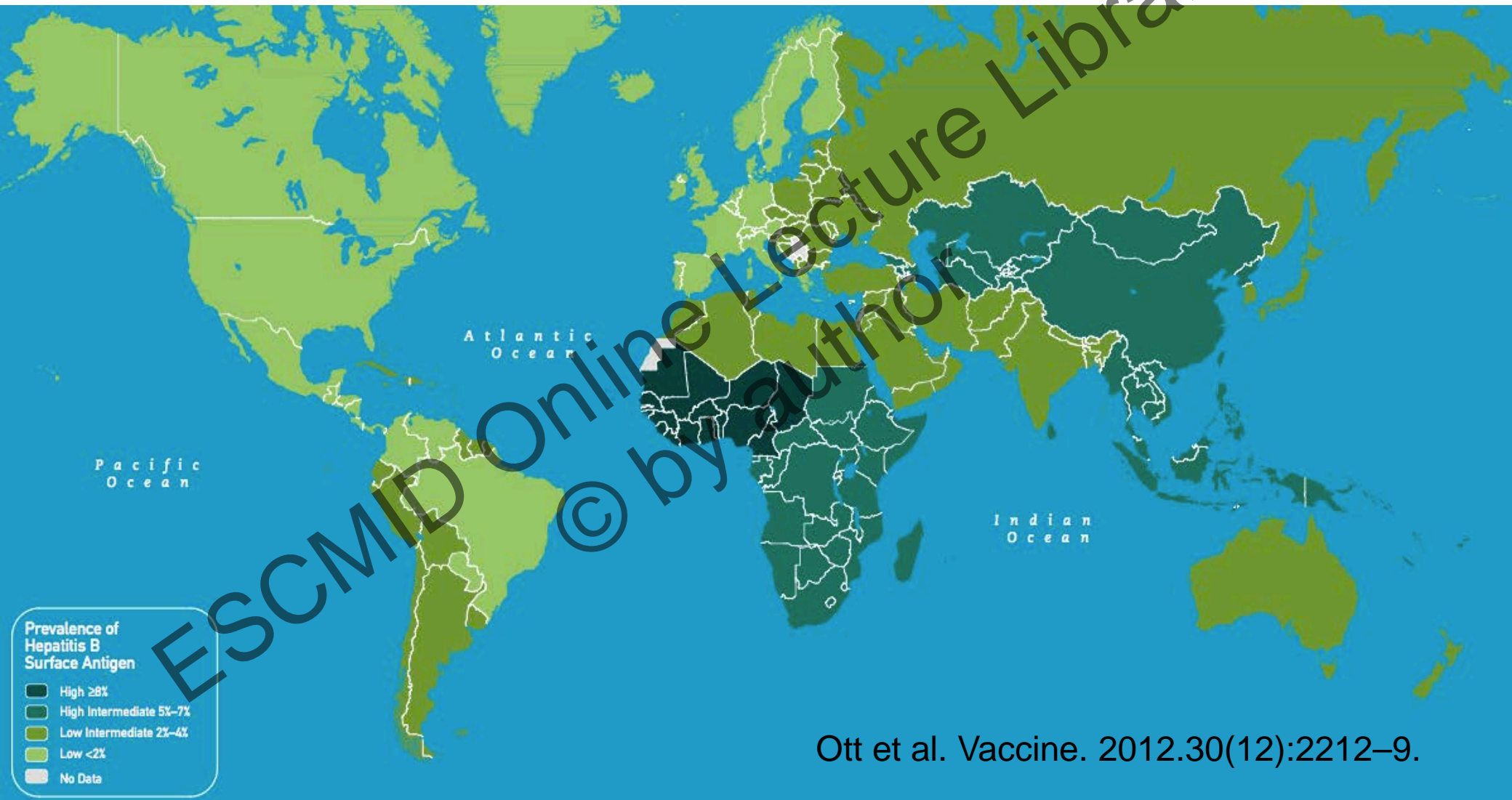
- 2 000 million people infected at some time of life
- 350 million carriers
- 600 000 deaths / year; cirrhosis and liver cancer
- 90% of healthy adults clear infection in 6 months
- 90% of infants develop chronic disease

# Hepatitis B

- Partially double-stranded circular DNA genome
- Reverse transcriptase
- cccDNA in hepatocyte nucleus
  - Persistence of infection



# HBsAg prevalence in adults 2005



# Hepatitis B serology - ELISA

- HBsAg

confirmation with neutralizing assay

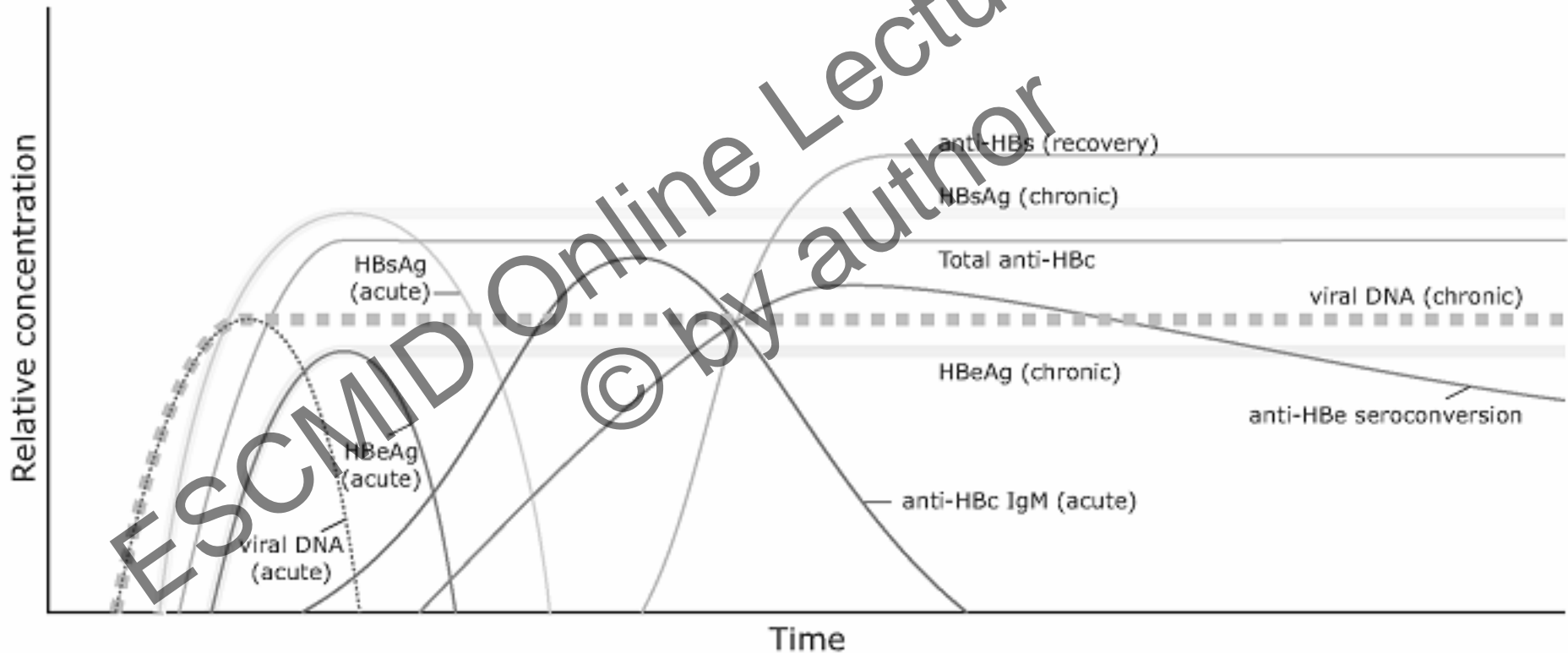
- AntiHBc

AntiHBc IgM

- AntiHBs

- HBeAg/AntiHBe

# Hepatitis B – acute/chronic



Sablon E, Shapiro F. *Int J Med Sci* 2005; 2(1):8-16.

# Hepatitis B – molecular methods

## ➤ HBV DNA PCR

Quantitative real-time PCR

IU/ml

How much virus is there in the blood?

What phase is the infection in?

May help diagnosis in complicated cases

# Phases of Chronic Hepatitis B

- Immune tolerant phase

HBeAg pos, HBV DNA high, ALT normal

- Immune reactive phase

HBeAg pos (wt) or HBeAg neg (mutants)

HBV DNA decreasing, ALT elevated, symptoms +/-

- Inactive carrier phase

HBeAg-negative, HBV DNA low, ALT normal

## Reactivation/HBeAg neg hepatitis



# Hepatitis B - treatment

What is the goal?

Prevent cirrhosis and cancer

Prevent mother-to-child transmission

Virological suppression

HBsAg clearance not primary goal !

# Hepatitis B - treatment

➤ PEG-Interferons

➤ Nucleos(t)ide analogues

Lamivudine, entecavir, telbivudine,

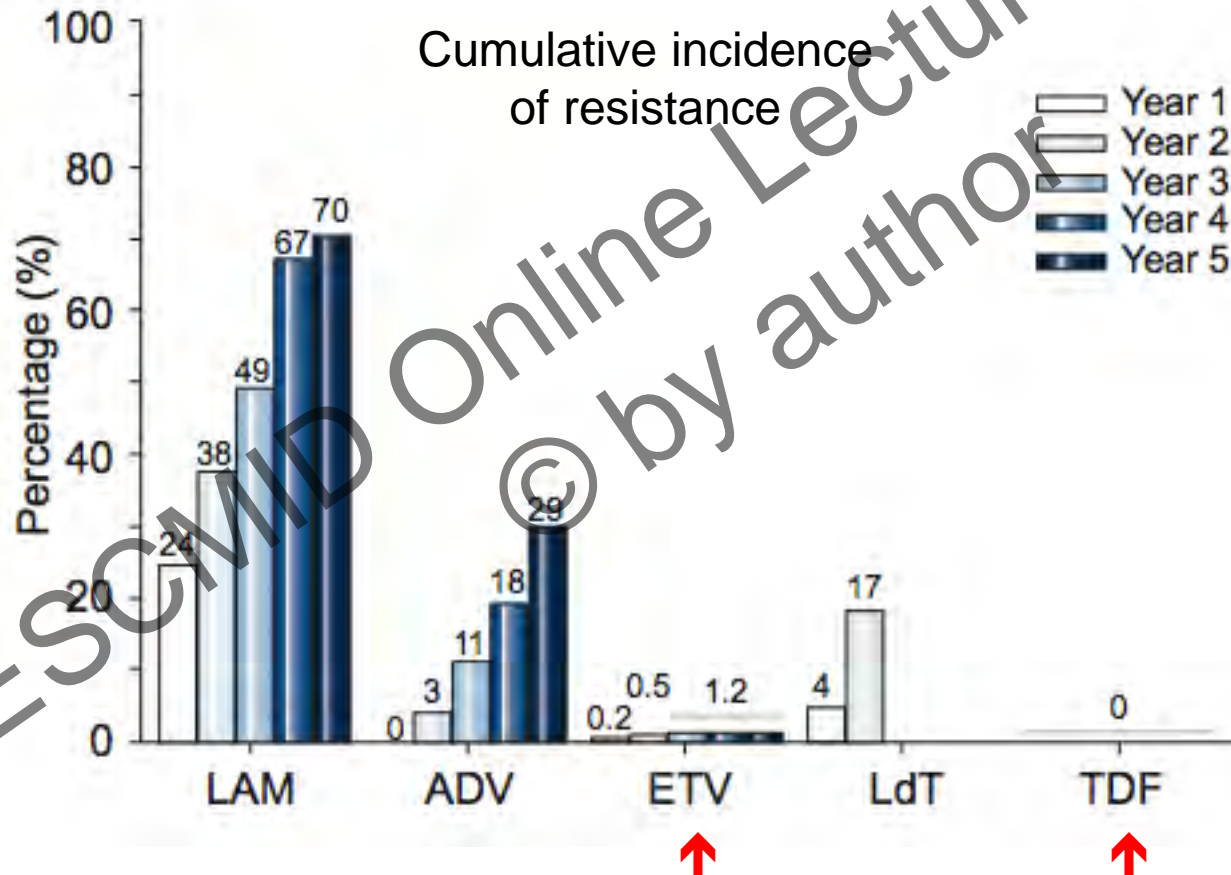
tenofovir

|               | (PEG)-IFN  | NAs   |
|---------------|--|---|
| Advantages    | <ul style="list-style-type: none"><li>• Finite duration</li><li>• Absence of resistance</li><li>• Higher rates of anti-HBe and anti-HBs seroconversion with 12 mo of therapy</li></ul> | <ul style="list-style-type: none"><li>• Potent antiviral effect</li><li>• Good tolerance</li><li>• Oral administration</li></ul>      |
| Disadvantages | <ul style="list-style-type: none"><li>• Moderate antiviral effect</li><li>• Inferior tolerability</li><li>• Risk of adverse events</li><li>• Subcutaneous injections</li></ul>         | <ul style="list-style-type: none"><li>• Indefinite duration</li><li>• Risk of resistance</li><li>• Unknown long-term safety</li></ul> |

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# Hepatitis B - nucleos(t)ides



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# Hepatitis B – nucleos(t)ide resistance

Sequencing of *pol* gene

→ genotype + resistance test

| HBV variants                            | Level of susceptibility |             |           |          |           |
|---|-------------------------|-------------|-----------|----------|-----------|
|   | Lamivudine              | Telbivudine | Entecavir | Adefovir | Tenofovir |
| Wild-type                               | S                       | S           | S         | S        | S         |
| M204V                                   | R                       | S           | I         | I        | S         |
| M204I                                   | R                       | R           | I         | I        | S         |
| L180M + M204V                           | R                       | R           | I         | I        | S         |
| A181T/V                                 | I                       | S           | S         | R        | S         |
| N236T                                   | S                       | S           | S         | R        | I         |
| L180M + M204V/I ± I169T ± V173L ± M250V | R                       | R           | R         | S        | S         |
| L180M + M204V/I ± T184G ± S202I/G       | R                       | R           | R         | S        | S         |

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# Monitoring Hepatitis B treatment

- HBsAg
- HBV DNA levels
- Resistance testing if viral failure on Nuc
- HBeAg + Anti-Hbe
- **Monitoring after treatment**

## **Clinical utility of quantitative HBsAg in natural history and nucleos(t)ide analogue treatment of chronic hepatitis B: new trick of old dog**

Tai-Chung Tseng · Jia-Horng Kao

- Correlates to amount of cccDNA in the liver
- Decline related to IFN response
- Predict HCC risk in HBV infection?
- Predict response to Nuc treatment?

# Hepatitis C

- RNA virus

“sloppy replication”, quasispecies

- 130-150 million people chronic infection

- 55-85% chronic infection

No persistence after cure, but reinfection possible

- 350 000 – 500 000 die from cirrhosis/HCC per year



# Hepatitis C - diagnostics

- Screening - ELISA

AntiHCV

- Active infection?

HCV RNA/HCV Ag

- Specificity of AntiHCV

Antibody confirmation - Immunoblotting

# Hepatitis C – choice of treatment

Everything is changing in the HCV business...

Almost!

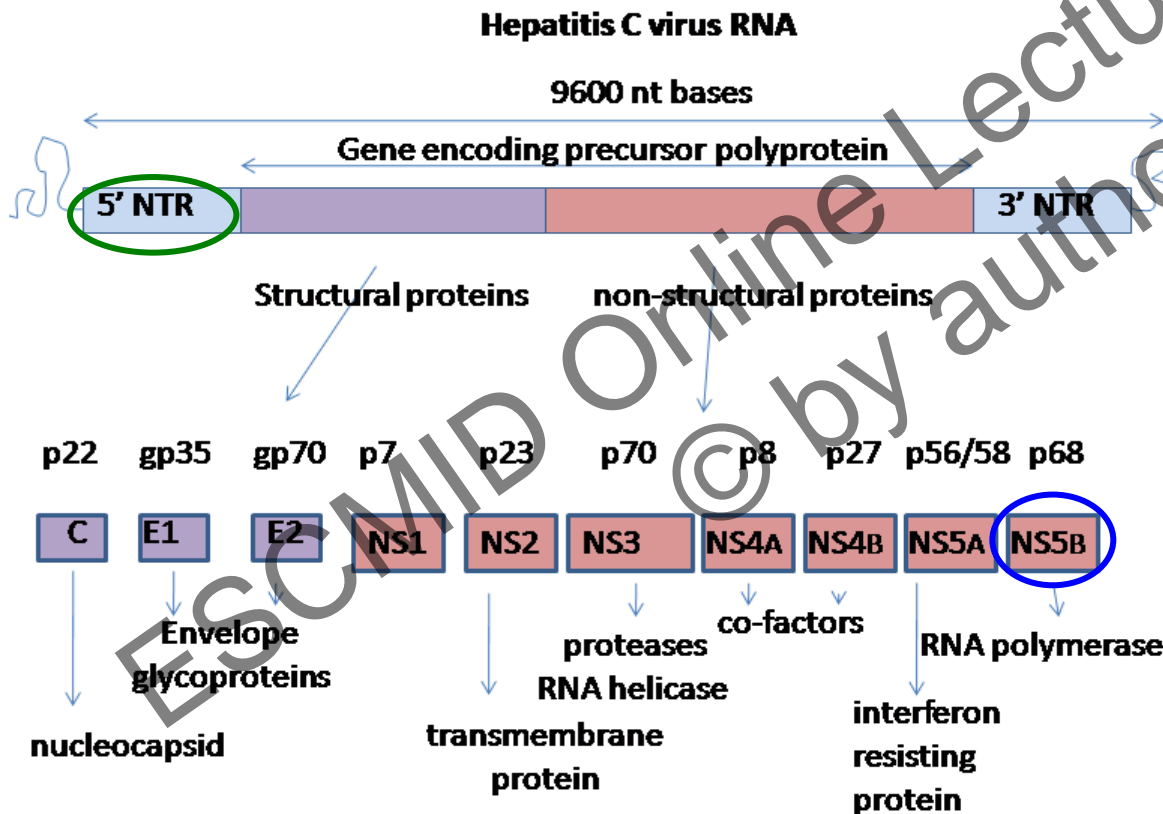
## ➤ Genotype

Before: Strong predictor of IFN/Ribavirin response

After: Guide choice of antivirals

## ➤ IL28B

# Hepatitis C - genotyping



➤ NS5B sequencing

➤ Hybridization of 5' NTR

# Hepatitis C – resistance testing

- Viral variants with resistance associated mutations exist pre-treatment
- Sequencing for resistance mutations
- NS3 protease inhibitors: Q80K
- Clinical significance?
- Pre-treatment / Pre-re-treatment resistance testing in the future?

# Hepatitis C – monitoring treatment

## ➤ HCV RNA PCR

Quantitative real-time PCR

IU/ml

During and post-treatment

