

HCV inhibitors

from bench to bedside

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This Talk will cover...

HCV (epidemiology, genome, pathogenesis, treatment)

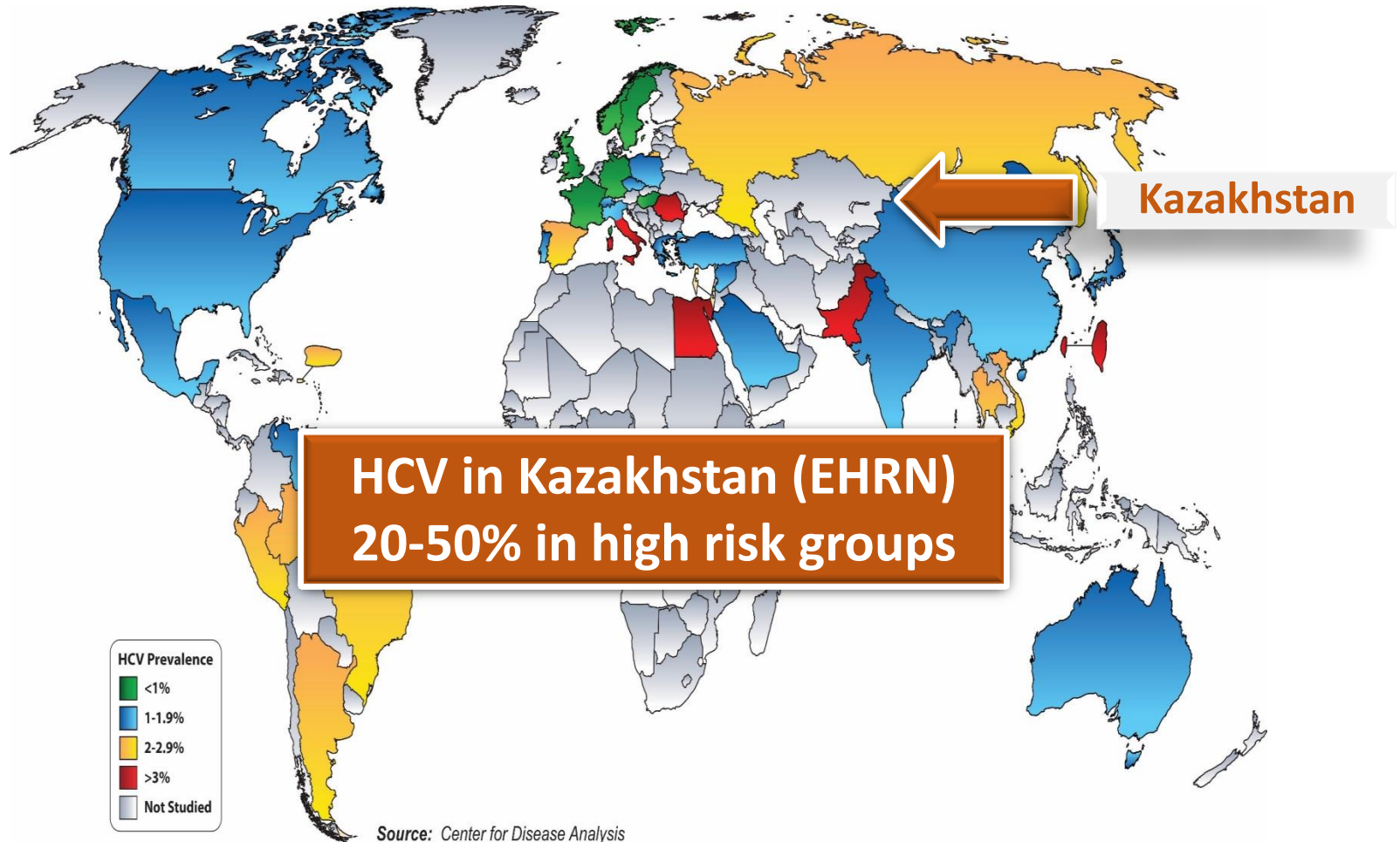


Drug Screening (in vitro, bioinformatics)

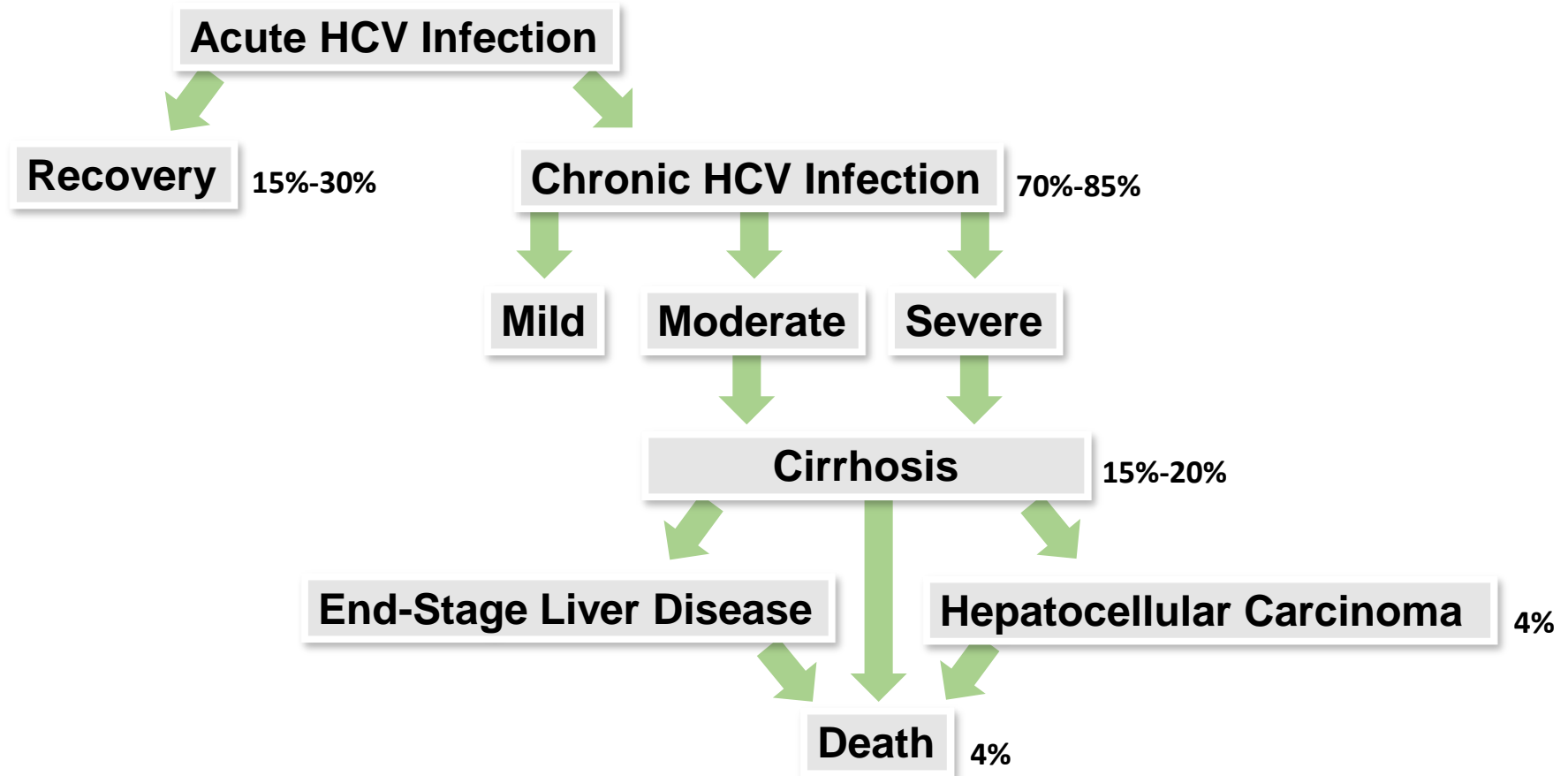


Clinical trial

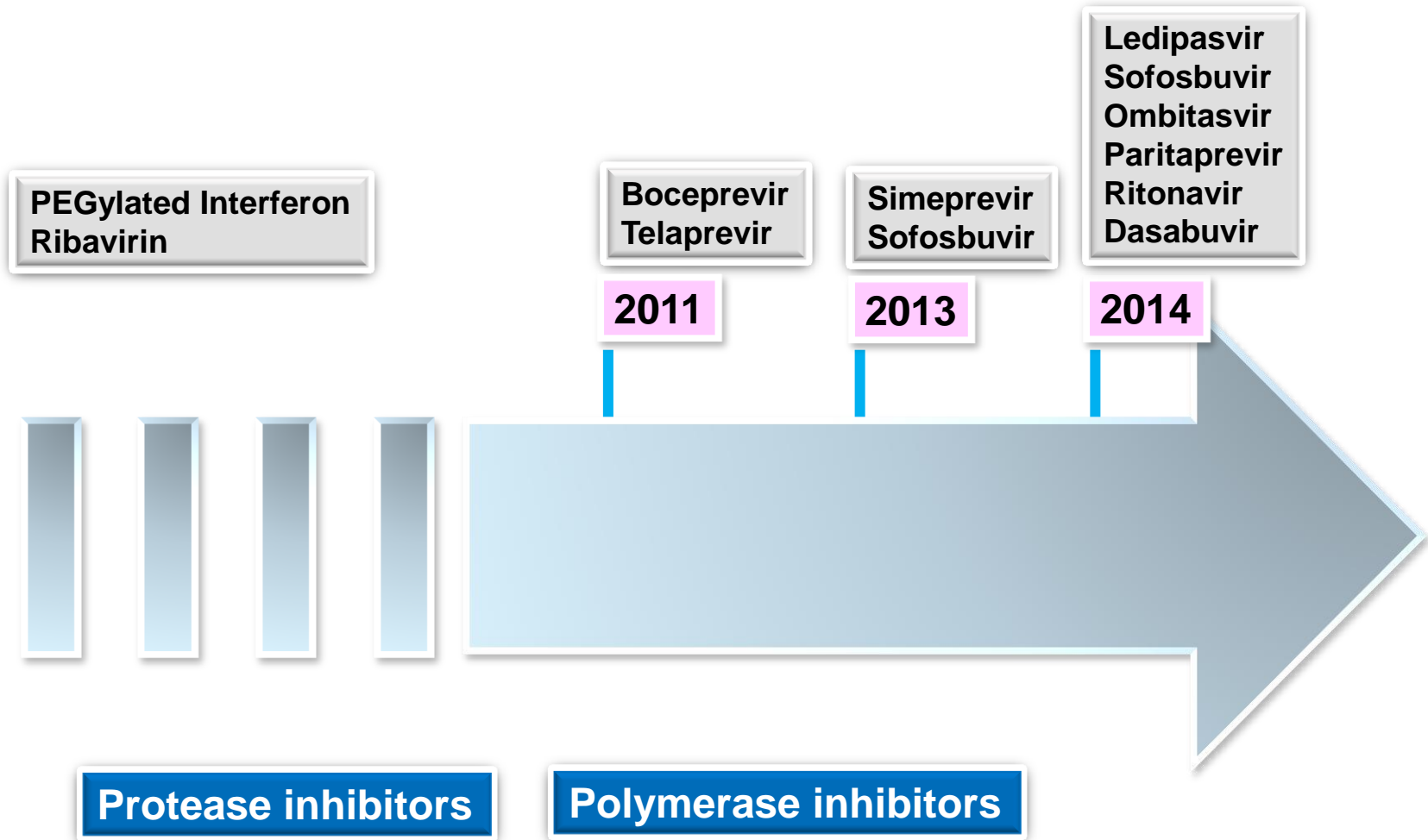
HCV Prevalence



HCV Pathogenesis



Treatment for HCV



Limitations of treatment

**PEGylated Interferon
Ribavirin**

Long duration

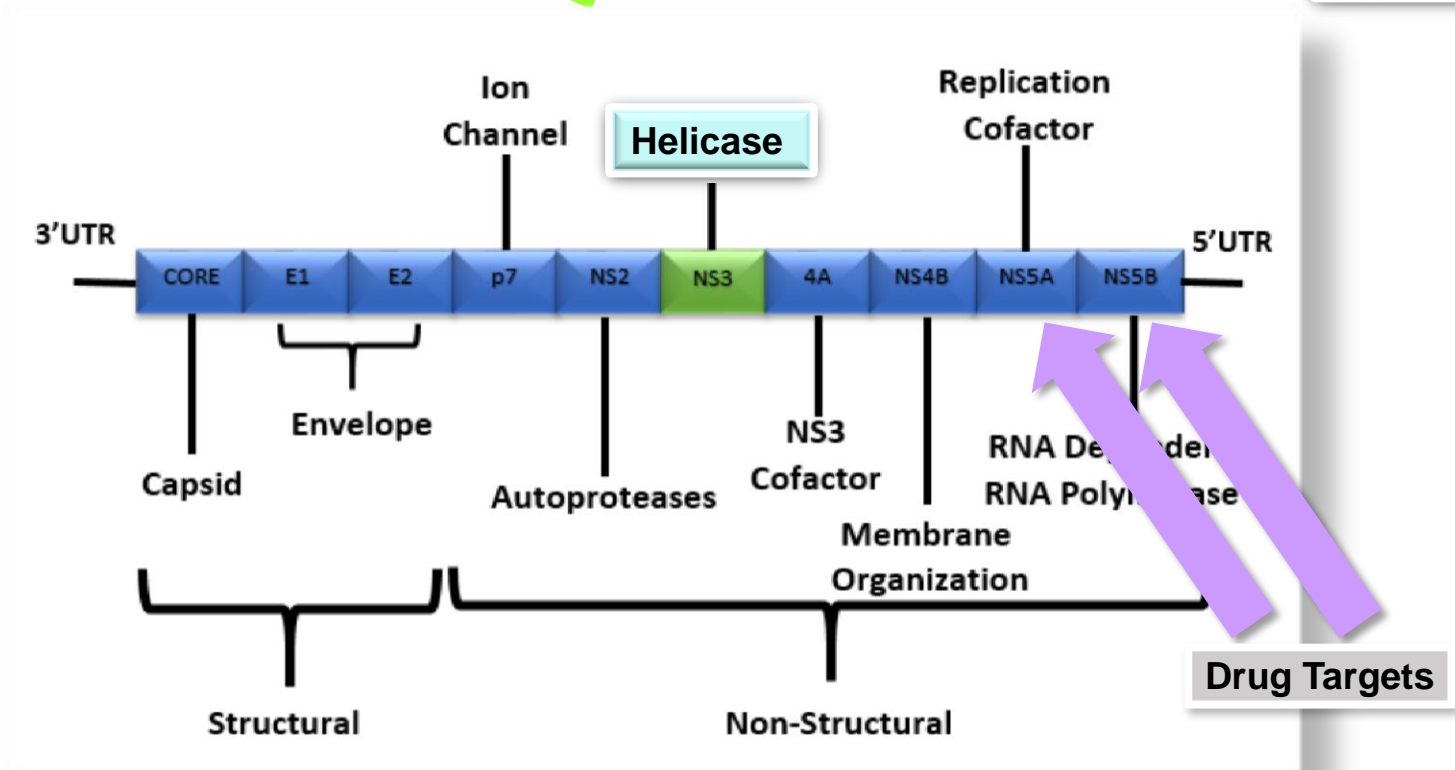
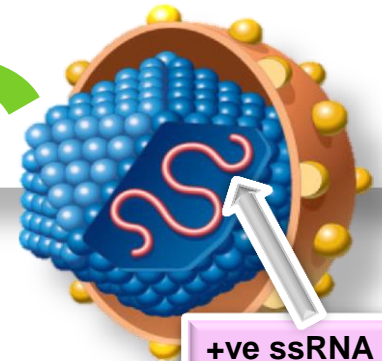
Adverse effects

Affordability

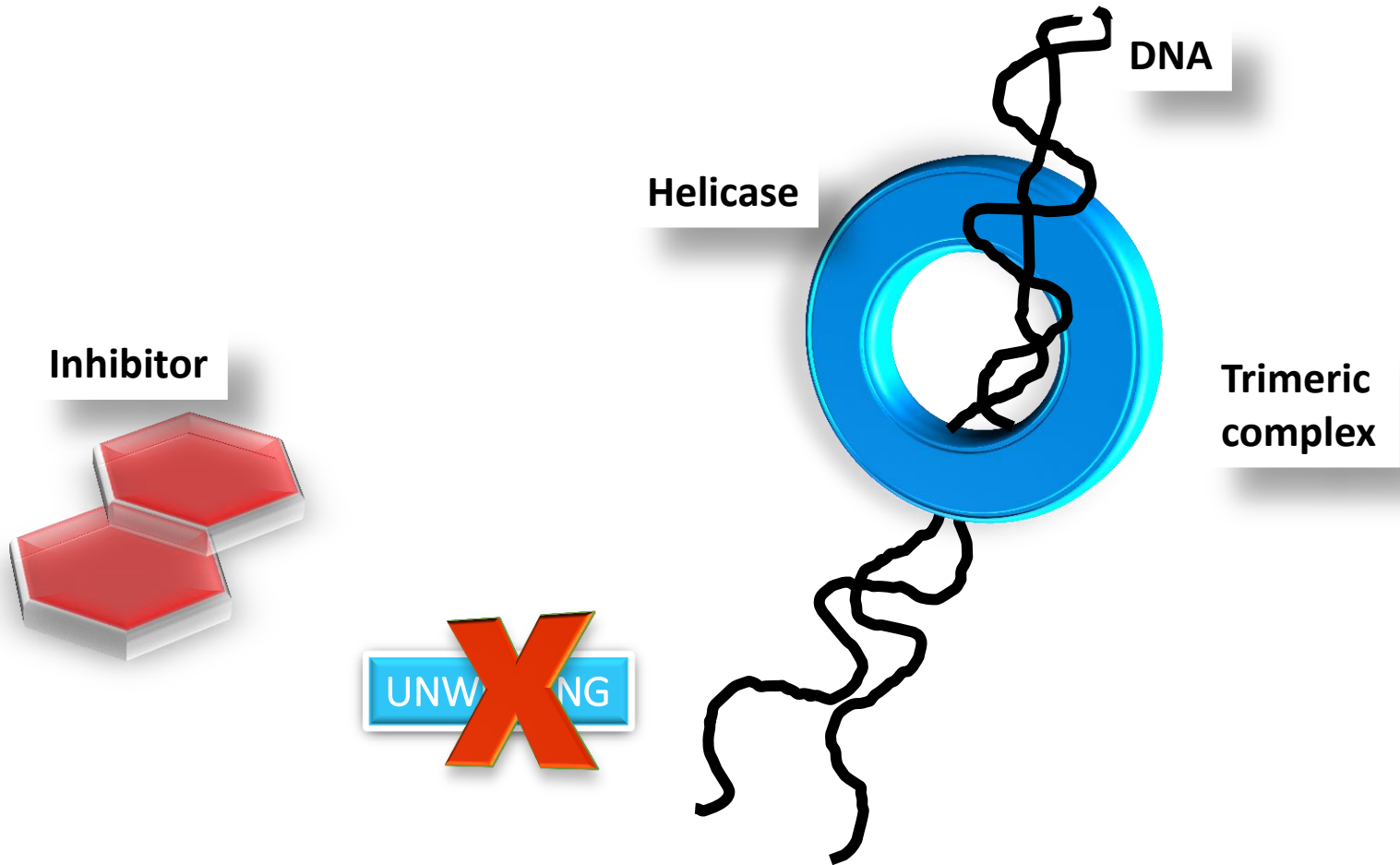
Resistance to treatment

Subtype variation

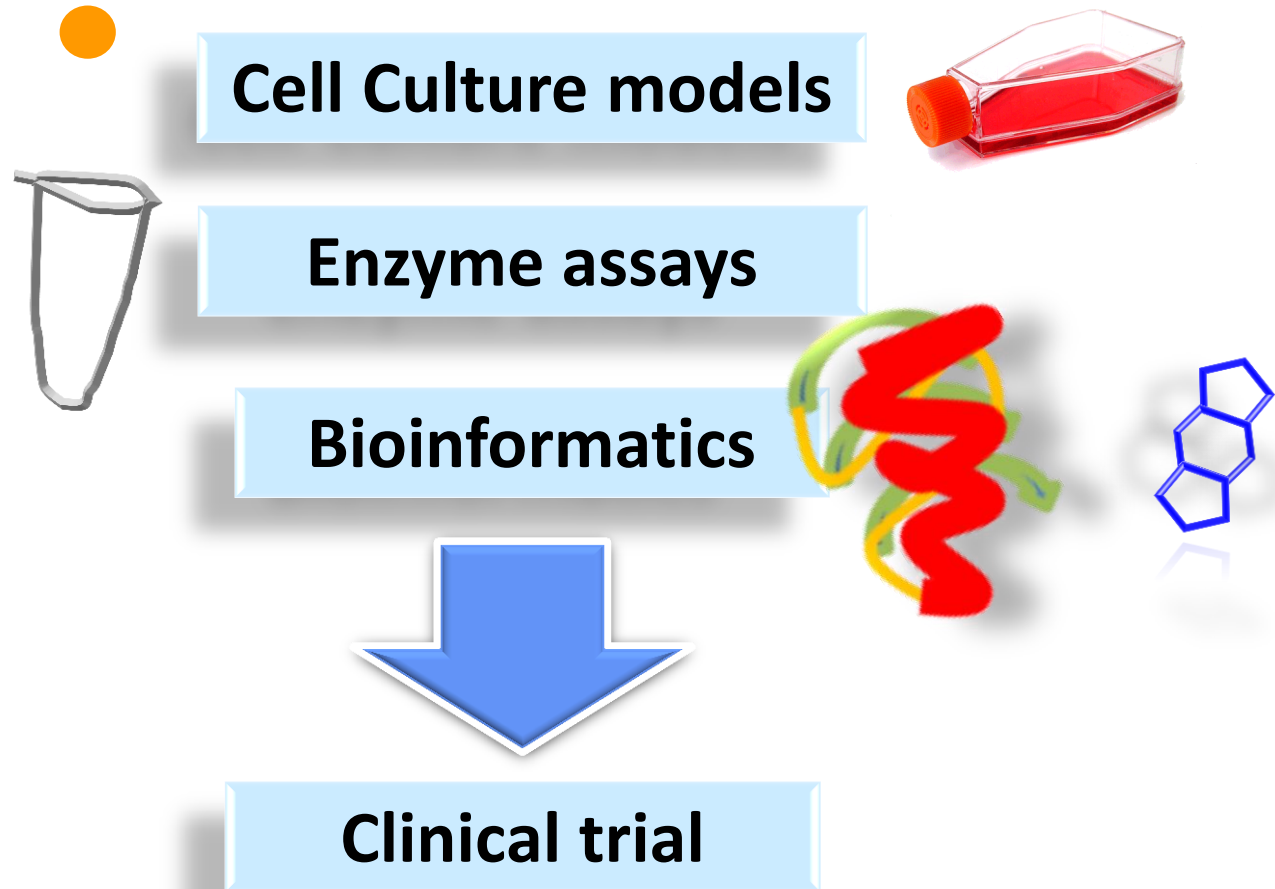
HCV Genome



Helicase Action



Drug Screening for HCV



Drug Screening for HCV

Huh8 cells

HCV Replicon

Huh7 cells

HCV virion

HCV NS3

Helicase

Drug Screening for HCV

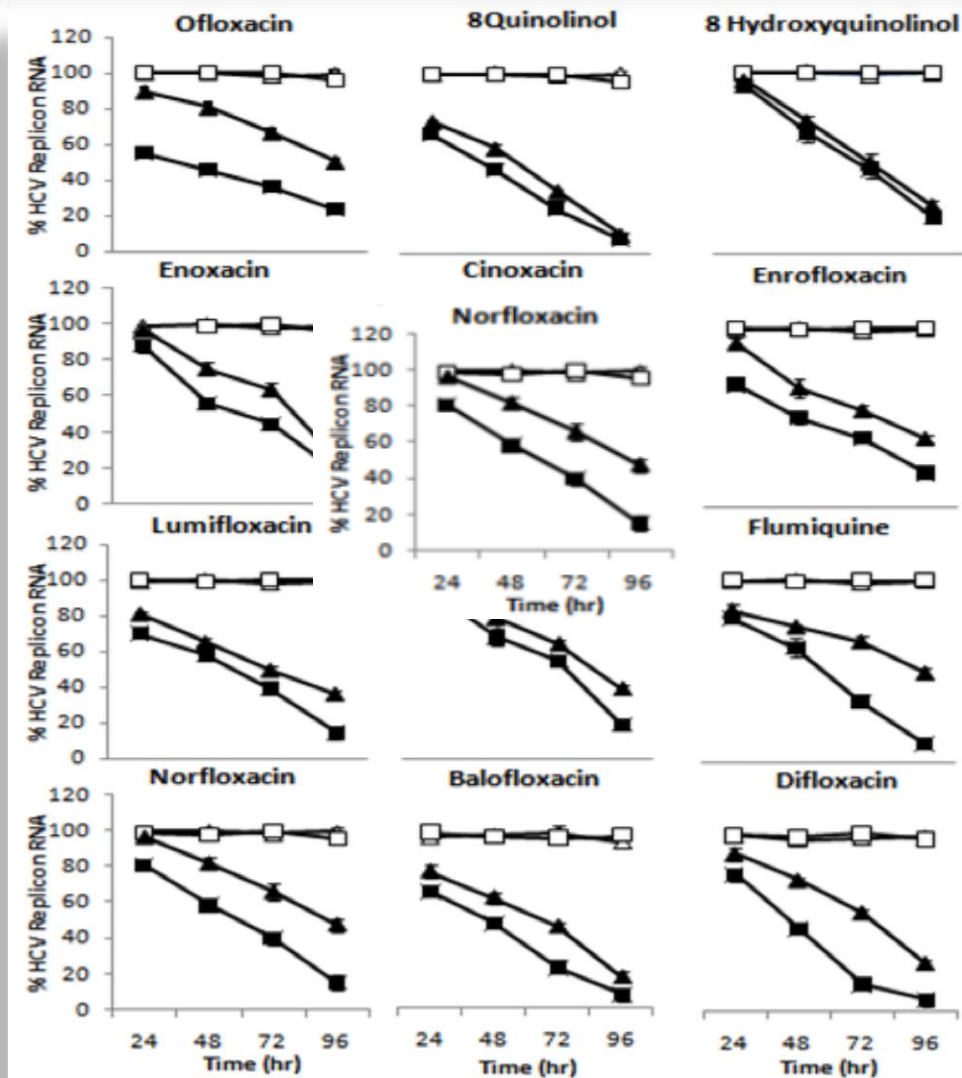
Huh8 cells
HCV Replicon



Incubate cells
with drug



Quantify
HCV RNA



Drug Screening for HCV

Huh8 cells

HCV Replicon

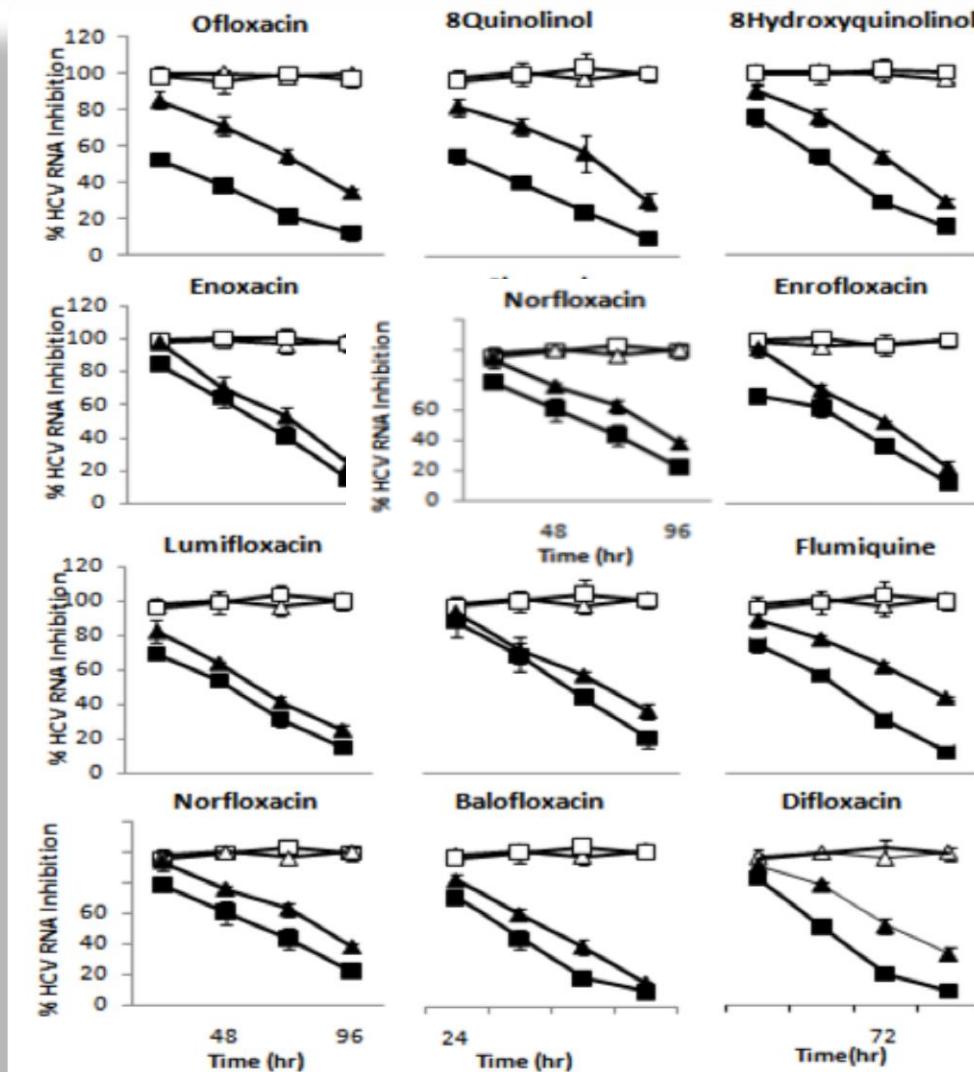
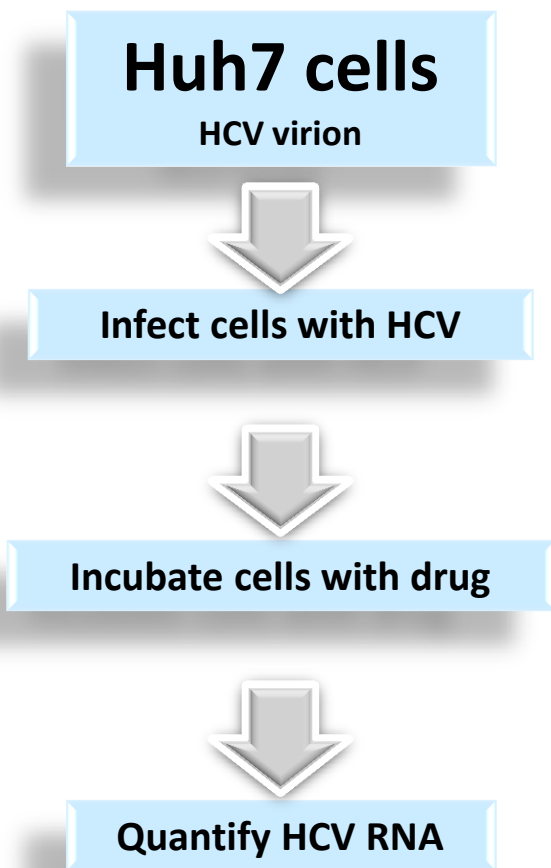
Huh7 cells

HCV virion

HCV NS3

Helicase

Drug Screening for HCV



Drug Screening for HCV

Huh8 cells

HCV Replicon

Huh7 cells

HCV virion

HCV NS3

Helicase

Drug Screening for HCV

HCV NS3

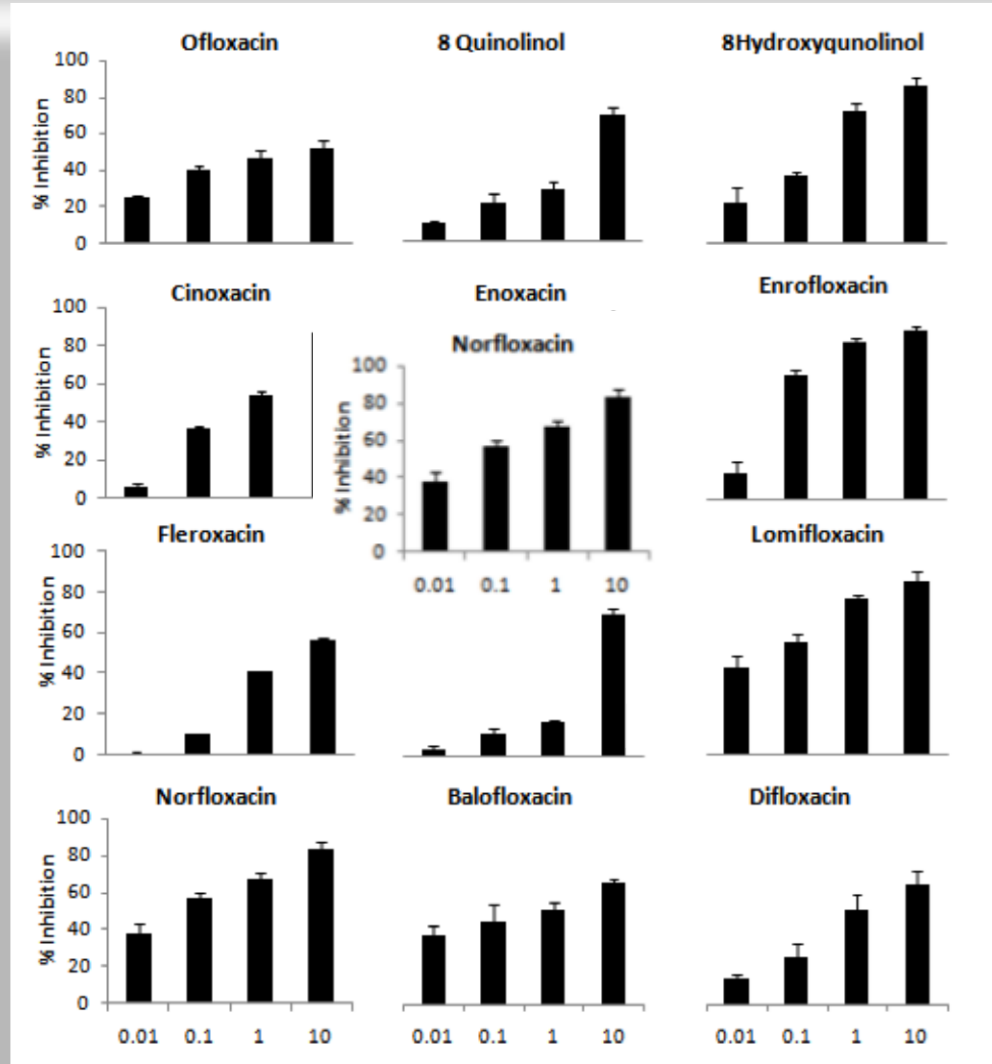
Helicase



Purify viral helicase

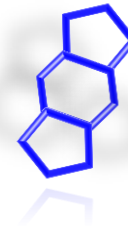


**Measure activity
With and without drug**



Docking Analysis

Bioinformatics

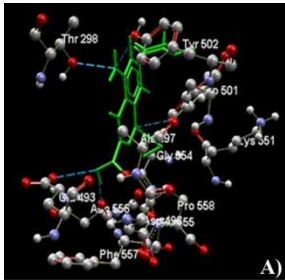


Drug-Target interactions

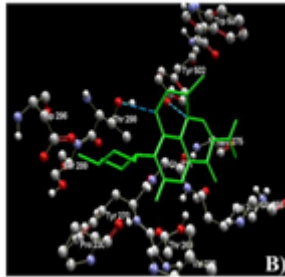
Ligand	Docking Energy (KJ/mol)	
	FlexX	Molegro
Sparfloxacin	-20.5	-86.6
Ofloxacin	-17.9	-85.1
Balofloxacin	-17.3	-81.0
Pefloxacin	-15.9	-79
Levofloxacin	-15.8	-75.6
Lomefloxacin	-15.6	-75.2
Ciprofloxacin	-15.4	-74.4
Enrofloxacin	-14.7	-74.1

Drug-Target interactions

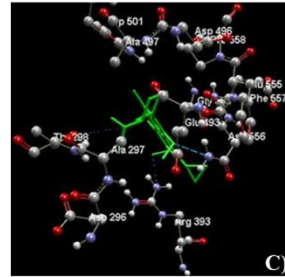
Sparfloxacin



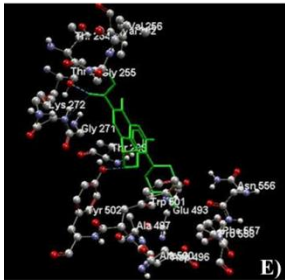
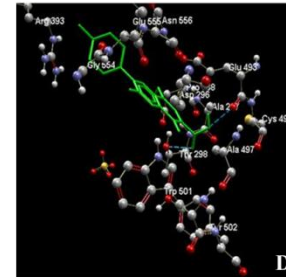
Ofloxacin



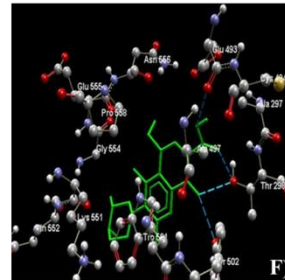
Balofloxacin



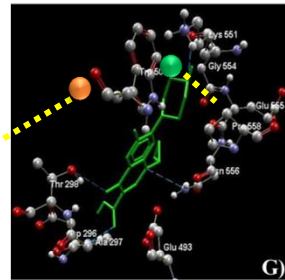
Pefloxacin



Levofloxacin



Lomefloxacin



Summary

HCV NS3 helicase inhibitors:

HCV replicon

HCV virion synthesis

HCV helicase

Computer modeling

Screening for novel inhibitors



CANCER & VIRUS LAB

