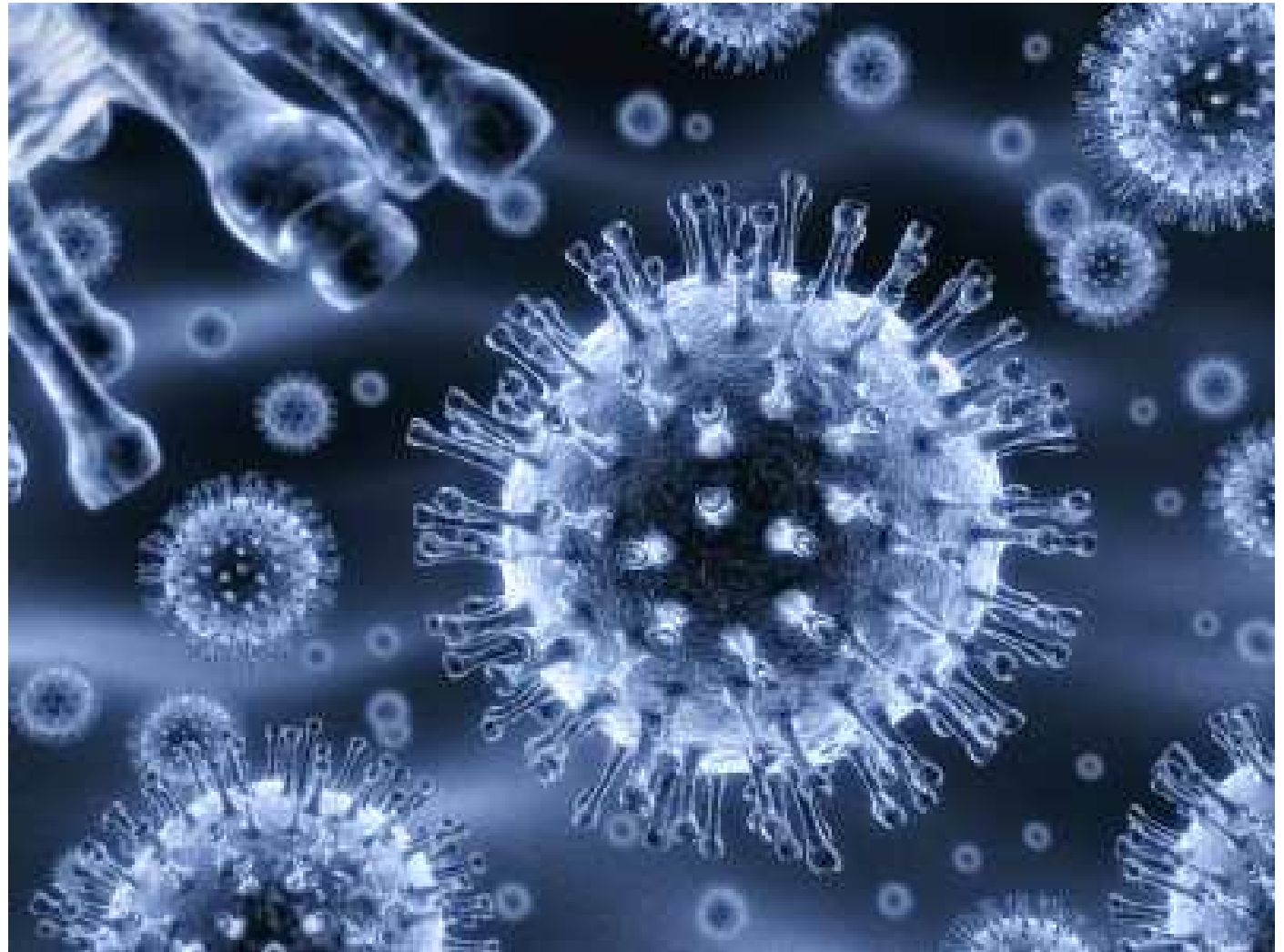
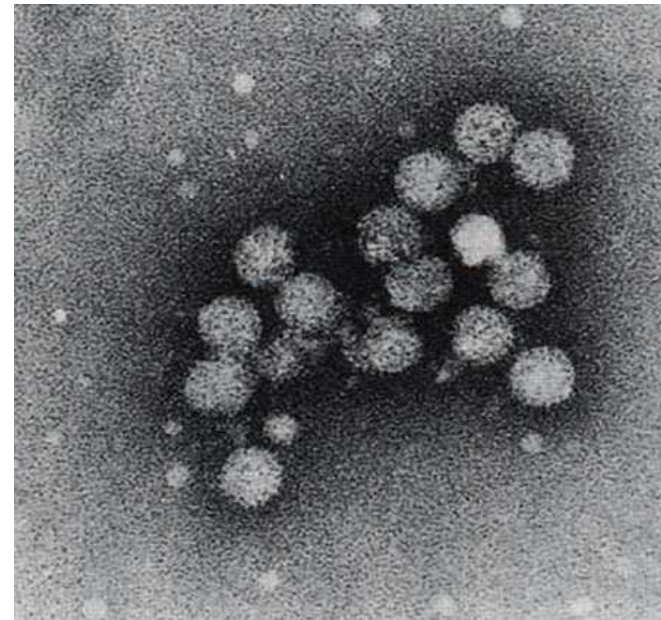
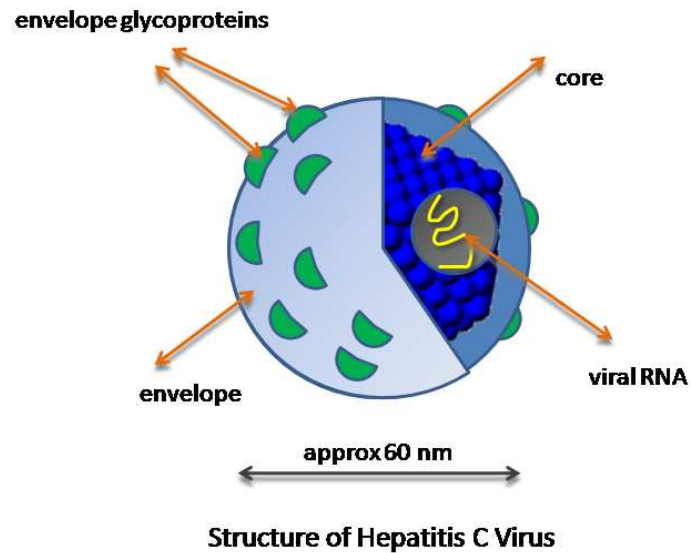




Virus Hepatitis C

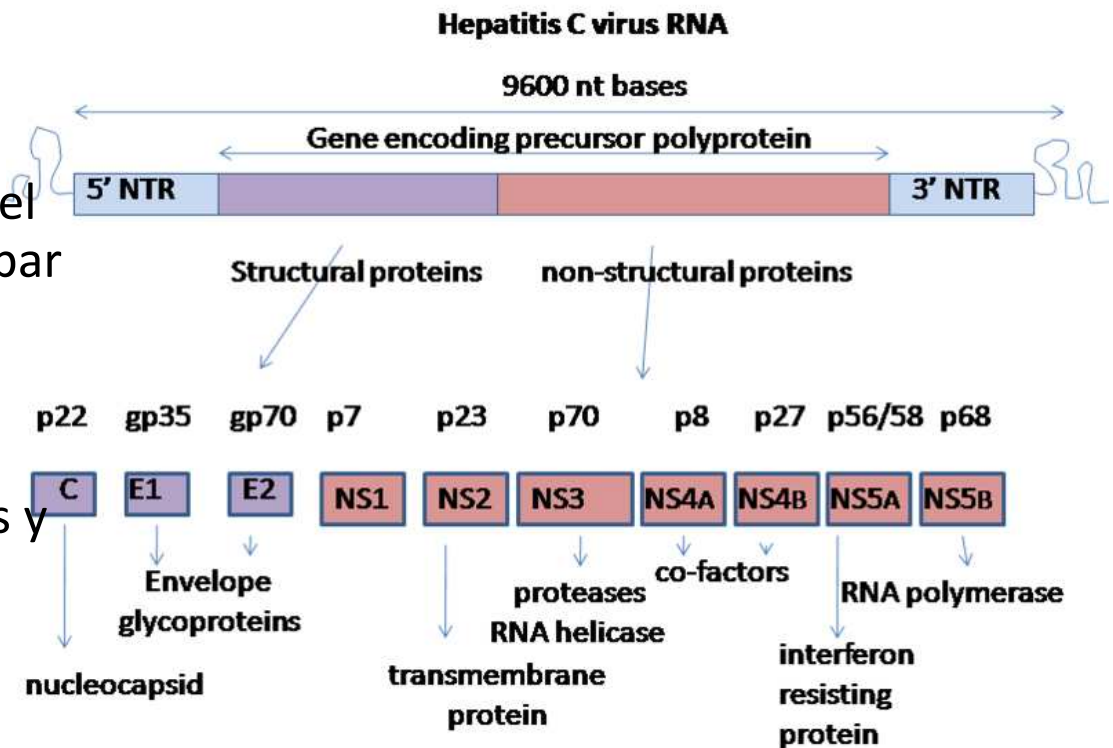
Características generales VHC

- Virus de pequeño tamaño (aprox. 50 nm)
- Posee envoltura
- ARN de polaridad +



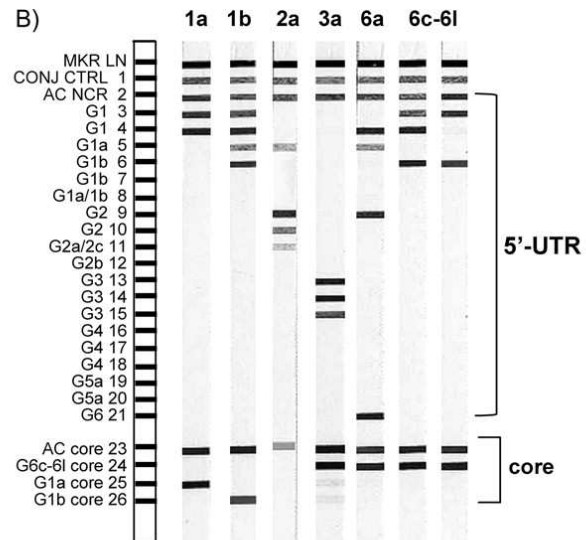
Características genéticas VHC

- Virus RNA con alta tasa de mutación en su replicación (cuasiespecies virales).
- Estos cambios genéticos en el virus hacen que pueda escapar al sistema inmune del hospedador.
- Existen 6 genotipos distintos y 15 subtipos descritos, sus prevalencias varían en cada región del mundo. Cada genotipo tiene sus propias implicaciones clínicas.

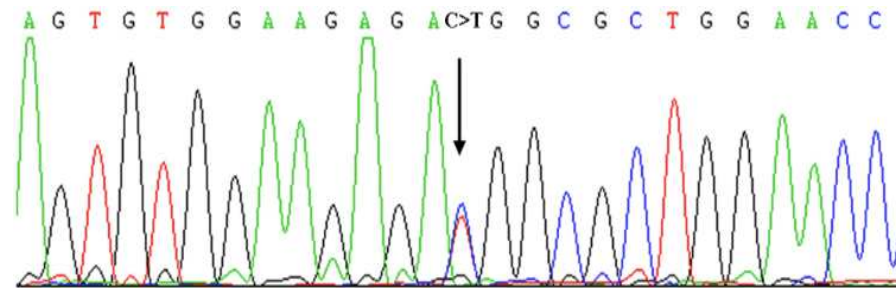
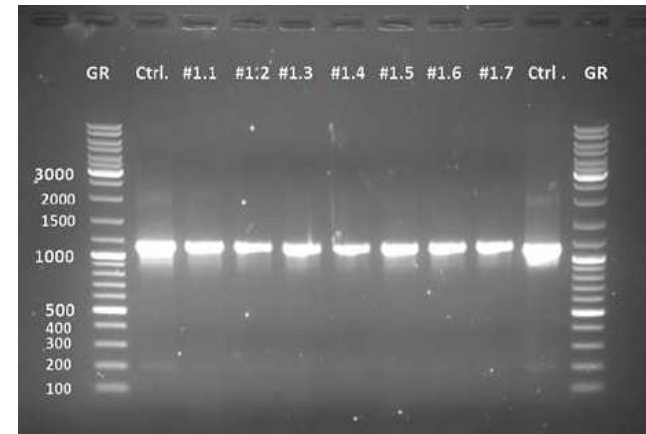


Tipado del VHC

- Métodos Moleculares
 1. Versant HCV Genotype 2.0
 2. RT-PCR-Secuenciación.

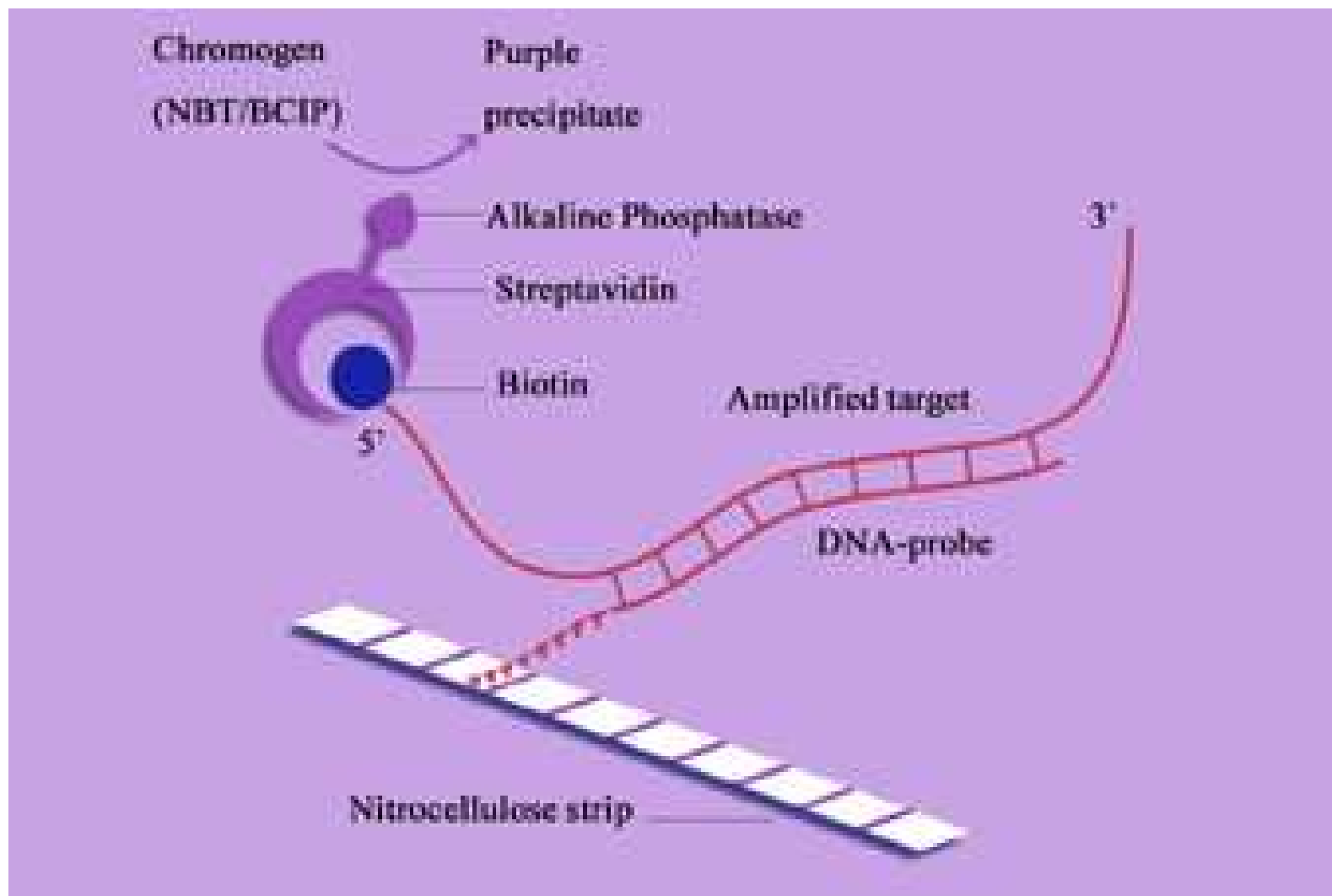


Versant HCV Genotype 2.0

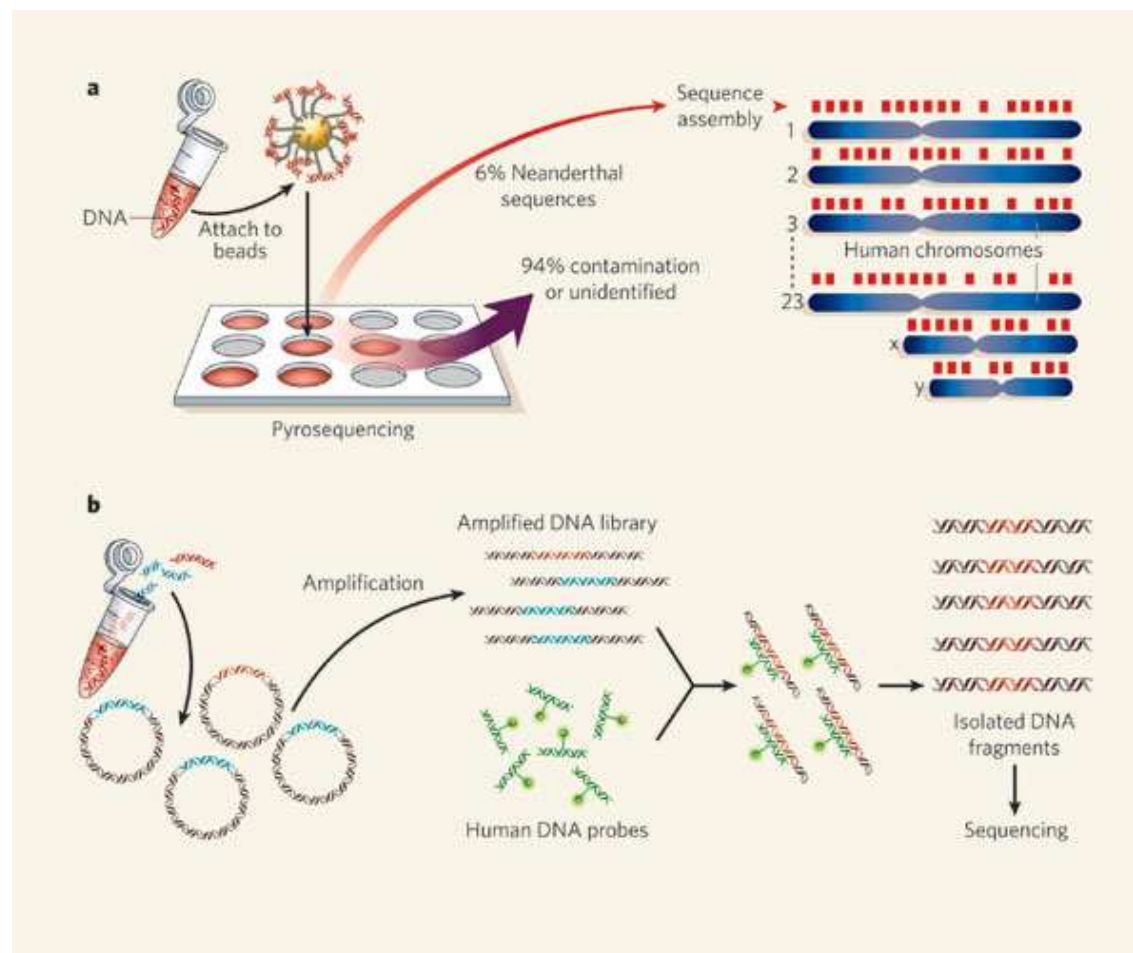


RT-PCR-Secuenciación

LIPA

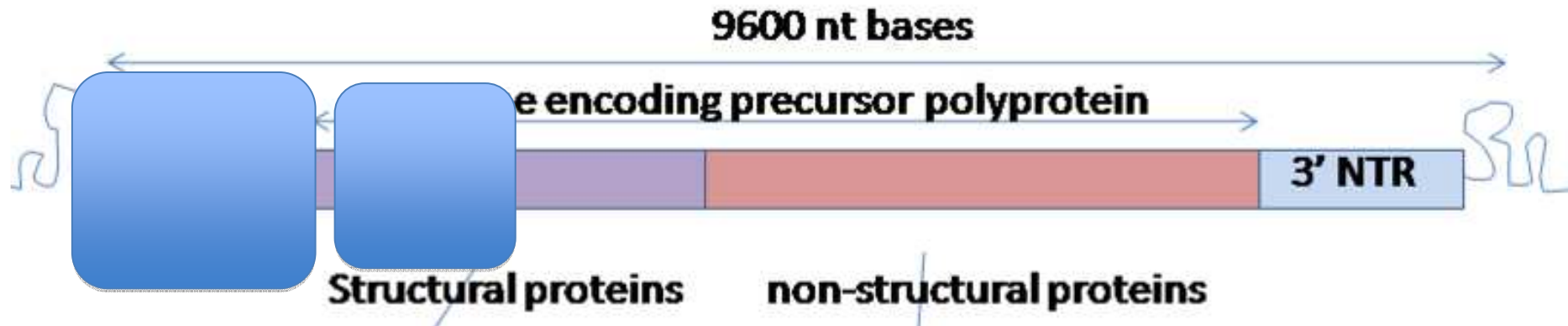


SECUENCIACIÓN



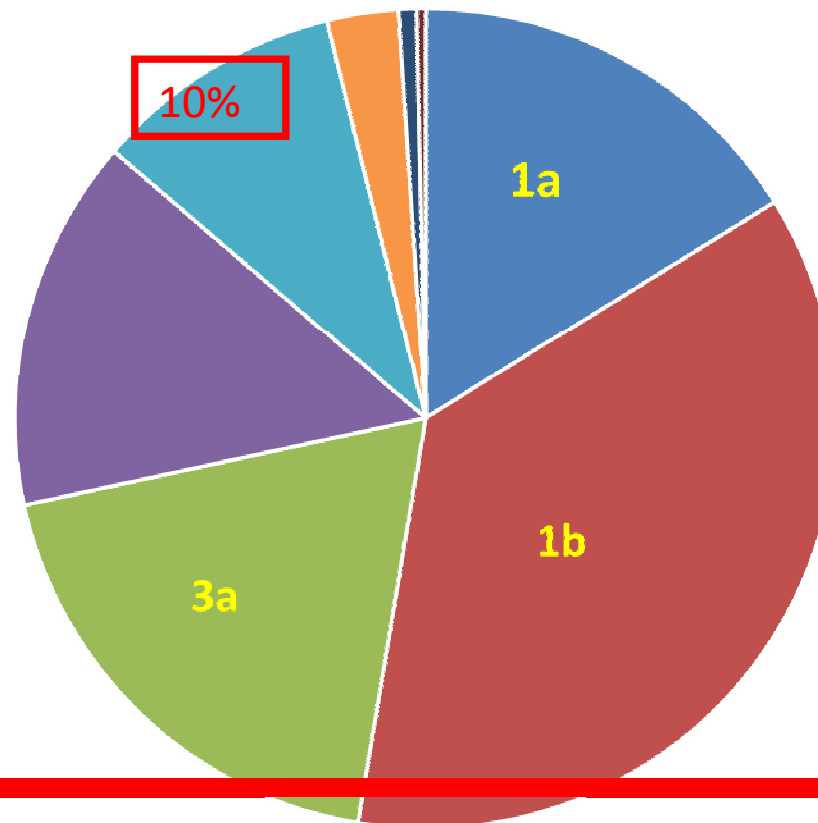
Versant HCV Genotype 2.0

Hepatitis C virus RNA



- Utiliza las regiones 5' UTR y parte del CORE
- No puede identificar o identifica erróneamente algunos subtipos
- No puede distinguir entre 1a y 1b en un 10% de los casos.
- No identifica mutaciones importantes como la Q80
- No puede determinar infecciones múltiples minoritarias

GENOTIPADO



■ 1a

■ 1b

■ 3a

■ 4

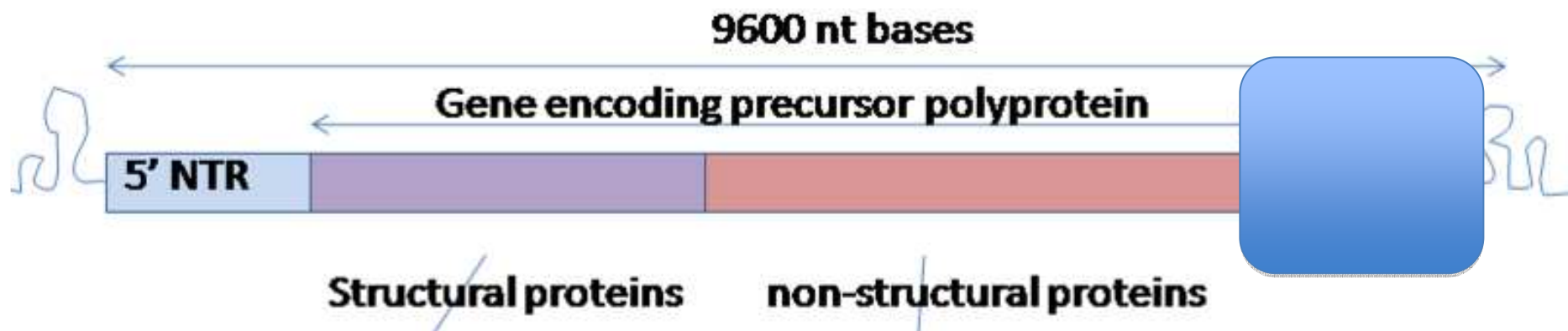
■ 1

■ 2

■ 5

■ 1+4

RT-PCR-Secuenciación



- Analiza la región NS5B de la zona 3' del VHC
- Identifica todos los genotipos y subtipos del VHC
- Distingue entre 1a y 1b
- No puede determinar infecciones múltiples minoritarias

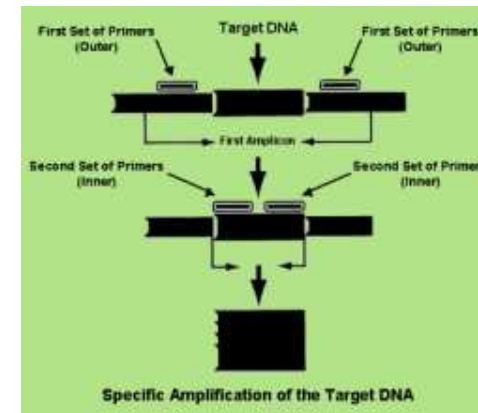
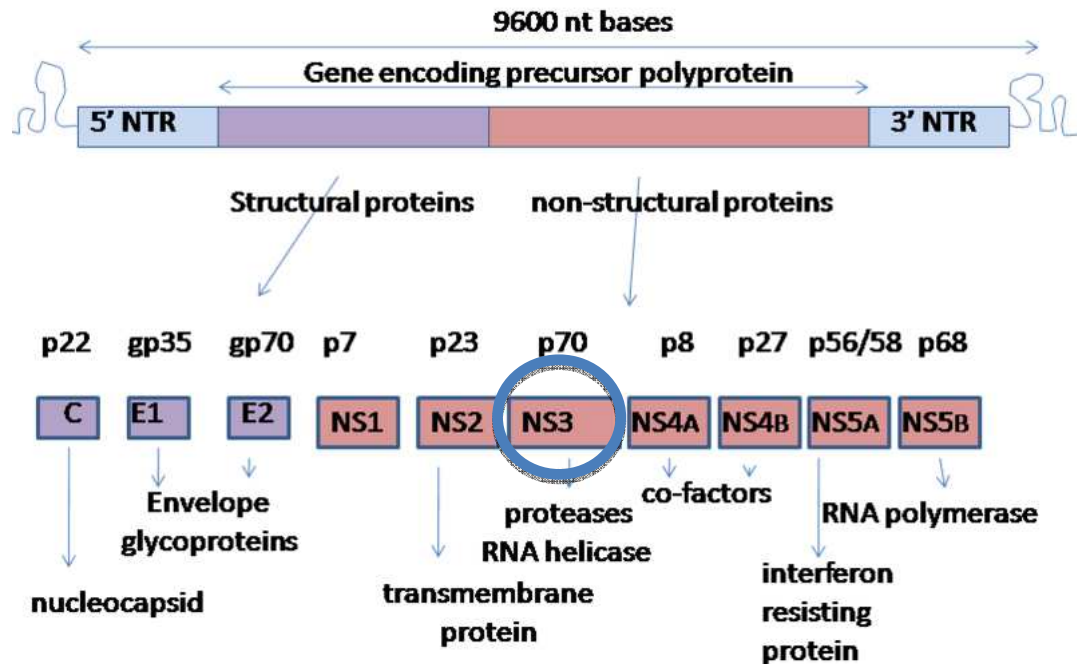
MUTACIÓN Q80K

GENO2PHENO

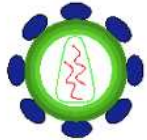
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Hepatitis C virus RNA



MUTACIÓN Q80K



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NEW

This is the new service geno2pheno[hcv]. Although we did several test-runs, we cannot guarantee for perfect stability at the moment. In case you observe any problems, please don't hesitate to contact us (beggel@mpi-inf.mpg.de). The list of rules may not be complete. Please stay tuned for some updates.

Submit below DNA sequences of the HCV *NS3* region, *NS5A* region or *NS5B* region.

- You will obtain a list of mutations and predictions of phenotypic resistance of the respective virus to antiviral drugs.
- You will obtain genotype and subgenotype prediction (and in case of 1a clade information) using a sequence alignments of the input sequence to HCV reference sequences.

By setting a [fold change](#) cutoff you will only obtain mutations with a higher maximal fold change than the threshold. Setting the cutoff '0' all mutations will be obtained. The fold change is based on the [IC50](#) values of the drugs for the different mutations and the wild type.

By changing the "Alignment width" you change the number of nucleotides printed per line in the alignment.

Please note that for reliable predictions the sequences must contain a substantial part of the *NS3*, *NS5A* or *NS5B* region.

No clinical decision should be based only on the result of the used algorithm.

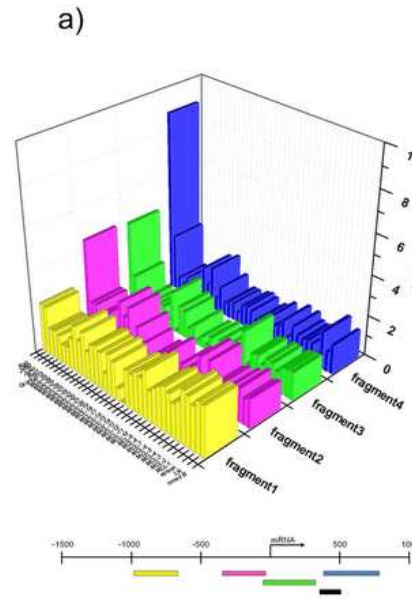
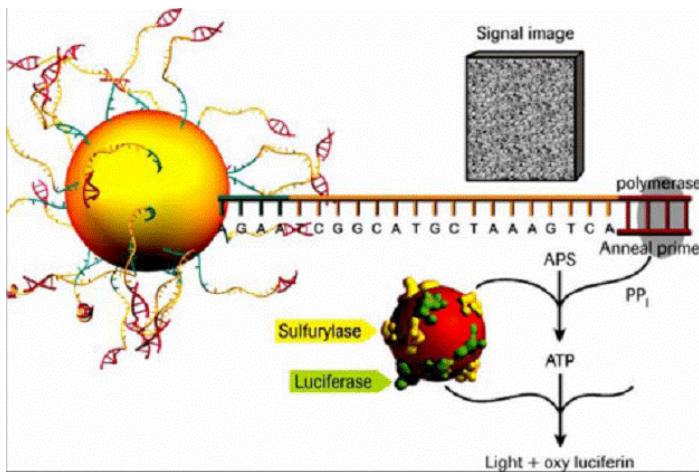
MUTACIÓN Q80K

Included <i>NS3</i> region codons:	13 - 167 (similarity to reference = 97.42%)		
Mutations <i>NS3</i> region:	T40A, Q89H, S91A, L153I		
Used reference for <i>NS3</i> region:	H77		
Drug Resistance			
Drugs	Scored mutations	Resistance analysis	Fold Change
Boceprevir	none	susceptible	-
Telaprevir	none	susceptible	-
Simeprevir	none	susceptible	-
Faldaprevir	none	susceptible	-
Detailed Mutation Information			
Mutation	Fold Change	Resistance analysis	

MUTACIÓN Q80K

Included <i>NS3</i> region codons:	13 - 167 (similarity to reference = 96.77%)		
Mutations <i>NS3</i> region:	T40A, Q80K, Q89H, S91A, L153I		
Used reference for <i>NS3</i> region:	H77		
Drug Resistance			
Drugs	Scored mutations	Resistance analysis	Fold Change
Boceprevir	none	susceptible	-
Telaprevir	none	susceptible	-
Simeprevir	80K	resistant	14
Faldaprevir	80K	resistant	2.2
Detailed Mutation Information			
	Mutation	Fold Change	Resistance analysis
Simeprevir			
	80K	14	resistant
Faldaprevir			
	80K	2.2	resistant

SECUENCIACION MASIVA



b)

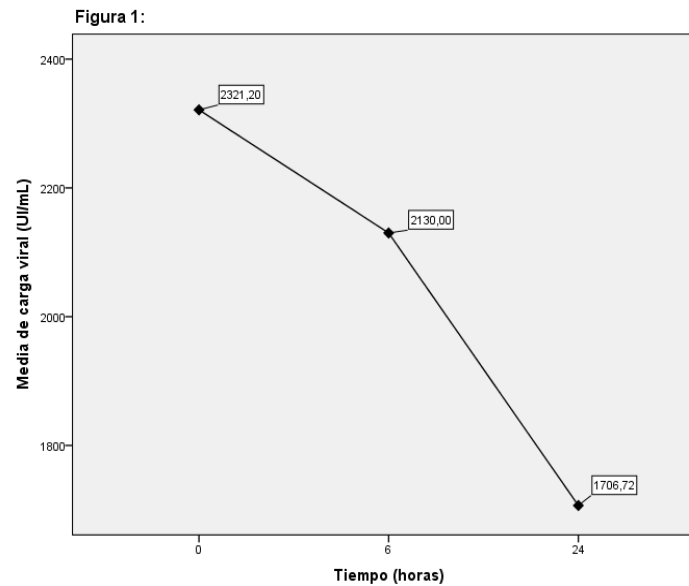
	CpG1	CpG2	CpG3	CpG4
tonsil B	7	7	18	13
LN	5	5	16	10
spleen	15	15	28	22
MCL-1	4	4	7	7
MCL-2	2	2	4	6
MCL-3	4	4	8	8
MCL-4	5	5	10	8
MCL-5	5	5	10	9
MCL-6	3	3	5	6
MCL-7	2	2	3	5
MCL-8	4	4	4	8
MCL-9	7	6	13	8
MCL-10	7	7	9	8
MCL-11	16	17	24	19
MCL-12	4	3	5	4
MCL-13	3	3	7	4
MCL-14	3	2	3	3
MCL-15	6	6	10	7
MCL-16	3	3	6	4
MCL-17	4	3	6	4
MCL-18	3	3	5	4
MCL-19	6	5	9	7
MCL-20	5	5	9	6
MCL-21	3	3	7	8
MCL-22	38	27	54	53
MCL-23	6	5	8	7
MCL-24	2	2	3	5
MCL-25	2	2	2	5
MCL-26	3	4	6	7
MCL-27	3	2	3	3
MCL-28	4	3	5	5
MCL-29	3	2	2	3
Granta519	2	2	3	4
Rec1	5	5	9	10
JeKo	1	2	2	4
JVM2	5	4	7	7
Raji	56	67	92	95

Permite detectar los genotipos y las mutaciones de las poblaciones minoritarias

CONSERVACIÓN Y TRANSPORTE

Table 1: Mean difference and Intraclass correlation coefficients* (ICC), limits of 95% confidence interval (95% CI)

	Mean difference, UI/ml (95% CI)	SD	CCI (95% CI)
Between 0 and 6 hours	-212.0 (-474.10; 50.10)	634	0.457 (0.099; 0.714)
Between 6 and 24 hours	-412.88 (-645.77; -179.99)	564.207	0.256 (-0.079; 0.564)
Between 0 and 24 hours	-624.88 (-871.95; -377.81)	598.558	0.207 (-0.101; 0.519)



CONCLUSIONES

- La genotipificación del LIPA es un método poco preciso para diferenciar entre los genotipos 1a y 1b
- Los resultados deben confirmarse, al menos, por secuenciación clásica
- Hay que caracterizar molecularmente todas las mutaciones que sean clínicamente importantes
- La secuenciación masiva es una técnica compleja pero permite:
 - Caracterizar poblaciones minoritarias
 - Estudiar el genoma completo del virus
- La toma, el transporte y la conservación de la muestra es clave para el correcto control del tratamiento