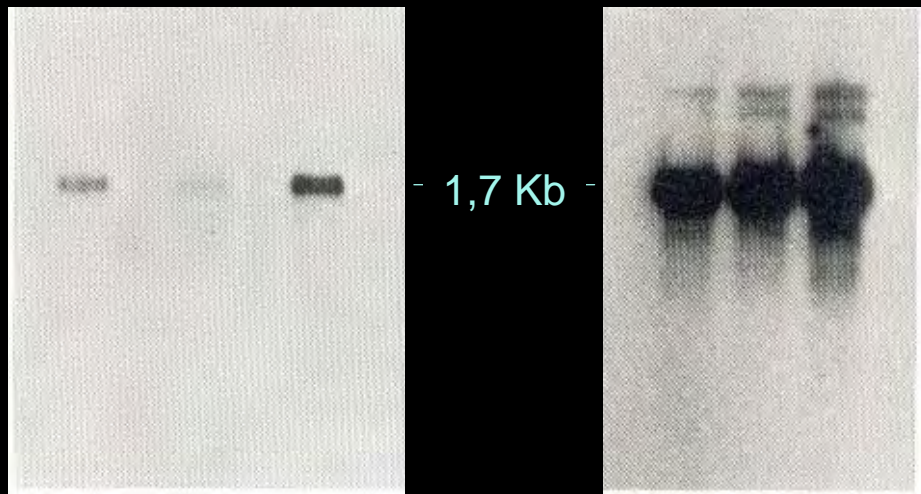


Génome 1672-1697 nt

Protéines sHD et LHD

Northern Blot



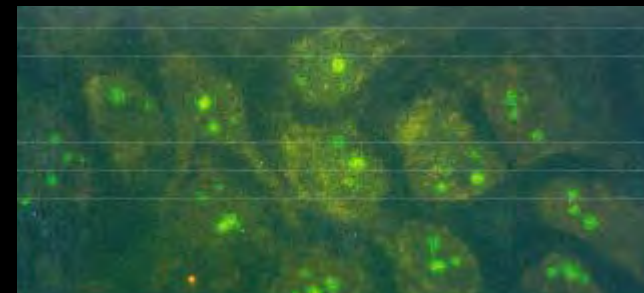
sérum

foie

chimpanzé

marmotte

IF anti-HD

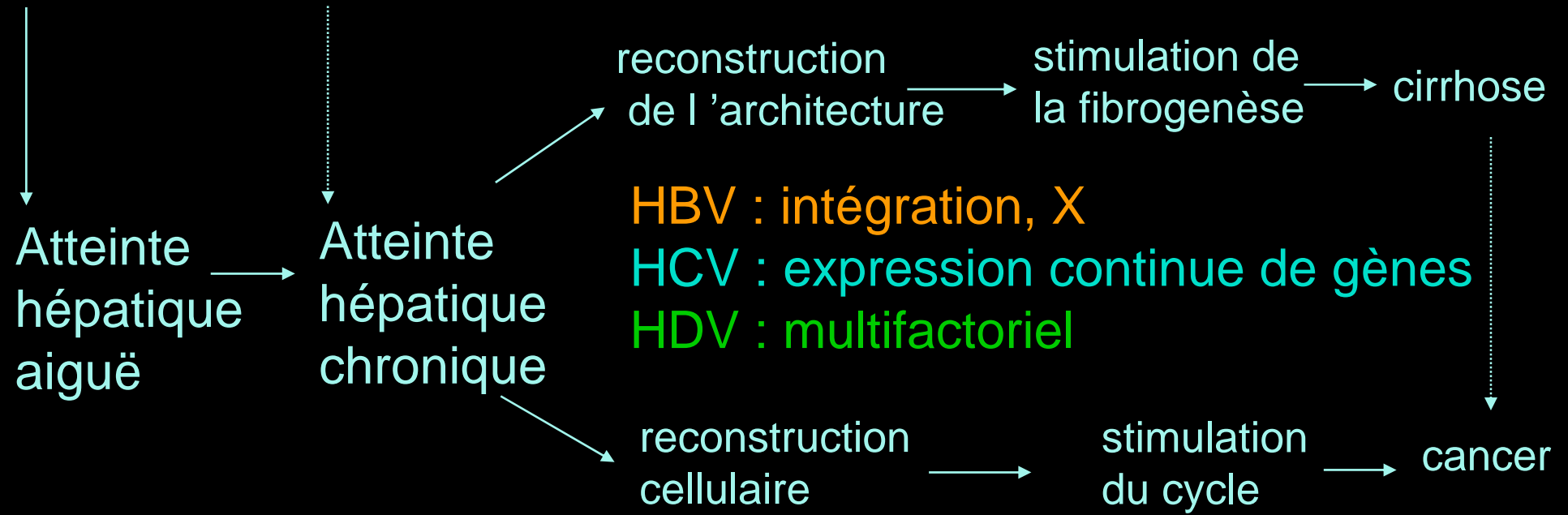


pCDNA3-sHD



pCDNA3-LHD

Transmission



HBV : intégration, X

HCV : expression continue de gènes

HDV : multifactoriel

HAV

HBV

HCV

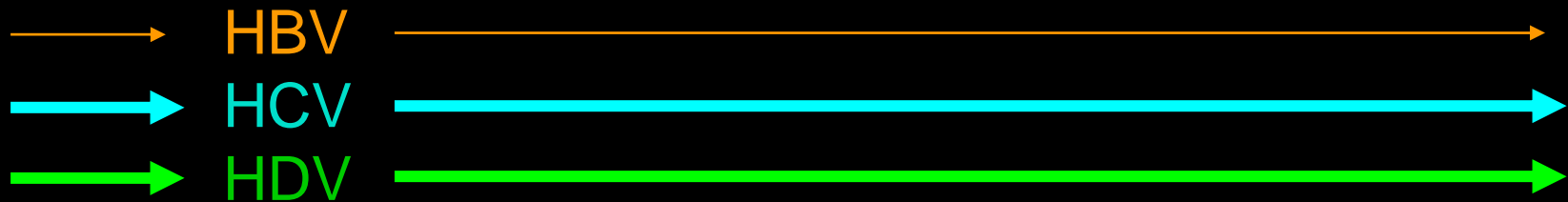
HDV

HEV

HBV

HCV

HDV



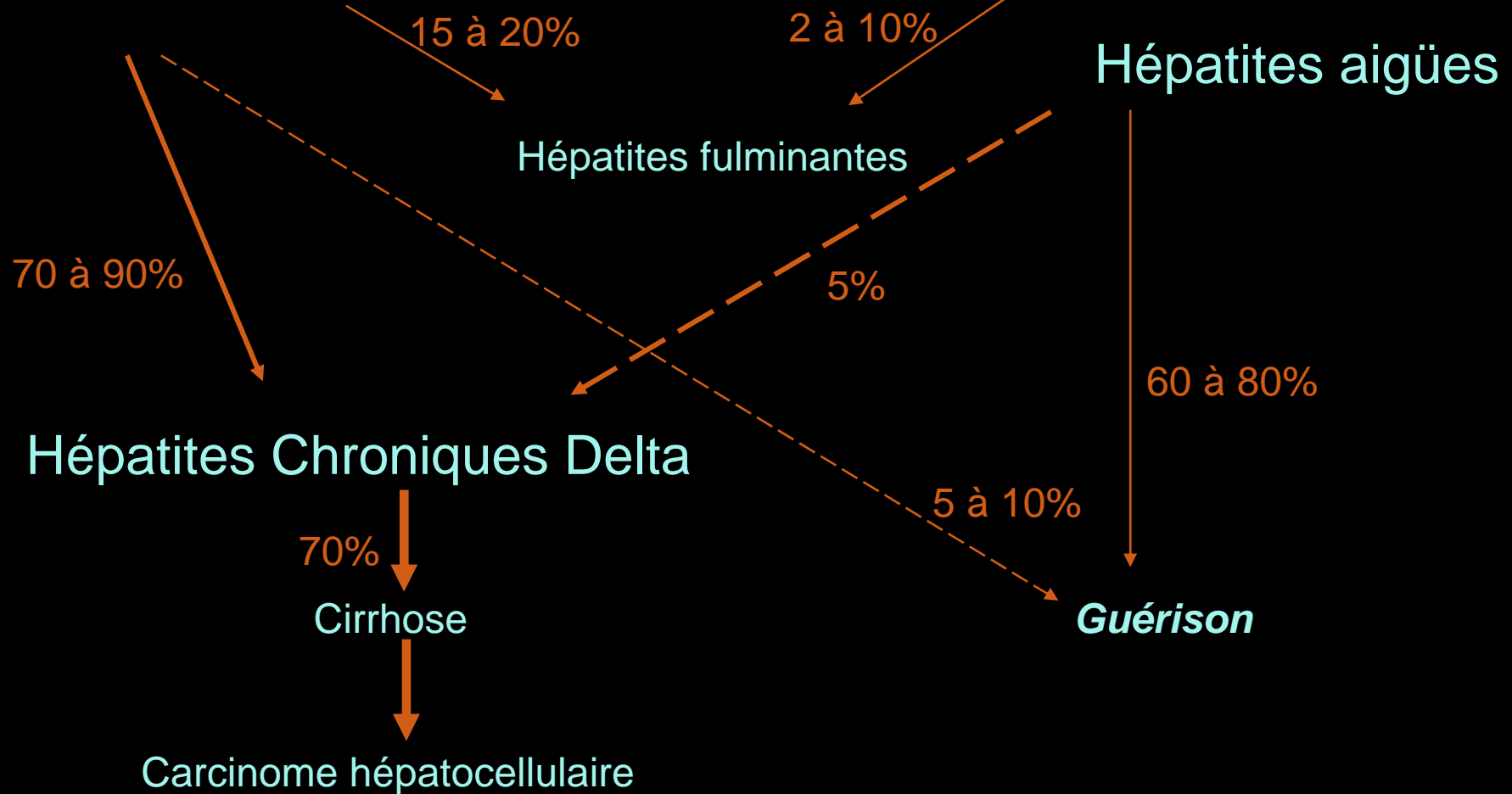
Porteurs chroniques B



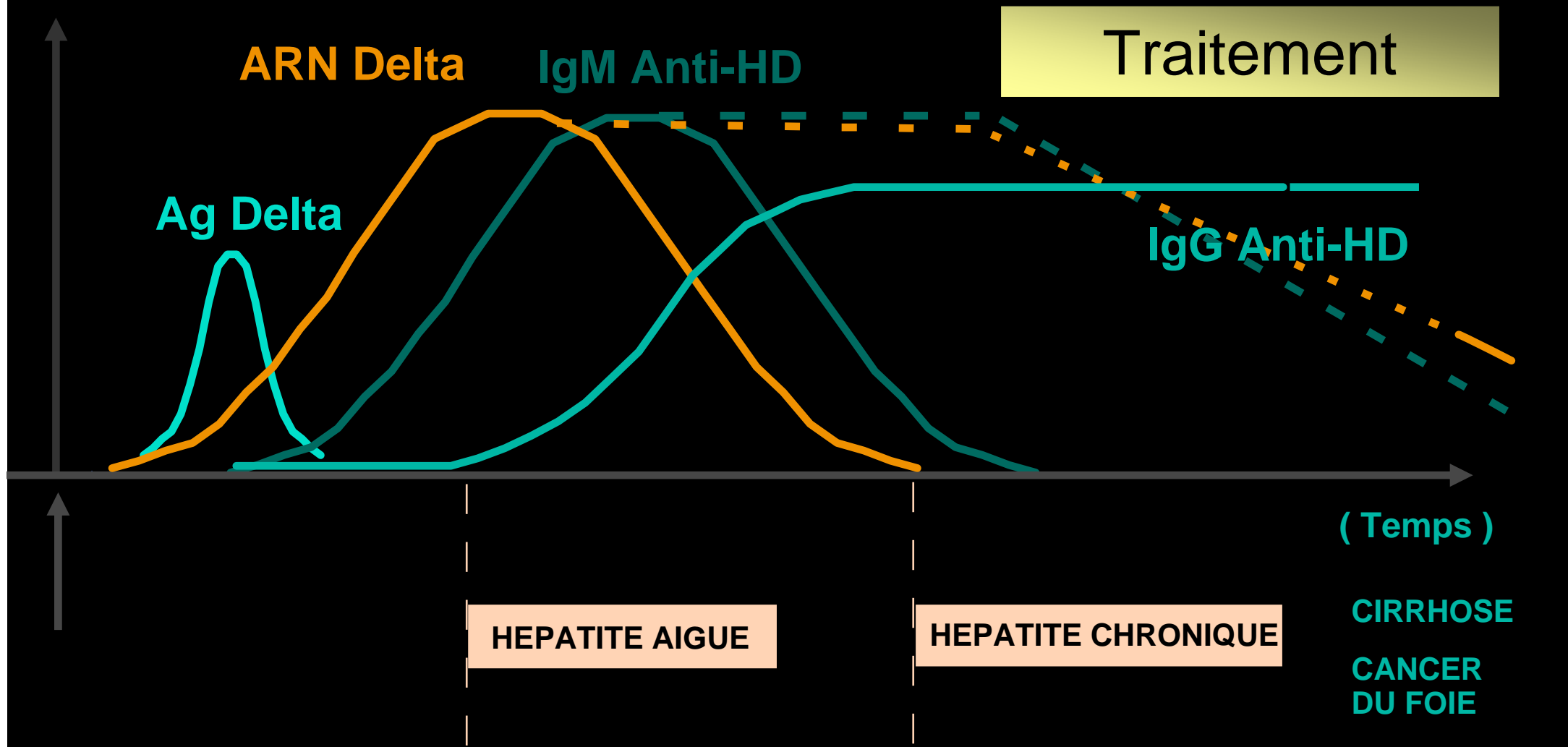
Surinfection

**Hépatite
Delta**

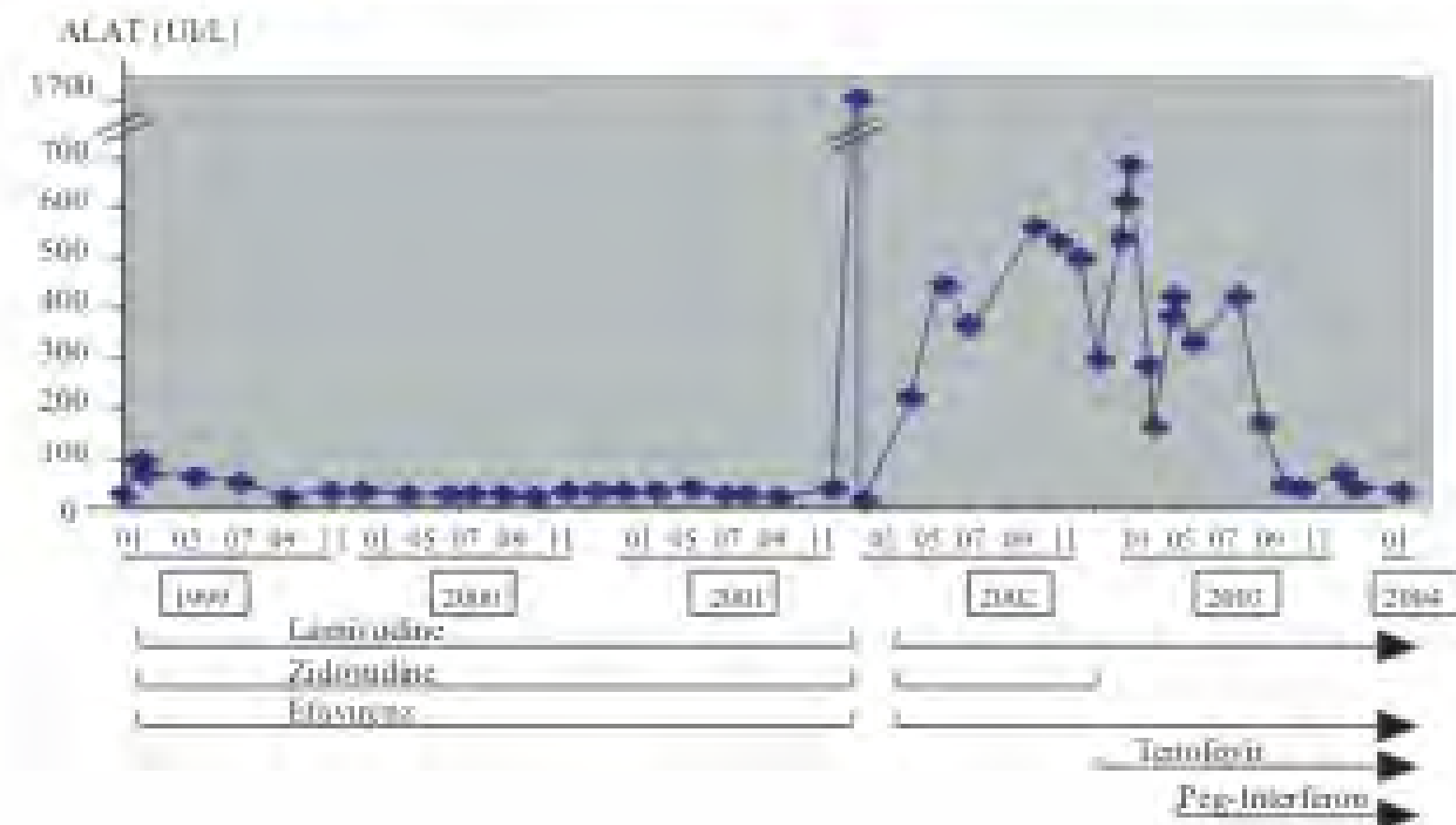
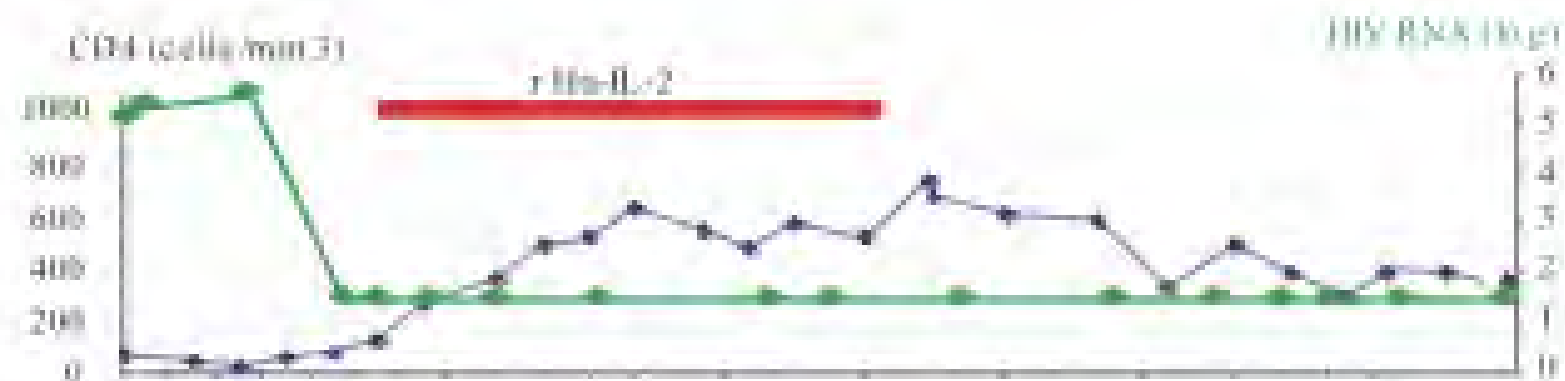
Co-infection



MARQUEURS VIRAUX



HDV toujours associé à une infection HBV ?



HDV INHIBE LA REPLICATION DE L'HBV

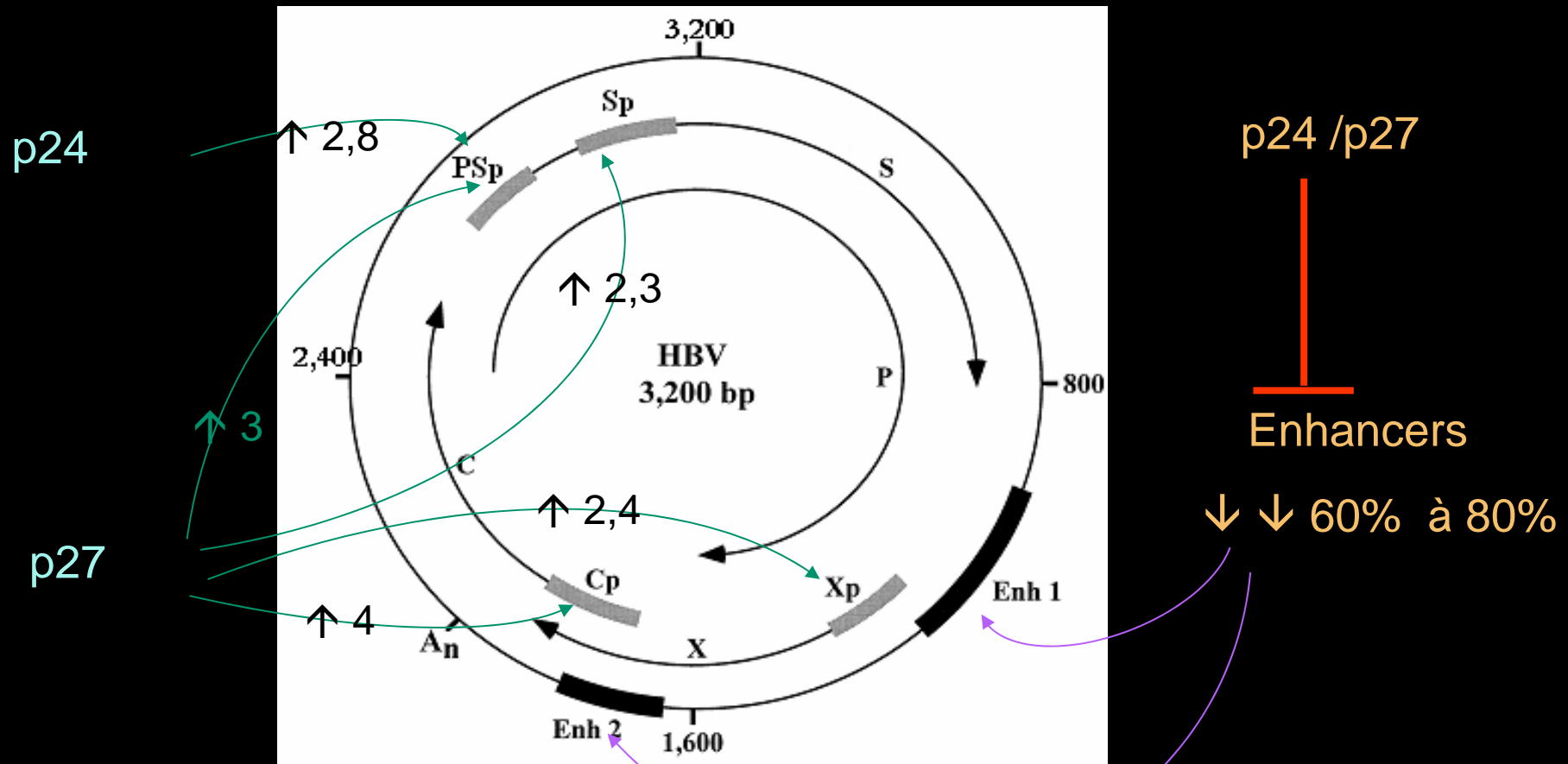


Effet anti-transcriptionnel

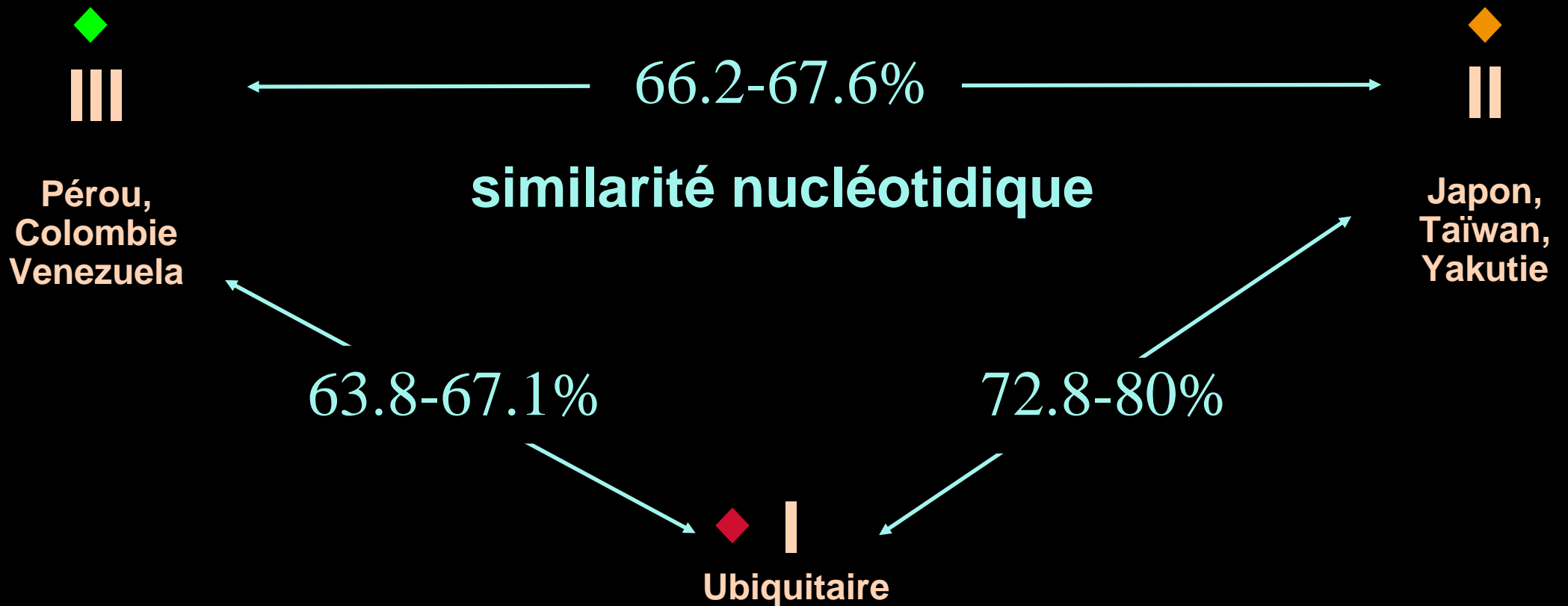
Compétition enveloppe

Cytokines (MxA ?)

Inhibition du HBV par HDV



HDV GENOTYPES



HDV GENOTYPES



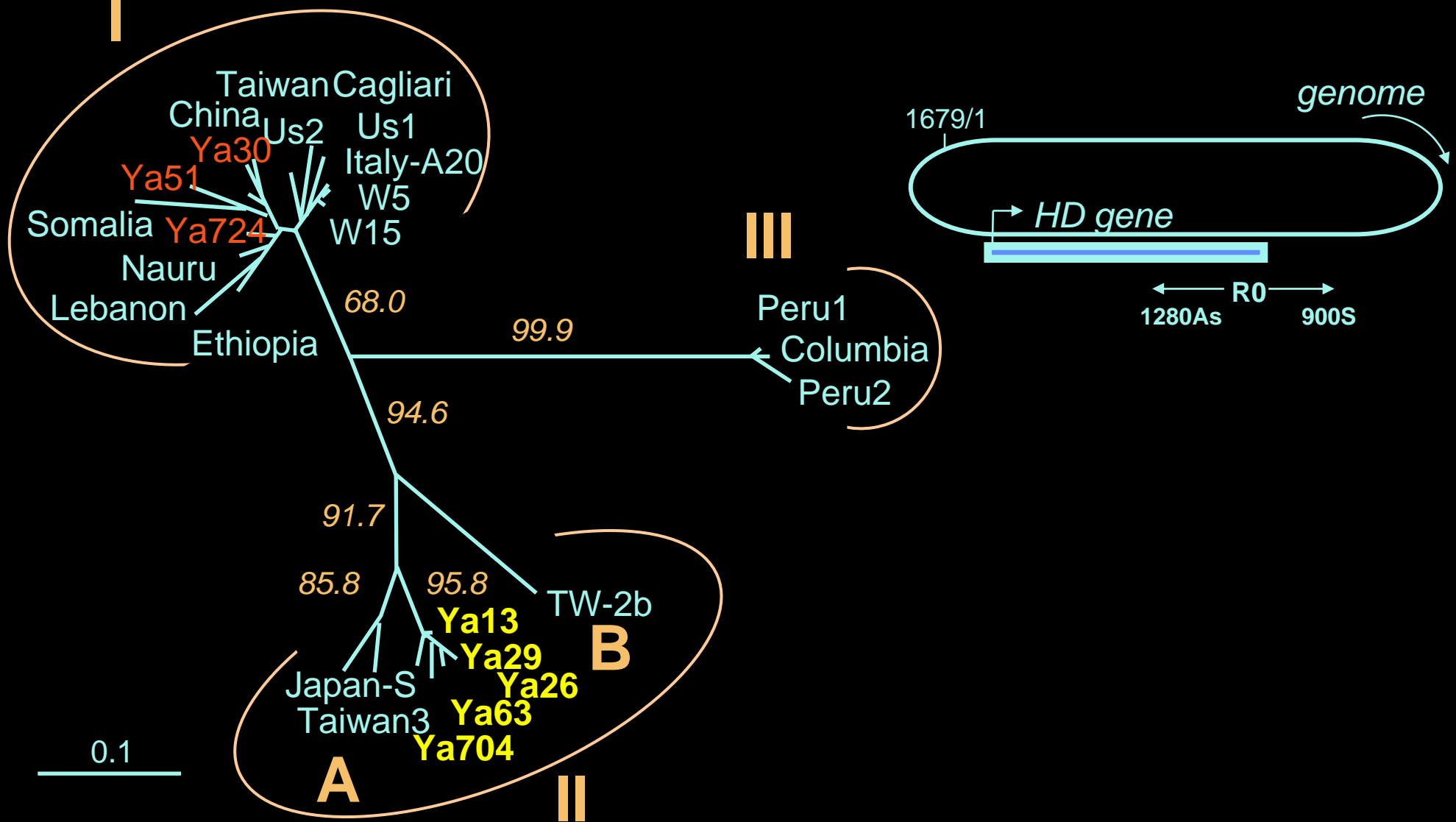
◆ | Ubiquitaire

◆ || Japon, Taïwan,
Yakutie

◆ ||| Pérou, Columbie
Vénézuéla

Wang, Nature, 1986; Imazeki, J Virol, 1990; Casey, PNAS, 1993, Wu J Gen Virol 1998, and many others

HDV sequences phylogenetic analyses



distance (R0) K2- NJ

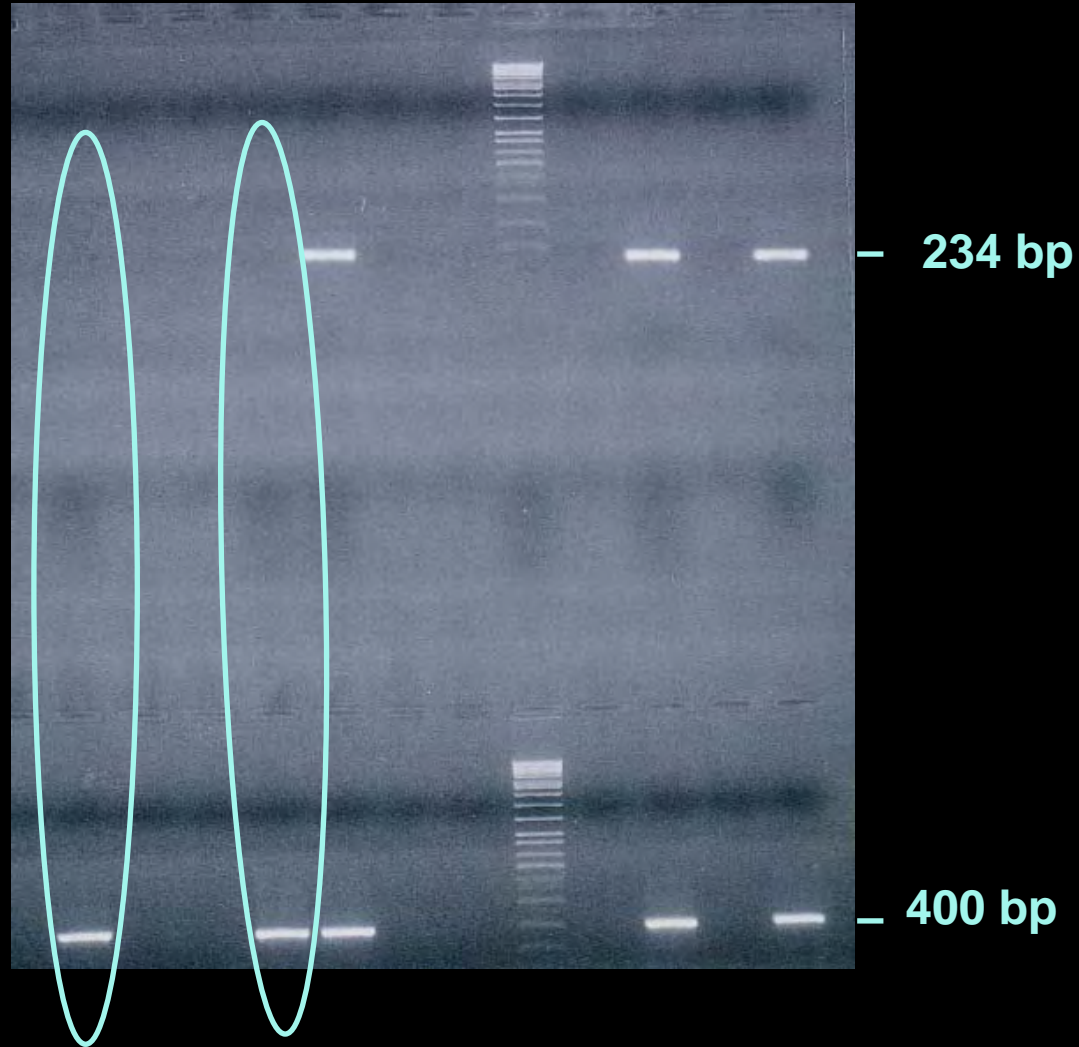
Ivaniushina et al, J Gen Virol 2001

ARN HDV PAR RT-PCR

1 2 3 4 5 6 7 8 9 10 11 12

1 : PCR CLASSIQUE

2 : PCR CONSENSUS



Angola	1
Cameroun	5
Republique Centre Africaine	1
Rep. Democratique du Congo	1
Egypte	2
Gabon	1
Gambie	1
Ghana	1
Guinée	2
Côte d'Ivoire	4
Mali	1
Republique du Congo	1
Pologne	1

SEQUENCE AND PHYLOGENETIC ANALYSES

RT-PCR amplification

- R0
- Full length (R1 et R2)

Cloning and sequencing

- Big Dye Terminator

Multiple Alignment (Clustal W1.8, ProAlign)

Phylogenetic approaches

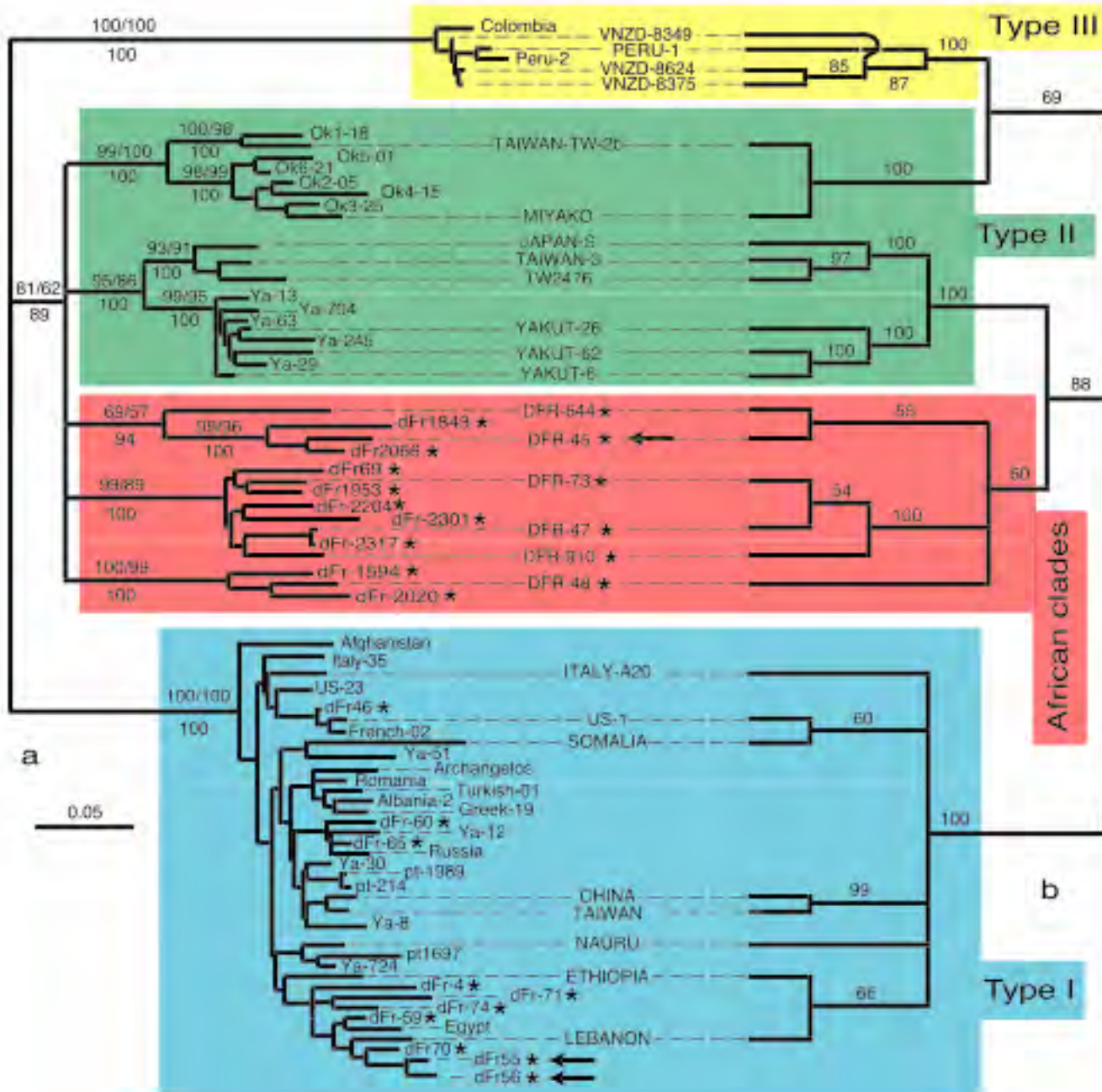
- Distance (K2/GTR) (PAUP* 4b6)
- MP (PAUP* 4b6)
- ML (GTR+ Γ)(PAUP* 4b6 / MetaPIGA)

Stability of the topology

- Bootstrap/ SOAP/ Proalign / MetaPIGA



R0



Full-length

Radjef et al.,
J. Virol. 2004

HD protein carboxy-terminal region

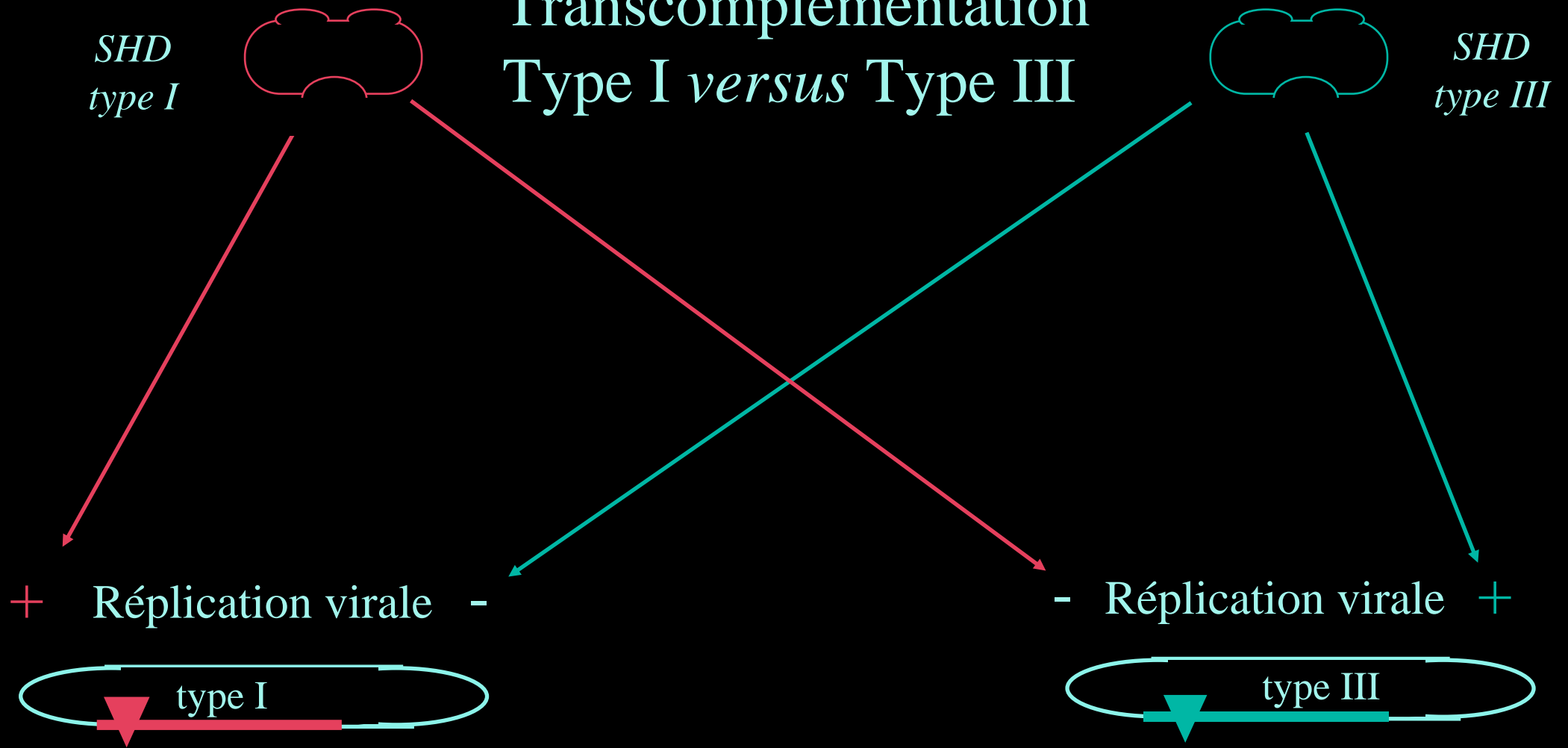
121

215

TW-2b KNLSREEEEELRRLTEEDERRRERVAGPRVGDVNPLDGGPRGAPGGGFVPSMHDIPESPFTRRGDGLDVRGAQEFPWVSPQPPPPRLPLLE-CTPQ
Miyako .V.....K.....E.A.....T.EGV.....S.....I..T.G..W.D.GR.S.....-.....
Taiwan3 .S.....V..E.K.....V..SG.....Q.EGV.....A.T.E...I..N.G..W.H.S..QQ.....-.....
Japon-S .I..K.....D..E.K.....SR.....Q.AGV.....S.T.E...I..T.G..W...S..QQ.....-.....
Yakut-62 .S..K.....I..DE.Q.....PG.S.....Q.TGV.....S.T.E...I..DRG..W.N.A..GQ.....-.....
Yakut-26PG.S.....Q.TGV.....T.E...I..T.G..W.N.V..GQ.....-.....
dFr910 .S.....K.....PE.P.....Q.L.V.....S.T.S.....N.Q..W.D.G.R.....-.....
dFr47 .S..K.....K.....PGTS.....Q.LGV.....S.T.E.....N.QY.W.N.G.R.....-.....
dFr73 .S..K....LG.....PQ.P.....Q.LNV.....T.E...I..N.Q..W...GA.S.....-.....
dFr644 .K.....G.....V..K.E.A..QD.G..PG.S.....R.LGV.....D..I..D.Q..WGQRP.....-.....
dFr45 .S..K.....K..AD..Q.A..I.....PE.P.....QLLGV.....S.T.E...I..DRQ..WGPSPT.....-.....
dFr48LG..G..Q.K.T.....PG.D.....T.LHV.....S.T.E.....T.Q..WGNTP.R.....-.....
Ethiopia .H.....LK.....A..P.G...E..Q.....QGV.....H.E.....TGG..WDILF..SD.PFSPQS-.R..
Italy-A20K.....P.G.I..E..S.....LQGV.....S.T.E...I..NRG..WDILF..AD.PFSPQS-.R..
SomaliaK.....AR..E.S..I..SA.G...E..S.....QG.....H..E...T.TGG..WDILF..SD.PFSPQS-.R..
Peru .H..Q.....ARD.DE...T...P.G..M..P.....LQGV.....S.T.E.I.I..T.Q..WYGFT....GYYWVPG..Q..
VnzD8375ARD.DE.....P.G..M..P.....LQGV.....S.T.E.I.I..T.Q..WYGFT....GYYWVPG..Q..
* * * . * * * * * : * : * : * * * * * * * * * * * : * * * * * * * * * * * * * * * * * *

sHD
LHD

Transcomplémentation Type I versus Type III



ARN VHD défectifs pour la synthèse de *sHD*

A
F
R
I
C
A
N

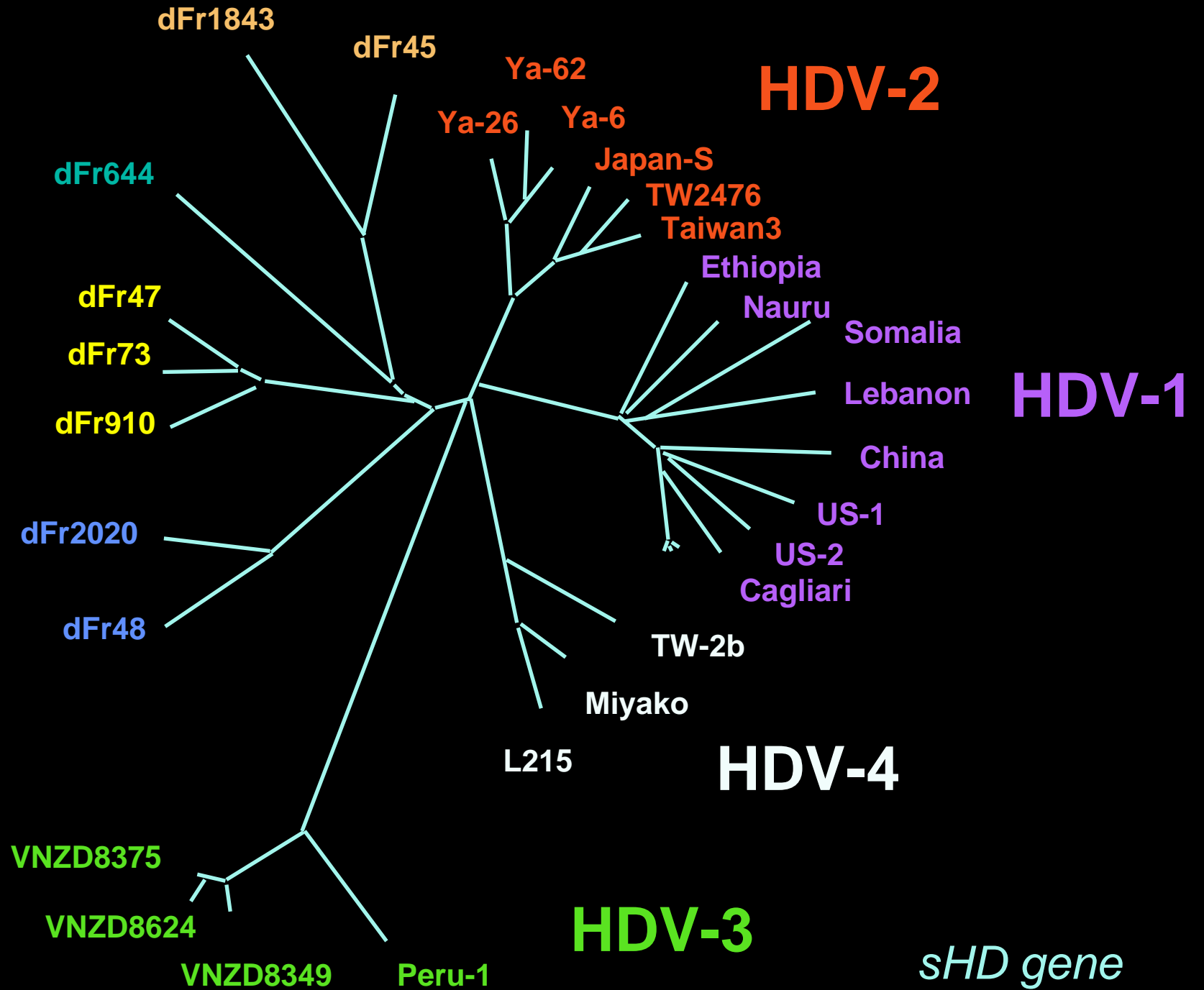
C
L
A
D
E
S

HDV-7

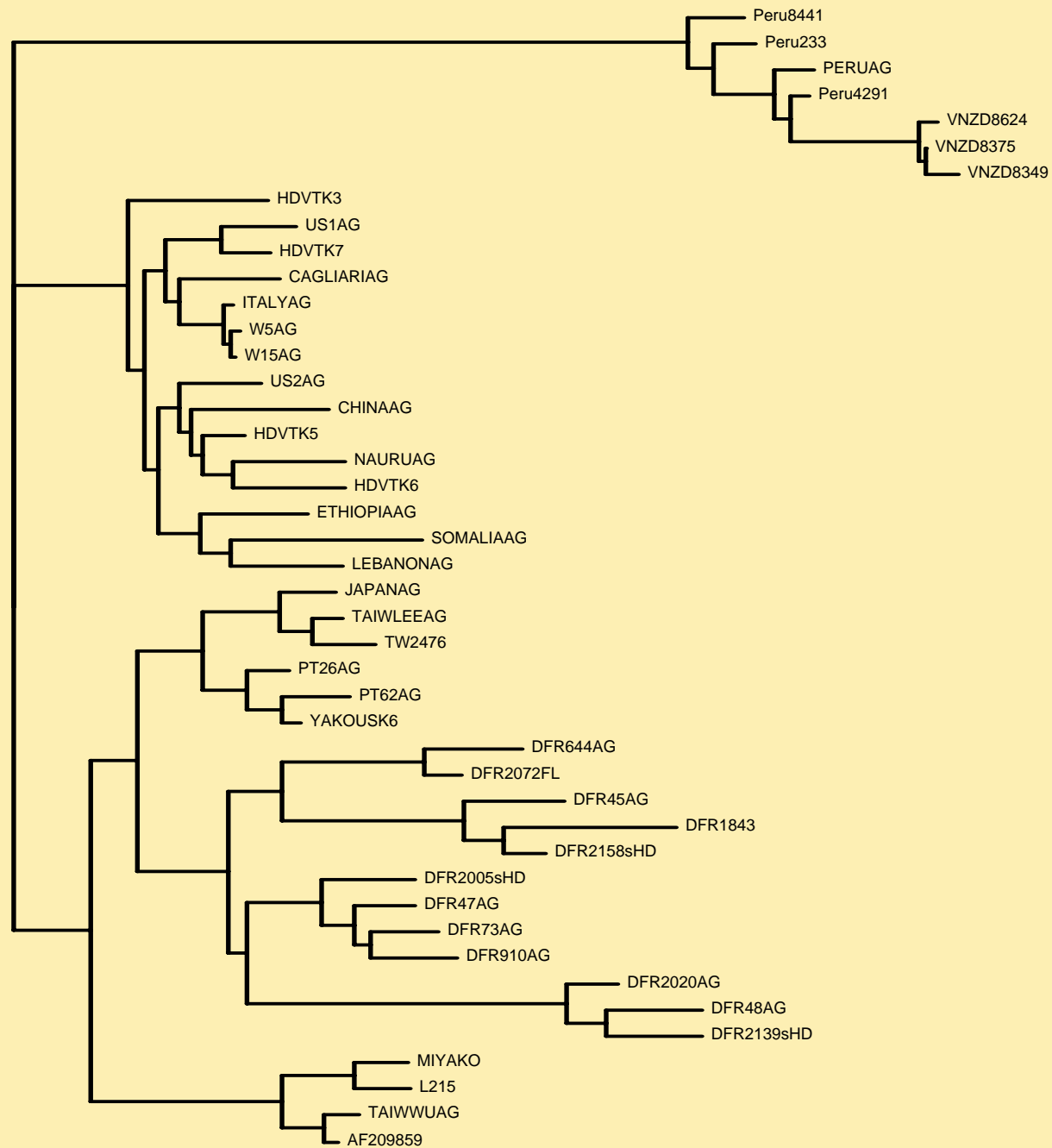
HDV-8

HDV-5

HDV-6

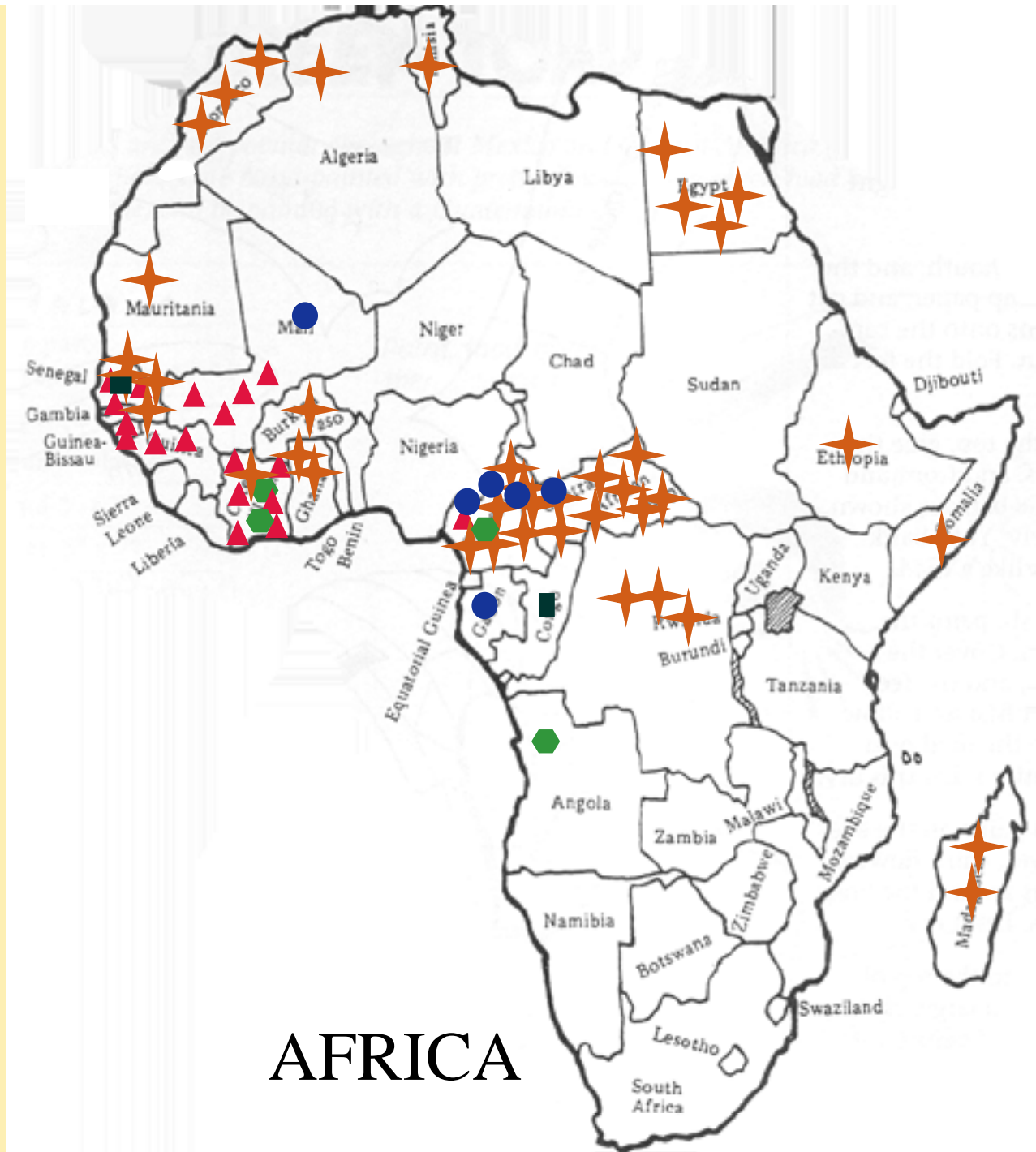


sHD gene

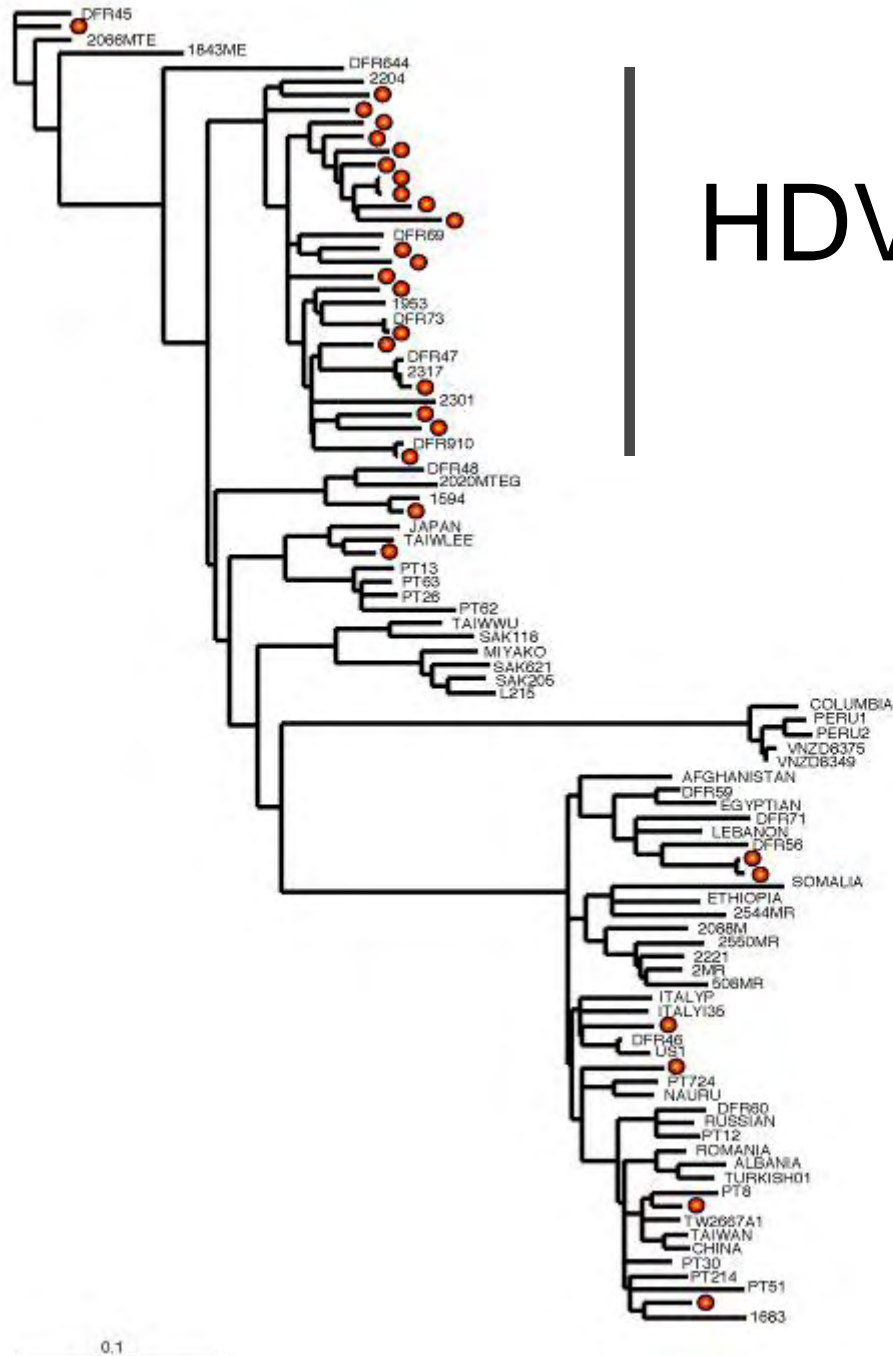


0.1

- ✦ HDV-1
- ▲ HDV-5
- ◆ HDV-6
- HDV-7
- HDV-8



En 2002



HDV-5

10,2%

Gordien et al., in preparation

DISCUSSION

Le genre *Deltavirus* : au moins 8 clades majeurs
suggestion ⁽¹⁾ HDV-1 → HDV-8

HDV / HBV co-(epidemiological)-speciation ?
8 HDV clades *versus* 8 HBV genotypes

HDV comme marqueur des migrations humaines ?

HDV variabilité : radiation Africaine large
suggérant une évolution ancienne ?

HDV

HBV

Clade 1

Ubiquitaire

HBV/D HBV/B^(1,2)
HBV/A HBV/C

Clade 2

Asie

HBV/B⁽²⁾
HBV/C

Clade 3

Amerique de Sud

HBV/F⁽³⁾

Clade 4

Asie

HBV/B⁽⁴⁾

Clade 5

Africa/France

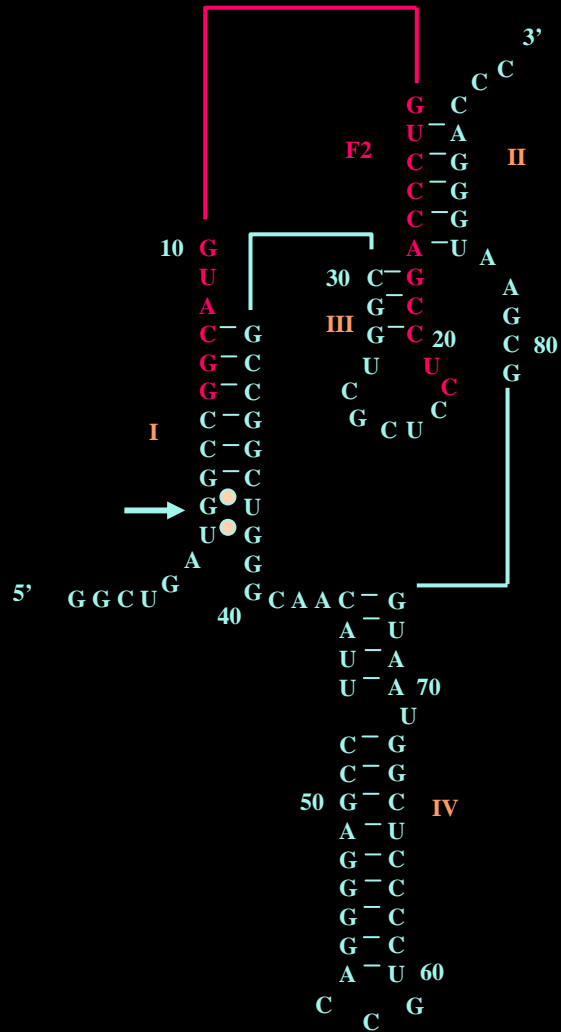
HBV/E⁽⁵⁾

Clade 6

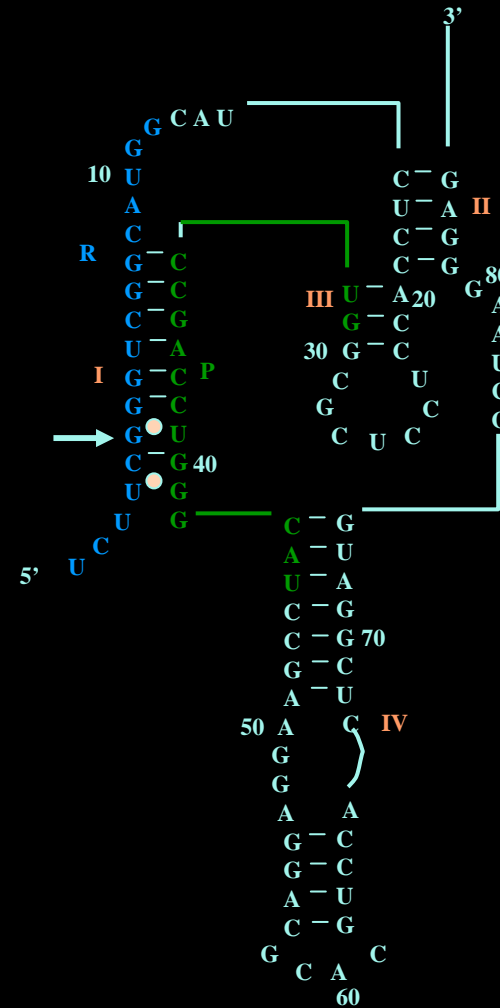
Clade 7

HBV/Aa

PCR Temps réel : amorces et sondes



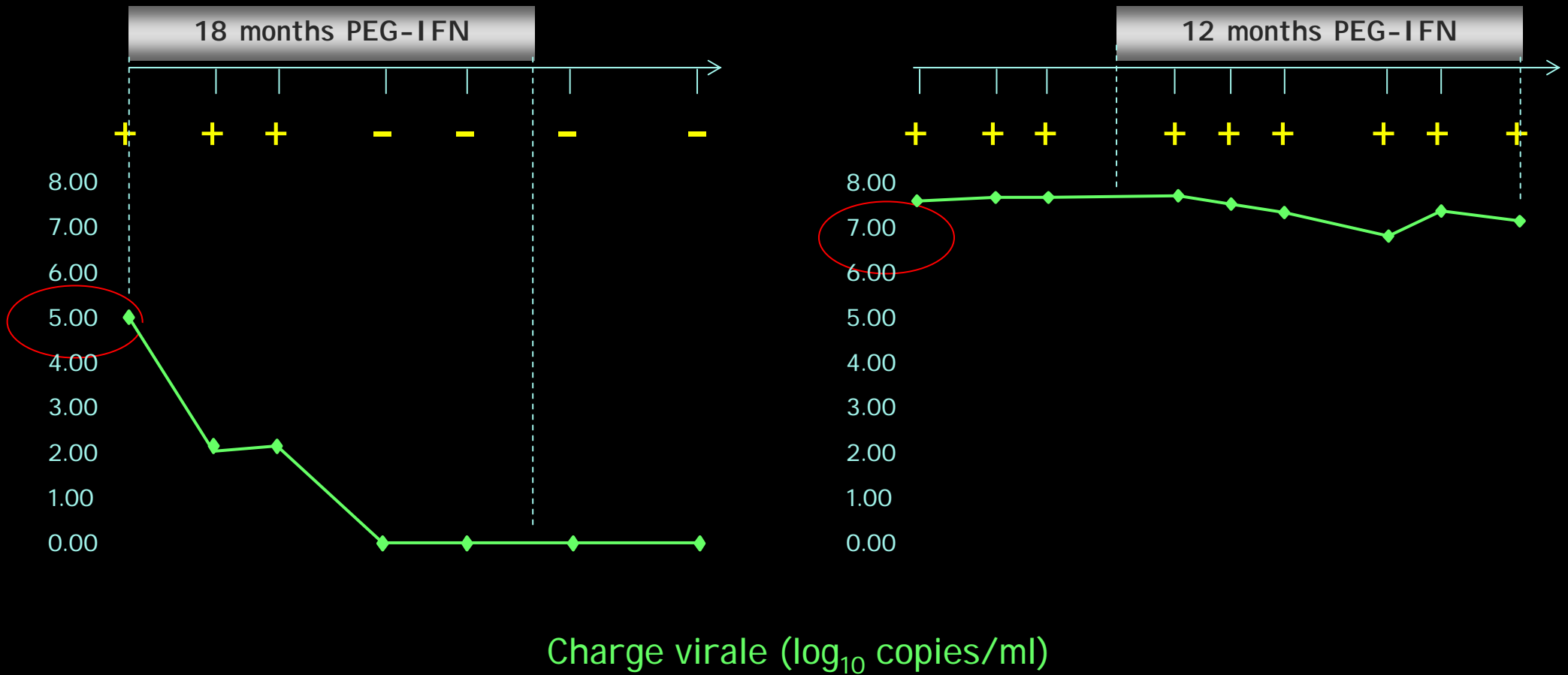
Ribozyme génomique



Ribozyme anti-génomique

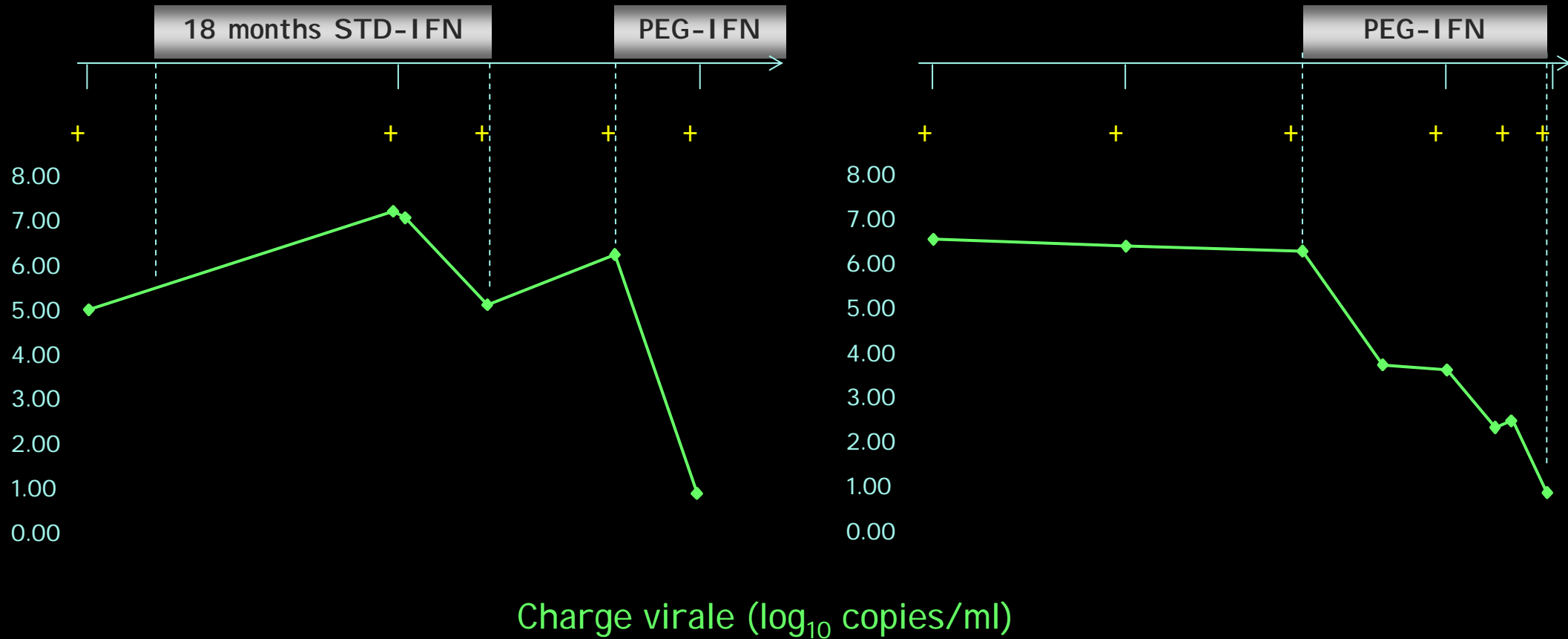
Intérêt du suivi de la charge virale de HDV

PCR qualitative



Intérêt du suivi de la charge virale de HDV

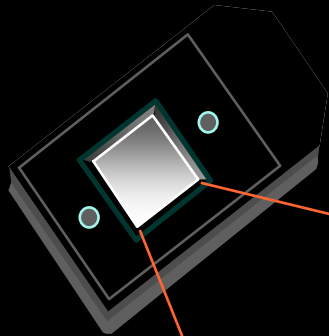
PCR qualitative





GeneChip[®] Probe Arrays

GeneChip Probe Array



1.28cm

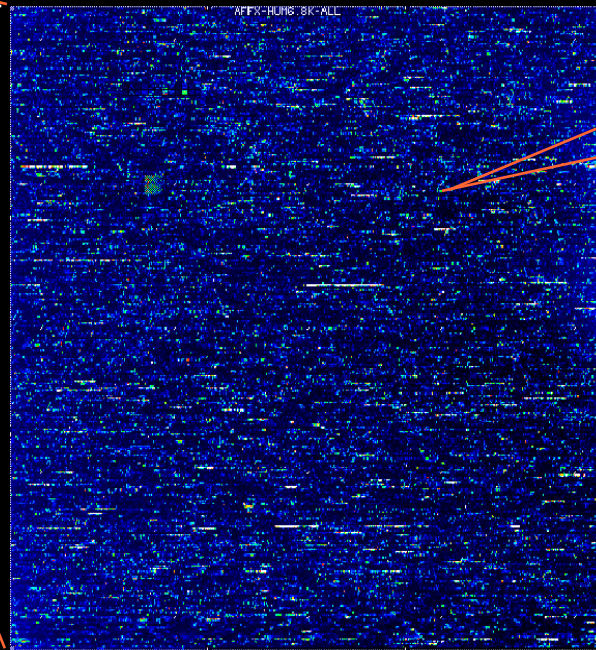
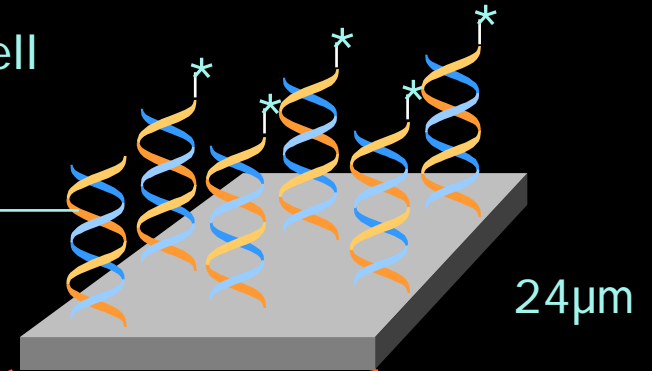


Image of Hybridized Probe Array

Hybridized Probe Cell

Single stranded, fluorescently labeled DNA target

Oligonucleotide probe



Each probe cell contains millions of molecules of a specific oligonucleotide probe

Over 250,000 different probes complementary to the genetic information of interest



Université PARIS 13
NORD

**Bactériologie, Virologie -
Hygiène, LACNR Hepatites
Hôpital Avicenne, AP-HP
EA 3406, Université Paris13
Bobigny, France**

Mariama Abdou
Dissou Affolabi
Chakib Alloui
Patricia Anaïs
Samira Dziri-Mendil
Maité Garcia-Rico
Elyanne Gault
Nasser Hawajri
Nadjia Radjef
Emmanuel Gordien
Frédéric Le Gal
Dominique Roulot
Virginie Williams
Marianne Ziol

**Unit of Evolutionary Genetics
Free University of Brussels,
Gosselies, Belgium**

Michel C Milinkovitch

**Univ. Medecine and Pharmacy
Cluj, Romania**

Tudor Drugan

**Influenzae Institute
St Petersburg, Russia**

Valeria Ivaniushina

**Institut National de Transfusion
Sanguine, Paris, France, U76**

Camille Sureau

Physicians, France

M Beaugrand
J Bernuau
L Bettan
O Bouchaud
N Boyer
D Capron
C Castelneau
N Ganne
V Grando
JM Guignard
D Guyader
C Féray
M Karmochkine
F Lacaille
C Lenaerts
C Mathieu
P Marcellin
G N'Kontchou
C Pallier
P Podevin
O Rosmorduc
D Samuel
JC Trinchet