

Vaccin(s) contre l'hépatite E

E NICAND

Service de biologie

CNR Hépatites entéro-transmissibles (VHE)

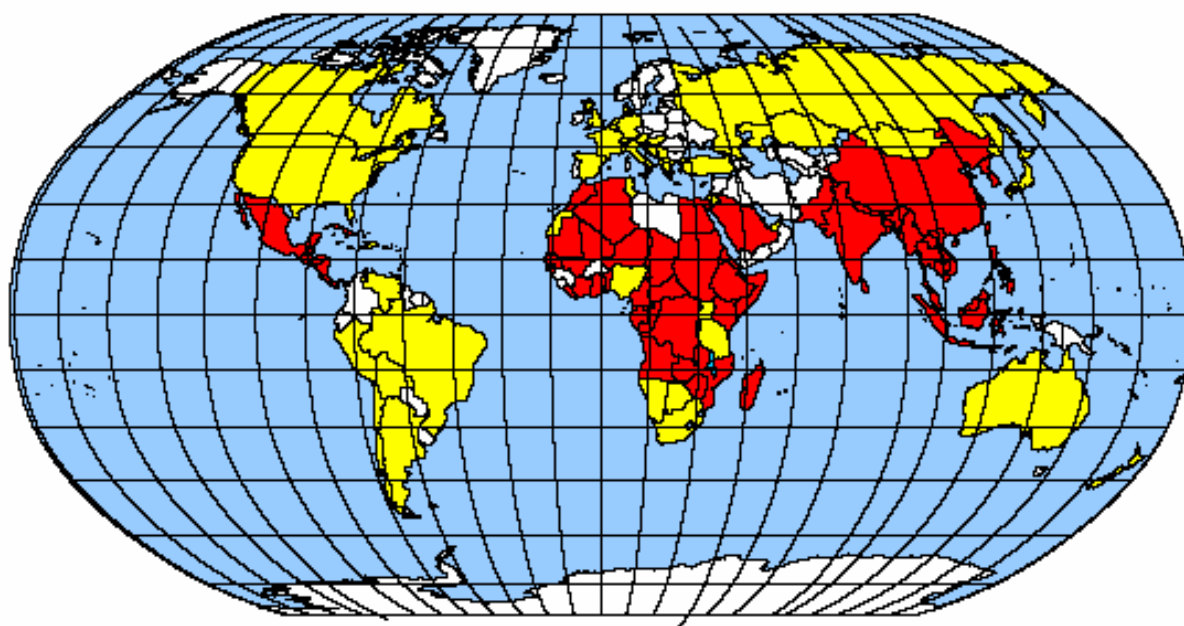
HIA Val de Grâce

Paris, France

<http://www.cnrvha-vhe.org>

CEMI 15 – 17 et 18 mai 2010 Institut Pasteur Paris

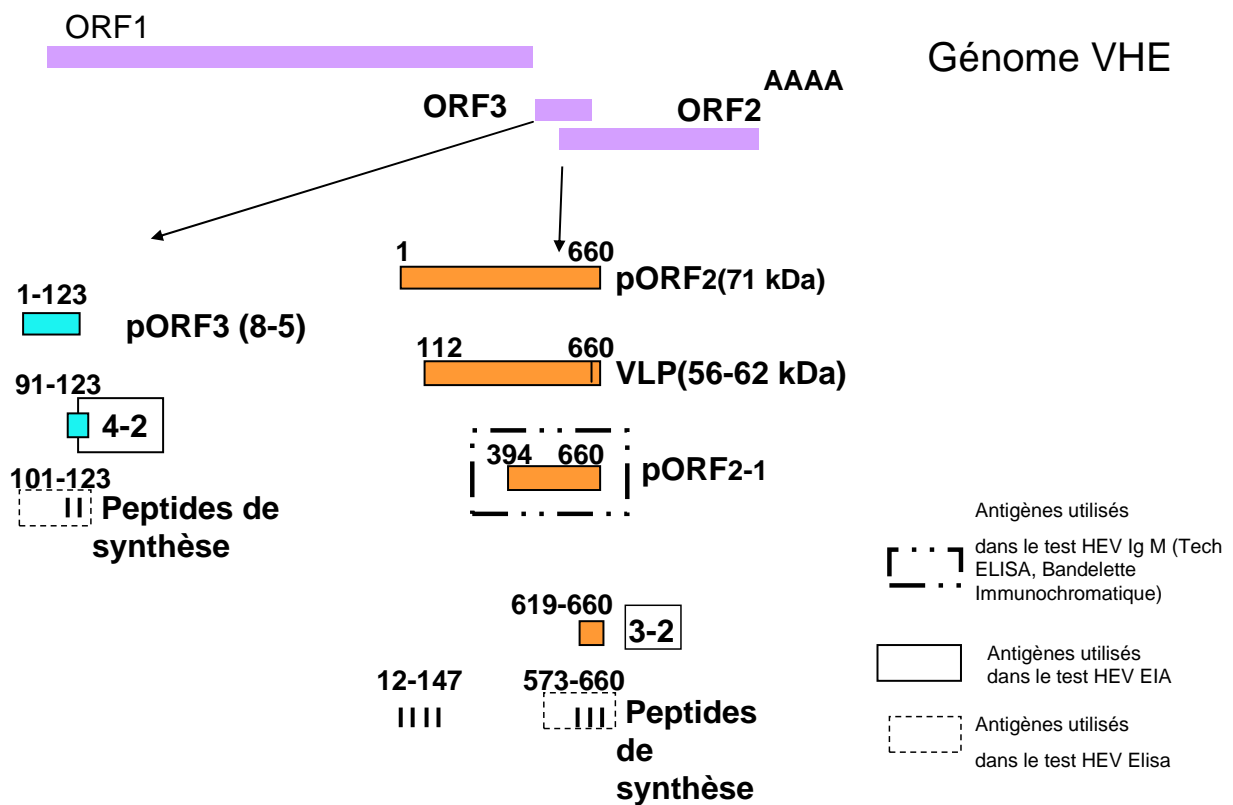
Répartition mondiale de l'hépatite E



- épidémies
- Cas sporadiques

Virus de l'Hépatite E

Cibles antigéniques du virus de l'hépatite E



Structure 3D VHE -VLP

S: AA 118-313

P1 : AA 314-453

P2: AA 454-606

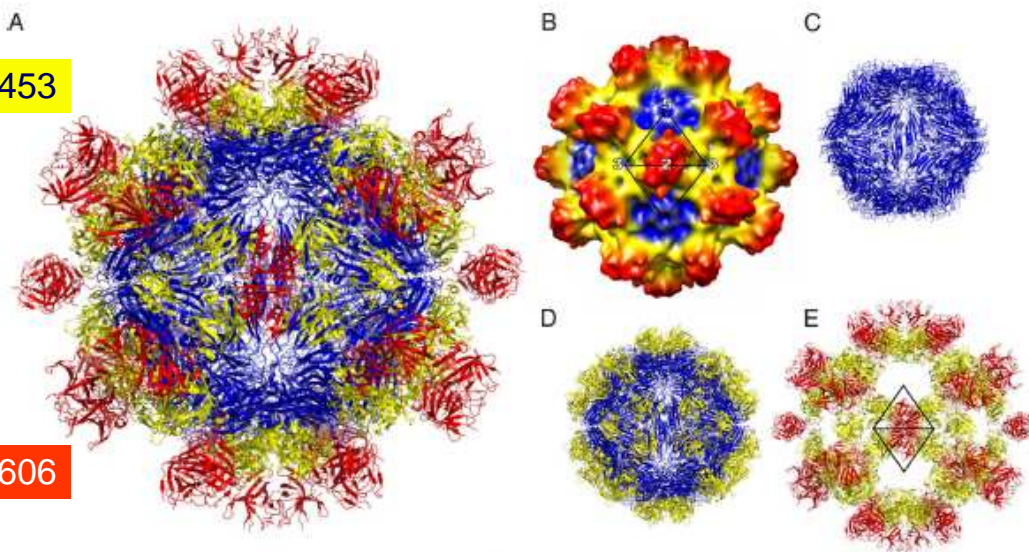
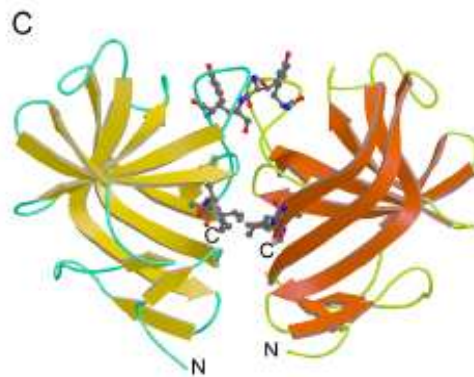


Fig. 1. Structure of the hepatitis E virus-like particle (VLP) ($T = 1$). (A) Crystal structure of HEV VLP. The 3 domains, S, P1, and P2 are colored blue, yellow, and red, respectively. The VLP is positioned in a standard orientation with the 3 2-fold icosahedral symmetry axes aligned along the vertical, horizontal, and viewing directions, respectively. (B) Cryo-EM reconstruction at 14 Å resolution. The surface is colored by radial depth cue from blue, yellow, to red. (C) HEV VLP with only the S domain. (D) VLP with S and P1 domains. (E) VLP with P1 and P2 domains.

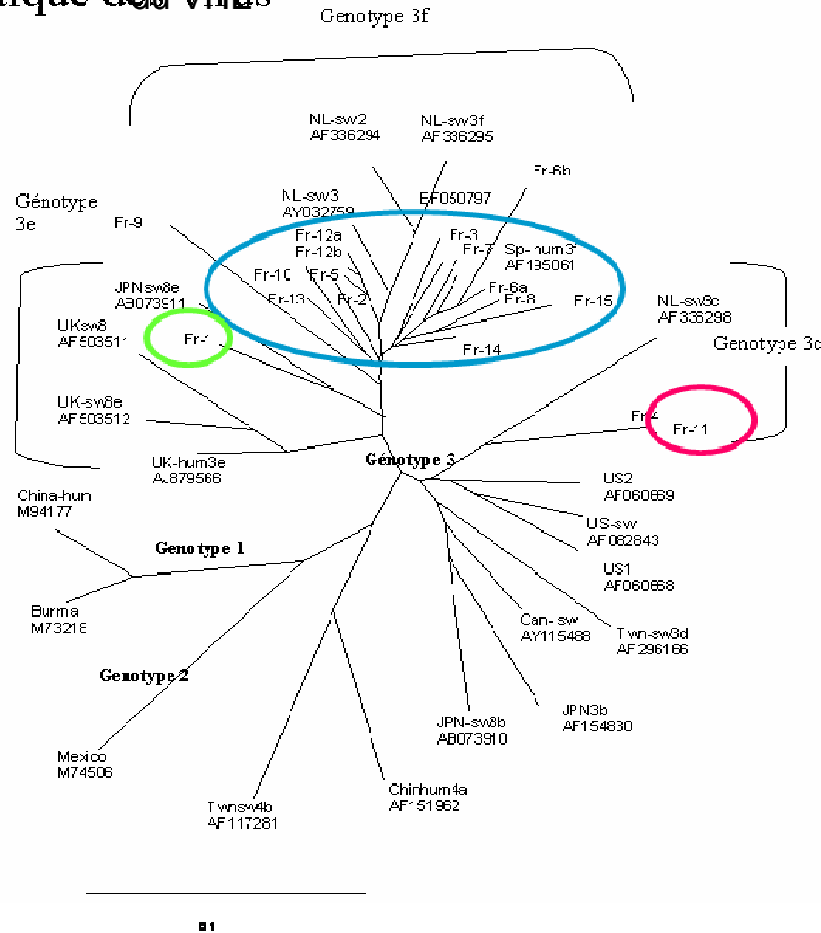
Guu et al., PNAS 2009

Structure 3D VHE domain E2 (aa 394-606)



Li et al., PLOS 2009

Diversité génétique des VHEs



Passage de barrière d'espèce des virus de l'hépatite E

Génotype	Hôte naturel	Modèle expérimental	Infection
1 et 2	Homme	Macaque	+
		Porc	-
		Rat	+
3	Homme	Macaque	+
		Porc	+
3	Porc	Macaque	+
		Porc	+
		Homme	ND
		Rat	ND

Prévention de l'infection à VHE

- Prévention spécifique: vaccination

Prévention non spécifique:

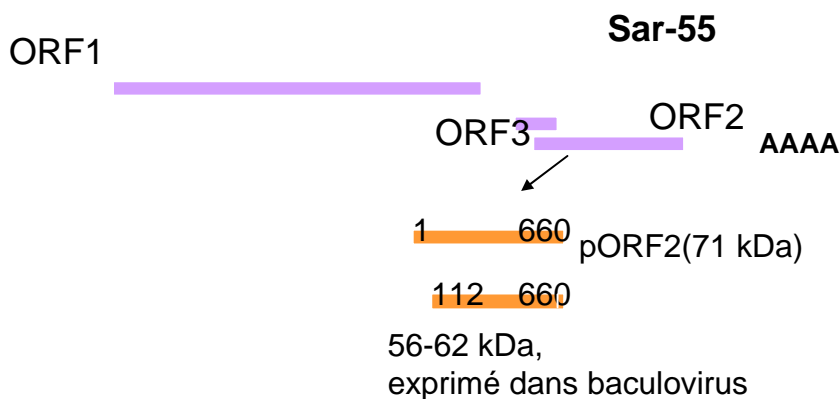


Prévention de l'hépatite E - Recommandations aux consommateurs

19 mai 2009

- hépatopathies chroniques sous jacentes**
- sujets ID**
- femmes enceintes**

Essais vaccinaux



- 2006: Essai phase2, double aveugle
- N= 2000 (1000 vaccinés contre le VHE, 1000 placebo)
 - Protocole: 3 doses (M0, M1, M6)

Candidats vaccins

Firme	Ag	Production	Adjuvant
GSK Belgique	Capside recombinante	Expression baculovirus	AI
Wantai (Chine)	Capside recombinante	E coli	AI

Table 1. Efficacy of the rHEV Vaccine against HEV.

Period of Observation	Subjects with HEV Infection		Vaccine Efficacy* % (95% CI)
	Vaccine <i>no./total no.</i>	Placebo <i>no./total no.</i>	
From 14 days after dose 3 until end of study (a priori primary end point)	3/898	66/896	95.5 (85.6 to 98.6)
From 14 days after dose 2 until dose 3 (a priori secondary end point)	1/960	7/961	85.7 (–16.0 to 98.2)
From 14 days after dose 2 until 14 days after dose 3 (a posteriori secondary end point)	1/960	8/961†	87.5 (0.1 to 98.4)
From dose 1 until end of study (exploratory end point)	9/1000	78/1000	88.5 (77.1 to 94.2)

* Efficacy was estimated as 1 minus the relative risk, with the 95% CI based on the Mantel–Haenszel CI for the relative risk.

† One additional case occurred 6 days after the administration of dose 3, before the surveillance period for the a priori primary end point.

Perspectives vaccinales

- Candidat vaccin: efficacité clinique
- Réaction croisée quelque soit le génotype?
 - G4 (Huang et al. Arch Virol 2009)

- Indications vaccinales ?