**Titre du Résumé (Arial 14)**

(Ajouter une traduction française du titre en anglais)

**Liste des auteurs (Arial 12)**

*Laboratoire de rattachement des auteurs (Arial 11)*

Texte du résumé en anglais (environ une demi page en simple interligne, Arial 11)

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***Nom et adresse email de la personne qui présente***

***Exemple***

**Caractérisation des interactions entre le virus de l’hépatite C et les héparanes sulfates**

**Characterization of Hepatitis C Virus interaction with Heparan Sulfates**

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Hepatitis C virus (HCV) infection is still a global health problem. HCV is a small enveloped virus with a positive stranded RNA genome. The virions are found to be associated with low- or very-low density lipoproteins (LDLs,VLDLs) forming a complex called lipoviroparticles (LVPs). Virally encoded envelope glycoproteins E1 and E2 as well as the lipoprotein components embedded on the virion surface play major roles in virus entry. HCV entry into hepatocyte is a multiple-step event. Initial attachment of the virion to the host cell involves cell surface Heparan Sulfate Proteoglycans (HSPGs) and Low Density Lipoprotein receptor (LDLR). It is then followed by the sequential interaction with specific receptors. Previous studies have shown that recombinant E2 protein interacts with HSPGs, suggesting a direct contact between the viral envelope protein of the virion and HSPGs (Barth *et a*l, JBC 2003). Furthermore, E2 hypervariable region1 (HVR1) has been proposed to contribute to this interaction (Barth *et al*. JVI 2006). However, recent studies demonstrated that ApoE mediates HCV cell attachment through interactions with HSPGs (Jiang *et al*, JVI 2012; Jiang *et al.* PloS One 2013). To discriminate the relative contribution of the HVR1 region of E2 glycoprotein and ApoE associated with the virion in HSPGs binding, we deleted the HVR1 region of E2 in the context of the HCVcc system (JFH1-ΔHVR1). This deletion does not affect HCV envelope proteins interaction with heparin-conjugated beads. We determined the cell surface binding of the HVR1-deleted viruses. Compared to the efficiency of binding of wild type virus (JFH1-WT), JFH1- ΔHVR1 virus did not show any decrease of binding to the cell surface, suggesting that HVR1 deletion does not affect virus-cell surface attachment. To determine if the JFH1- ΔHVR1 virus still relies on HSPGs for cell surface attachment, we performed infection in presence of increasing dose of heparin. Our data indicate that the binding of both viruses is equally inhibited by heparin. These results suggest that the HVR1 region is not required for attachment of the virion to HSPGs. We then analyzed the role of ApoE in HCV entry. Infection with JFH1 and JFH1-∆HVR1 viruses were inhibited by anti-ApoE antibodies and kinetics studies showed that anti-ApoE antibodies block HCV infection at the binding step. These data suggest that ApoE associated with the virus is likely responsible for HCV-HS interaction. Then, to investigate the role of sulfation of HS in HCV infection, we analyzed the expression profile of enzymes involved in HS sulfation in Huh7 cells. Our results show that the NDST-1 isozyme mRNAs are expressed abundantly in hepatoma cell line Huh7 cells. N-sulfation is the first and obligatory step for the following HS modifications. Through specific RNA knock-down assays, we found that inhibition of NDST-1 expression decreases HCV infection suggesting that sulfation of HS is required for HCV entry. By using chemically modified heparins, we found that 2-O sulfation is not required for HCV infection but that 6-O sulfation may be involved. Then, we defined the minimum HS oligosaccharide length required for HCV infection. We found that heparin oligosaccharides with the size of dp10 have the same effect as heparin, both can efficiently inhibit HCV infection.

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