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## Cooperation between syndecan 1 and CD81 contributes to *hepatitis C virus* infection of hepatocytes

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**Background & Aims:** The hepatocyte microenvironment at the vicinity of cell surface (a.k.a. glycocalyx) is rich in membrane-anchored proteoglycans which are receptors for extracellular matrix proteins, cytokines, growth factors, lipoproteins and infectious agents. The *hepatitis C virus* (HCV) infects hepatocytes, after its initial attachment to the heparan sulfate proteoglycan syndecan-1. Here we investigated the link between the hepatocyte microenvironment, HCV entry and infection.

**Methods:** Studies were carried out by RNA silencing, immunoprecipitation, proximity ligation assays, immunofluorescence and confocal imaging, coupled to cross-correlation and statistical analyses.

**Results:** Hepatocyte infection by cell culture-grown HCV or clinical isolates was inhibited after knockdown of syndecan-1 or xylosyltransferase-2, a key enzyme of proteoglycan biosynthesis. Simultaneous knockdown of syndecan-1 and CD81, a receptor of HCV entry, strongly inhibited infection, suggesting their concerted action. At early infection stages, syndecan-1 and virions colocalized at the plasma membrane, and were internalized along with CD81 in endosomes. Direct interactions between syndecan-1 and CD81 were revealed in primary and transformed hepatocytes by immunoprecipitation and proximity ligation assays. This underpins the relevance of this interaction to HCV internalization and infection. Expression of syndecan-1 and xylosyltransferase-2 was altered within days post-infection, and the remaining syndecan-1 pool colocalized poorly with CD81.

**Conclusions:** Syndecan-1 plays an important role in HCV entry and infection, and may act in concert with CD81, as syndecan-1 is detected in complex with CD81. Infection modulates syndecan-1 and xylosyltransferase-2 expression, underscoring a profound reshuffle of the hepatocyte glycocalyx early in infection, likely required for settling optimal conditions of viral propagation.

### Biography

Eve-Isabelle Pecheur has completed her PhD in 1997 from University Paris XI and Post-doctoral studies from Groningen University of Medical Sciences (Netherlands). She leads her research group at the Cancer Research Center of Lyon. She has published more than 50 papers in reputed journals. She is serving as an Editorial Board Member of *Antiviral Research*, and as an academic Editor of *PLoS ONE*.

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