Biochemical And Biophysical Studies Of The Interaction Between Hepatitis C Virus Core Protein And P53

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INTRODUCTION: The major cause of viral hepatitis is the Hepatitis C Virus (HCV), it is estimated that 210 million people are infected wordwide. No vaccine was approved to human use until today and the treatment is ineffective in many cases. This shows how important it is to investigate this virus and its interaction with cells. With this aim, facing the difficulty to study the infeccious particle, here we study the viral proteins separately. The HCV core protein (HCVcp) assembles the viral capsid protecting the RNA and participates in several viral and cellular processes. Previous studies show that HCVcp interacts with the supressor tumoral protein 53 (p53) and is able to modify its post-translational function. This interaction suggests to be the reason why hepatocellular carcinoma (HCC) is present in so many HCV-infected patients. OBJECTIVES: Here, we investigated the interaction between HCVcp (truncated form with 124 amino acids) and p53 (central domain [p53C] and full length [p53 Full]) by biochemical and biophysical techniques. MATERIALS AND METHODS: Both proteins were obtained by heterologous expression, and the interaction between them was investigated by nuclear magnetic resonance (NMR), surface plasmon resonance (SPR) and Immunoblotting. RESULTS AND DISCUSSION: NMR data show alterations in the chemical shifts pattern in the $^{1}H/^{15}N$ HSQC spectra of HCVcp protein, isotopicaly labeled, when obtained in the presence of p53C, suggesting changes in the chemical environment of some HCVcp amino acid residues, possibly induced by HCVcp and p53C interaction. Additionally, ITC measurements suggest an exothermic interaction between the two proteins at 25 °C. SPR and immunoblotting assays corroborate our hypothesis, showing the HCVcp-p53 interaction. SPR analysis can give us information about stoichiometry. CONCLUSIONS: These data help us to better understand the HCVcp-p53 interaction, and consequently the HCC, gaining insights for the development of more efficient treatments and possible vaccines against Hepatitis C.

Keywords: Hepatitis C Virus, core protein, p53 protein

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