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## Designing drugs that simultaneously target viral and human helicases

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**Background:** Hepatocellular carcinoma (HCC) is the most prevalent type of primary liver cancer and the second leading cause of cancer death globally. The principal risk factor for HCC is chronic infection with hepatitis C or B virus. Although direct-acting antivirals are effective in reducing viral load in chronic hepatitis, HCV-infected patients still remain at risk of developing HCC. Therefore, new therapeutic strategies need to be developed for this detrimental condition. Recently, it was found that Ruvbl2, an ATP-dependent DNA helicase, is overexpressed in HCC and is associated with poor prognosis. On the other hand, HCV also utilizes a helicase, NS3, to replicate its genome. These human and viral helicases share evolutionarily conserved motifs that are involved in important functions of the enzyme. Here, we propose simultaneous targeting of HCV helicase NS3 and human helicase Ruvbl2 in the liver for, respectively, treating HCV infection and preventing HCC.

**Objective:** The primary objective of this study was to identify and functionally characterize evolutionarily conserved amino acid sequence motifs in HCV helicase NS3 and human helicase Ruvbl2.

**Methodology:** To identify conserved motifs in NS3 and Ruvbl2, we used the MEME computational tool. To discover the functions of the motifs, we performed a literature search and protein structure analysis. Location of the motifs in the protein 3D structures was performed using the Discovery Studio software.

**Result:** We found 10 evolutionarily conserved, functionally important motifs in NS3 and Ruvbl2 involved in ATP and/or substrate binding.

**Conclusion:** The evolutionarily conserved motifs we identify here may be used as targets for the future design of next-generation drugs that could be used for simultaneous treatment of HCV infection and prevention of HCC.

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