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Bivalent candidate vaccine against HCV and HIV-1: Construction and biological evaluation

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Objectives: Hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infections are a global health concern. Therefore, they are considered for the huge number of studies looking for effective vaccines. In the previous study, we introduced a single cycle replicable (SCR) HIV system that, completely maintained the antigenic structures of HIV-1, through its one cycle replicating properties represented a good implication as a potential vaccine candidate, Herein, we constructed a novel HIV-1 virion, capable of expressing non structural 3 (NS3) protein of HCV as potential bivalent candidate vaccine that provides a more immunogenicity, while preventing any pathologic effects with further evaluated its biological properties.

Methods: The pIPNL4-3/NS3 containing HIV genome of NL4-3 strain with a 2-kb deletion in reverse transcriptase (RT) and integrase (IN) genes and replacement of the deleted fragment with NS3 was constructed, confirmed by sequencing reactions and transfected into HEK 293T cell line. By further co-transfection of psPAX2 and pMD2.G plasmids, which encoded HIV Gag-pro-pol and vesicular stomatitis virus surface glycoprotein, into the same pIPNL4-3/NS3-harboring cells, pseudotyped virions were produced, evaluated by electron microscopy, quantified using P24 end-point ELISA assay and western blotting. Infectivity of recombinant virions and their efficiency towards the syncytium formation was evaluated on HIV-sensitive MT-2 cells.

Results: Production of HIV virions was indicated by the level of P24 protein in culture supernatant of transfected cells and was further confirmed by electron microscopy. Also, expression of NS3 protein was confirmed using western blotting. Formation of syncytia in MT-2 cells also evidenced for the functionality of the surface glycoproteins in produced pseudotyped virions. Interestingly, infectivity analysis verified that the second generation virions were completely non-replicative.

Conclusion: The results were shown that a new recombinant virion with capable to express NS3 protein completely maintained the antigenic structures of HIV-1, by its one cycle replicating properties, and represented a good implication as a potential bivalent vaccine candidate. Moreover, this guarantees further investigations toward the assessment of its immunogenicity, which are currently under process. It may also present another interesting approach towards the improvement of its application in bivalent HIV and HCV vaccine researches.

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