

(data not shown), respectively. Furthermore, induction of ISG15 by treatment with IFN- α was almost comparable between Huh7 and FU97 cells (Fig. 5A), and expression levels of IFN- α receptor in the cell lines were the same (data not shown), suggesting the involvement of other factors in the difference in the IFN responses between FU97 and Huh7 cells.

Cyclophilins possess peptidyl-prolyl *cis/trans* isomerase (PPIase) activity and are involved in protein folding and assembly. Cyclophilin A (CypA), the most abundant cyclophilin, localizes in the cytoplasm and interacts with the immunosuppressive drug cyclosporine (82). In addition, CypA has been shown to be involved in the propagation of human immunodeficiency virus (83, 84), hepatitis B virus (85, 86), influenza A virus (87), and HCV (88). Replication of HCV RNA was inhibited by suppression of the PPIase activity of CypA by treatments with cyclosporine, mutation in the active site of CypA, and knockdown of CypA (55, 89–91). The same level of CypA expression in Huh7 and FU97 cells (data not shown) suggests that the difference in inhibitory effect of cyclosporine in the cell lines may be attributable to other reasons, such as a difference in PPIase activity of CypA in these cell lines. The differences in the efficacy of anti-HCV drugs between Huh7 and FU97 cells were small; however, FU97 cells have the possibility to possess antiviral activity different from that of Huh7 cells.

In summary, we identified novel permissive cell lines for complete propagation of HCVcc without any artificial manipulation. In particular, gastric cancer-derived FU97 cells exhibited a much higher susceptibility to HCVcc/JFH-2 infection than observed in Huh7 cells, suggesting that FU97 cells would be useful for further investigation of the HCV life cycle, as well as the development of therapeutic agents for chronic hepatitis C.

ACKNOWLEDGMENTS

We thank M. Tomiyama for her secretarial work and M. Ishibashi and Y. Sugiyama for their technical assistance. We also thank M. Hijikata, R. Bartenschlager, S. Akira, F. Chisari, and M. Whitt for providing experimental materials.

This work was supported in part by grants-in-aid from the Japanese Ministry of Health, Labor, and Welfare (Research on Hepatitis), the Japanese Ministry of Education, Culture, Sports, Science, and Technology, the Naito Foundation, and the Takeda Science Foundation.

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