عنوان مقاله:

The Coagulation Factors Effect on Adenoviral-mediated Innate Immunity

محل انتشار:

سیزدهمین کنگره بین المللی میکروب شناسی بالینی استاد البرزی (سال: 1398)

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خلاصه مقاله:

Background and Objectives: As innate immunity inducing by Adenovirus remained a challenging issue in clinic and during gene therapy, understanding the underlying mechanism is beneficial. Some ambiguous points regarding the role of coagulation factors in this mechanism need to be clarified. To better understand the contribution of coagulation factors to the extent of Adenovirus mediated innate immunity on the hepatocyte. Materials & Methods: Adenovirus-36 (AD) and Adenovector-5-GFP (Ad5-GFP) were prepared and tittered; then, they were loaded with coagulation factors VII and X. A standard Adenovirus-36 (AD) was propagated and then became complex with FVII or FX factors. Afterwards, they were evaluated for size and charge parameters. After adding AD-VII and AD-X complexes, the levels of innate inflammatory genes including PKR, IL-1β, IL-8 and IL-18 were measured by Real-time PCR (qPCR) on a hepatocellular carcinoma cell, HepG2. Results: The loading of coagulation factors VII and X on Ad5-GFP enhanced the transduction rate up to 50% and 60% ($P<0.05$), respectively, compared to the vector alone (30%). The formation of coagulation factors-virus complex leads to multimodal size distribution with an increase in average hydrodynamic size and absolute zeta-potential. The qPCR results showed that PKR expression increased significantly after treatment with all adenoviruses. These findings also showed that AD had a significant ($P=0.0152$) inflammatory impact on Hep-G2. However, AD which was loaded with FX (AD-X) exhibited the most inflammatory effect ($P=0.0164$). Significantly, the expression of IL-1β ($P= 0.0041$), IL-8 ($P= 0.0107$) and IL-18 ($P= 0.0193$) was enhanced by AD-X. On the other hand, AD-VII complex showed the least effect of immune induction when compared to the negative control ($P<0.05$). Conclusion: The complex of coagulation factors-virus, especially with FX, could increase the transduction rate of Ad5-GFP. It was also suggested that Adenovirus loaded with FX exhibited more innate .immunity in the hepatocytes, while it was not the case for FVII

کلمات کلیدی: