Mesenchymal stem cells enable delivery of an oncolytic adenovirus specifically to the tumor without posing any risk associated with systemic administration of naked virions to the host

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Background: Systemic delivery oncolytic virus to tumors remains a major challenge due to its poor tumor tropism and immunogenicity.

Methods: In this regard, we hypothesize that mesenchymal stem cells (MSCs) with low immunogenicity and tumor-homing property could serve as a promising systemic delivery tool for oncolytic viruses.

Results: We showed that MSCs could be effectively infected by oncolytic adenovirus (oAd) and the virus replicated efficiently in the MSC carrier. Importantly, systemically administered oAd loaded in MSCs (oAd/MSC), which were initially infected with a low viral dose, led to significantly and preferentially elevated viral accumulation in tumor tissues, while attenuating virus detection in normal organs in respect to systemically administered naked oAd. Efficient retargeting of oAd to tumor tissues prevented the induction of oAd-associated hepatotoxicity that arise due to native hepatic tropism of systemically administered oAd. Further, pharmacokinetic profiling of oAd/MSC revealed that cell carrier improved and prolonged oAd retention in blood circulation compared with naked Ad. Importantly, these attributes enabled oAd/MSC to elicit potent antitumor effect, while attenuating systemic toxicity.

Conclusions: Collectively, these results demonstrate that MSC-mediated systemic delivery of oAd is a promising strategy for achieving synergistic antitumor efficacy with improved safety profiles.

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