Abstract

A challenge to develop adenovirus (Ad)-mediated therapeutics has been issued to treat metastatic cancer via systemic administration. Systemic administration of conventional naked Ads leads to the acute accumulation of Ad particles in the liver, induction of neutralizing antibody, short blood circulation half-life, nonspecific biodistribution in undesired organs, and low selective accumulation in the target disease site. Versatile strategies involving the modification of viral surfaces with polymers and nanomaterials have been designed to maximize Ad antitumor activity and specificity by systemic administration. Modification of the Ad surface allows Ad to circulate in the bloodstream for a longer time, to be not targeted to the liver, and to passively accumulate in tumor sites via enhanced permeation and retention effects. The addition of affinity tags results in active targeting and high efficacy. Biodistribution, blood circulation time, immune response, and therapeutic efficacy of functionalized oncolytic Ad nanocomplex will be discussed, proposing the future direction of viral/nonviral combinatory delivery for cancer therapy.