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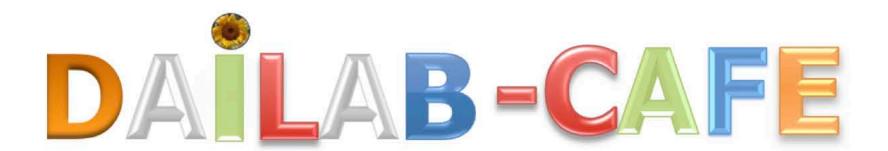


DBT -AIST International Laboratory for Advanced Biomedicine



Classroom for Advanced & Frontier Education





Series - 33

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Venue: Central 5-41 5F (5015)

Speaker: Chae-Ok Yun

Affiliation: Professor, Hanyang University

E-mail: chaeok@Hanyang.ac.kr



Title: Hydrogel system-mediated delivery of oncolytic adenovirus overcomes short half-life, adverse inflammatory response, and nonspecific shedding of conventional local delivery route

Currently, intratumoral injection of an oncolytic adenovirus (Ad) remains the conventional administration route in clinical trials. Nonetheless, the locally administered Ad disseminates to the surrounding normal tissues and has short biological activity due to immunogenicity of Ad, which inadvertently promotes rapid clearance and insufficient intratumoral retainment of the virus. These shortcomings necessitate multiple injections of oncolytic Ad for sufficient therapeutic index to be achieved. To address these problems, a hydrogel can be utilized as a delivery platform. Our findings show that hydrogel system attenuates oncolytic Ad-mediated antiviral immune response while preserving the viruses' ability to induce robust antitumor immune response in tumor tissues. A hydrogel as a reservoir can promote a high concentration of oncolytic Ad to be retained in tumor tissues over an extended period and restricted nonspecific shedding to normal tissues. One of the hydrogel, which is capable of efficiently co-delivering and protecting both therapeutic dendritic cells and oncolytic Ad in tumor tissues, enabled the combination therapy to induce a stronger antitumor immune response than either immunotherapeutic administered alone, showing that the biological activity of both immunotherapeutic agents could be preserved over a considerable time period in immunosuppressive and hostile tumor microenvironment that significantly diminishes the efficacy of immunotherapeutics. These findings have significant clinical importance as clinical studies have attributed strong induction of antitumor immune response via oncolytic viruses as one of the key determinants defining the overall potency of these therapies in cancer patients, whereas robust antiviral immune response is associated with adverse side effects and subpar patient response.

