IS-106 Vascular Shutdown Effects by Tetraarsenic oxide in TC-1 cells Implanted C57BL/6 mice

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Purpose: Arsenic trioxide (As203, diarsenic oxide) potential anticancer activity has been demonstrated in a wide range of solid tumors. In this study, we investigated the antivascular effects of As203 and tetraarsenic oxide (As406) in the cervical cancer animal model. Methods: In the cervical cancer animal model using C57BL/6 mice and HPV16 E6/E7 immortalized hosts, PBS, As203 and As406 were injected into the peritoneal when the tumor size reached 200-250 mm3. After the injection, the tumor size was caliperated every 2-3 days, and the studies of anti-vascular effects were assessed by two separate methods. Evans blue extraction and Hoechst 33342 uptake. Histopathological changes of the tumors after As203 and As406 treatments were also observed with hematoxylin and eosin (H&E) staining. Results: After the injection of As203 and As406 into the peritoneal, the tumor growth suppression was noted in comparison with control group. Moreover, As406 demonstrated a significant suppression of tumor growth. Also, injection of arsenic compounds produced a preferential vascular shutdown in the tumor, leading to massive necrosis in the central part of the tumor. Conclusion: This study shows that As406 has vascular shutdown effects in TC-1 cells implanted mice.

IS-107 Nanodot Arrays Modulate Cell Adhesion and Induces an Apoptosis-like Abnormality in NIH-3T3 Cells

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Objective: To evaluate the cellular response to a nano-scaled surface. Methods: NIH 3T3 cells were grown on nanodot arrays with dot diameters ranging from 10 to 200 nm. The nanodot arrays were fabricated by AAO processing on TaN-coated wafers. A thin layer of platinum, 5 nm in thickness, was sputtered onto the structure to improve biocompatibility. Immuno-staining using antibodies against vinculin and actin filament was performed. Results: The cells grew normally on the 10-nm array and on flat surfaces. However, 50-nm, 100-nm, and 200-nm nanodot arrays induced apoptosis-like events. Abnormality was triggered after as few as 24 hours of incubation on a 200-nm dot array. For cells grown on the 50-nm array, the abnormality started after 72 hours of incubation. The number of filopodia extended from the cell bodies was lower for the abnormal cells. Immunostaining also showed reorganization of cytoskeleton and reduced number of focal adhesions. In summary, nanotopography, in the form of nanodot arrays, induced an apoptosis-like abnormality for cultured NIH 3T3 cells. The occurrence of the abnormality was mediated by the formation of focal adhesions. Conclusion: Nanotopography of nanodot arrays induced apoptosis for cultured NIH 3T3 cells. The apoptotic signaling was closely associated with nanotopography-induced retardation for the formation of focal adhesions. It is possible to evaluate the invasion potentials of cancerous cell lines using this working platform.

IS-108 Integrin, Serotype 3 Receptor–Targeted Virotherapy with Genetic Fiber Modified Adenovirus Vector for Ovarian Cancer Treatment

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[Objective] Conditionally replicative adenovirus (CRAd) is a ovarian cancer gene therapy strategy which seeks to achieve selective viral replication in tumor cells. However, ovarian cancer cells are relatively resistant to infection by adenovirus (Ad), thus limiting the capability of CRAd agents to achieve effective lateralization within the tumor. [Methods] We have developed Ad by replacing the knob region of Ad serotype 5 fiber with Ad serotype 3 knob (Ad5/3 chimera) and by putting an Arg-Gly-Asp (RGD) -4C motif in the HI loop of the Ad fiber knob region (RGD modification) to enhance the infectivity to the ovarian cancer cells. We employed recombinant Ad vectors containing luciferase reporter genes with or without fiber mutation (Ad5/3LucRGD and Ad5Luc) to evaluate transductional activity in ovarian cancer cell lines in vitro. Then, we evaluated the oncolytic effect of CRAd in ovarian cancer cell lines by both an MTS assay and crystal violet assay. [Results] Ad5/3Luc–RGD Ad showed an increased reporter gene expression in ovarian cancer cell lines. Moreover, oncolysis CRAd in ovarian cancer cells was much enhanced in Ad5/3RGD retaining the specificity. [Conclusion] These results suggest that infectivity enhancement with mutant fiber is especially effective for enhancing oncolysis. This infectivity-enhanced CRAd may thus be useful in the gene therapy of ovarian cancer.