xenograft models, the magnetofection-mediated HmT/PCION complex displayed significantly enhanced anti-tumor efficacy in the presence of an external magnetic field by 2.74- and 2.10- fold than cancer cell killing effects in the absence of an MGF and Ad alone, respectively. These results demonstrate that magnetofection-mediated oncolytic Ad infection is able to overcome CAR-dependent infectivity while producing higher antitumor efficacy.

363. Laser-Triggered Gold Nanoparticle-Assisted Cell Poration for Selective Gene Delivery

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We present an innovative approach using laser-triggered plasmonic gold nanoparticles to selectively transfect cells. This method emerged from the combination of the recent progress in photonics and nanotechnologies. To perform the laser-triggered delivery, spherical gold nanoparticles (d=100 nm) were first dispersed onto cells *in vitro* in a medium containing fluorescent molecules or exogenous genes, and then irradiated with a scanning picosecond laser beam at high repetition rate (f = 76 MHz, wavelength λ =1064 nm, pulse width τ = 7.5 ps). When irradiated under appropriate conditions, the gold nanoparticles locally amplify the laser energy (plasmonic effect) and create transient pores on the cell membranes, allowing the penetration of surrounding molecules or genes through the plasma membrane by fluid exchange. After the delivery, the cell membranes rapidly self-reseal and the cells continue to thrive. Our technique presents several advantages: First, the method is safe. Gold nanoparticles are biocompatible and are believed to be non-toxic both *in vitro* and *in vivo* at low concentration. The emitted laser energy in the near infrared is weak and harmless to the tissue, and is only amplified in the near-field of gold nanoparticles within submicron distance. Second, the transfection is temporally and spatially controlled by the pattern of irradiation. Gold nanoparticles can be conjugated to selectively target and transfect desired cell populations. We performed experiments on different cell types including breast cancer cells, ocular epithelium cells and neurons. Cell poration efficiency increased with laser energy up to a certain threshold, and decreased as mortality became important at higher irradiation fluence. The optimal conditions for irradiation vary from one cell line to another. The general poration efficiency could reach 30-70% depending on the cell line, with mortality as low as < 3%. Ongoing *in vitro* and *ex vivo* experiments will be presented. Our studies suggest that the laser-triggered gold nanoparticle-assisted cell transfection is a promising physical delivery method enabling efficient, safe and selective gene delivery in a variety of cells. It is anticipated that it would be an increasingly useful tool for the development and improvement of new gene therapy for prevalent diseases such as cancers or neural degenerative diseases.

364. Impact of Injection Volume on Hydrodynamic Delivery To the Liver in Mice

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Hydrodynamic gene delivery is a widely prevailed method for gene delivery to the liver especially in rodents, because of its efficiency and simplicity. A transient enlargement of the liver derived from physical force, which is generated by a rapid injection of a large amount of solution through the tail vein of a mouse, plays an important role for the gene transfer.

We previously demonstrated that the expansion speed of the liver is a primary determinant for gene transfer efficiency, because the liver volume at the end of the injection (final volume) was not significantly different between hydrodynamic (5 sec) and slow (60 sec) injections, as long as the same amount of volume of 9% of body weight (BW) was injected (kanefuji, et al. Mol Ther Methods Clin Deve 1;14029). However, the relationship between the injection volume and final volume has not been clarified.

The present study aimed to evaluate volume-dependent physical impacts on the liver in hydrodynamic injection. Physical impacts to the liver were quantified in mice by measuring the final volume using a cone beam computed tomography (CBCT) and serum concentration of alanine aminotransferase (ALT). Hydrodynamic (9% of BW/5 sec), half-hydrodynamic (5% of BW/5 sec), and half-slow (5% of BW/60 sec) injections were performed with contrast medium including 300 mg/ml of iodine through the tail vein of mice. Just after the injections, CBCT studies were performed without any surgical intervention to collect volume data of the liver, and the final volumes were shown as the relative volume of that of control mice. Blood samples were collected for the assay of serum concentration of ALT at the time points of 1, 4, 24, 48, and 168 hours after the injections.

The average final volumes were 125.8 ± 11.5 and 119.7 ± 4.8% in half-hydrodynamic and half-slow injections, and were not significantly different from each other, while they were significantly lower than that of 173.1 ± 10.4% in hydrodynamic injection ($p>0.99$ and <0.05, respectively, Kruskal-Wallis followed by Dunn's Multiple Comparison test). The average levels of ALT 4 hours after the injections were 82.6 ± 72.4 U/L and 1582 ± 701.5 U/L in half-hydrodynamic and hydrodynamic injections, which were significantly different from each other ($p<0.01$, Mann-Whitney test), and returned to the normal level within 48 hours after the injections.

These results clearly indicate that the final volume evidently depends on the injection volume but not speed in both hydrodynamic and half-hydrodynamic injections. Furthermore, the reduction of the injection volume markedly suppressed the elevation of liver enzyme in serum after the injection.

From a safety viewpoint, there is no doubt that an injection with less volume is advisable as far as sufficient gene delivery is guaranteed. A further study is on going to make the efficacy of half-hydrodynamic injection comparable with that of hydrodynamic injection.