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Research Article

Collloidal Gold with Camostat Mesylate Powder Remove DNA and RNA from Living Object

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Abstract:

Gene therapy using foreign DNA, RNA such as CRISP-CAS9 system, cause incidental insertion into the host genome. Nontoxic drugs that irreversibly remove gene fragments inhibit insertion into the host genome. We recently gold nanoparticles with sulfonic acids (mesilate) to prevent incidental insertion into the host genome. On the anaphase stage of the cell cycle, thiolated colloidal golds bind 3.4nm DNA pitch between the histone octamers. In the nucleus during transcription, breakage of the hydrogen bonds between the double strands of the genes can dissolution of gold–sulfur bonds which expel the DNA-thiolated colloidal gold complexes out of the nucleus and excrete out of the body from several hours to days.

Key words: collloidal gold; camostat mesylate powder; lung adenocarcinoma; pd-1 inhibitor; xenograft mouse model

Introduction

Gene therapy has resulted in the use of plasmid DNA as a drug substance. Viral and non-viral vectors and delivery systems developed to transfer therapeutic genes into target cells [1]. In the case of non-viral approaches plasmid DNA, promising gene delivery vector, makes production easy in comparison to other gene delivery vectors.

mRNA-based drugs have potential as clinical treatments, however, a major challenge in realizing this drug class safely delivering the bioactive agents with high efficiency and without activating the immune system [2]. Researchers have modified the mRNA structure to enhance its stability and promote systemic tolerance of antigenic presentation in non-inflammatory contexts. Delivery of naked modified mRNAs is inefficient and results in low levels of antigen protein production. As such, lipid nanoparticles have been to improve delivery and protect the mRNA cargo from extracellular degradation [3]. Many mRNA-based drugs have been proposed for a variety of diseases. mRNA-based drugs have emerged as an attractive therapeutic class, which is expected to revolutionize cancer treatment through different approach.

We report herein the results of investigation, in nude mouse xenograft settings, Collloidal gold with Camostat Mesylate powder was able to achieve therapeutic cures against a human lung cancer cell lines.

Materials and Methods

Chemicals

Camostat mesylate (Foipan) powder was purchased from Ilsung Pharmaceuticals (South Korea). Colloid gold (Crystal Colloidal Gold) was purchased from Crystal Colloidals (Roermond, Netherlands).

Cell Culture and Reagents

Murine Lewis lung carcinoma cells were purchased from the American Type Culture Collection. Cells were cultured in RPMI1640 supplemented with 10% fetal bovine serum and 1% penicillin/streptomycin (Gibco) in humidified incubators at 37 ◦C with 5% CO2. The tumor cells, 10 *passages*, over 3 months in culture, are grown to *70–85% confluence* before being harvested. After 48 and 72 h incubation, 20 µL of MTT solution (5mg/ml) was added to the each well and incubated at 37°C for 4 hours. Then, the supernatant was removed and 100 µL of DMSO was added and absorbance of plates were read on an ELISA reader at a wavelength of 570 nm.

Mouse Xenograft Model

Athymic nude mice (nu/nu) obtained from National Cancer Institute were used in all human tumor xenograft therapeutic studies. Tumors were implanted. The tumor size was measured periodically at specified times, and treatment when tumor size reached 80 mm^3 or larger. Tumor size and body weight were recorded. An inoculum of 3×10^5 LLC lung carcinoma cells was injected subcutaneously on the flank of C57BL/6 mice in 100 µL serum-free media. Four days after injection, the treatment was initiated per orally. The tumor volume was calculated as $0.5 \times \text{length} \times \text{width}^2$. The tumors were allowed to grow [4]. This study was reviewed and approved by the Institution of Animal Care and Use Committee (IACUC) of Ewha Womans University (approval number: IACUC-21-005). 100% viability

of the cancer cell was starting from the day of seeding.

Caliper measurements of subcutaneous xenografts

The two longest perpendicular axes in the x/y plane of each xenograft tumor were measured to the nearest 0.1 mm by three independent observers (reviewers 5–7) familiar with collecting caliper measurements of xenograft tumors in mice. The depth was assumed to be equivalent to the shortest of the perpendicular axes, defined as y. Measurements were made using a digital vernier caliper while mice were conscious and were calculated according to equation as is standard practice: Xenograft volume = $xy^2/2$

Results

Nude mice bearing LLC lung carcinoma [5] xenografts were treated orally beginning on day 1, after tumor implantation, with 50 µl of 10 cc colloidal gold and 100mg camostat mesylate powder solution daily. Transcriptional differences, the different growth ratios, and multiple genes are involved in these differences. In this study, saline served as a negative control.

Body-weight gain (Figure 1) observed in this course of treatment for colloidal gold with camostat mesylate powder. Treatment with the solution led to 42% suppression on day 20 (Figure 2).

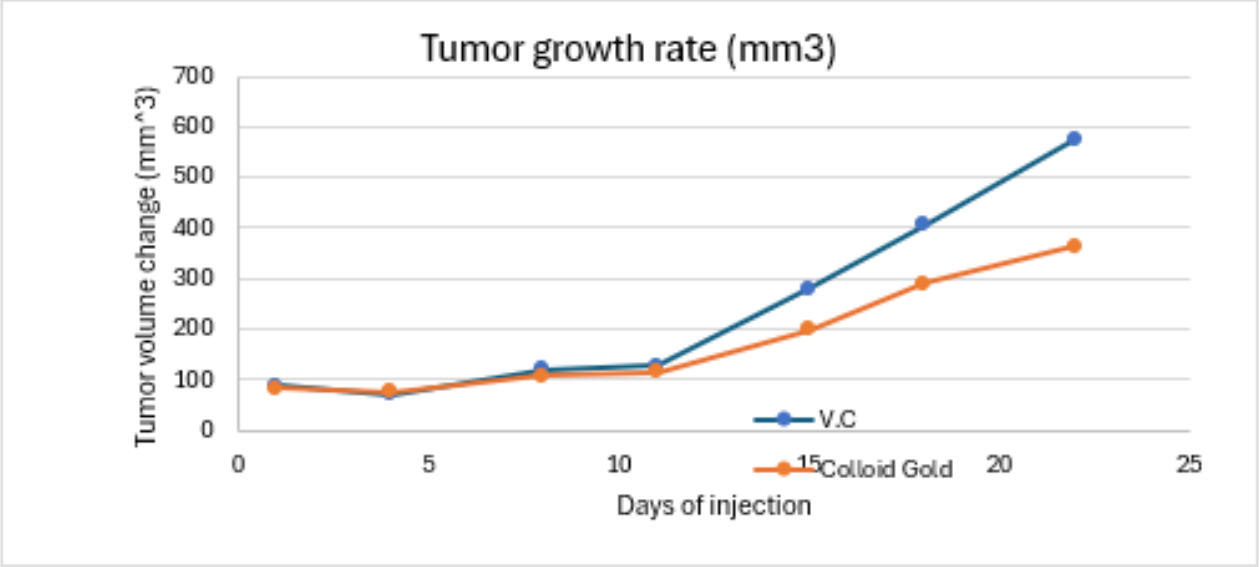


Figure 1: Body weight gain by intaking the solutions of saline and colloidal gold with camostat mesylate.

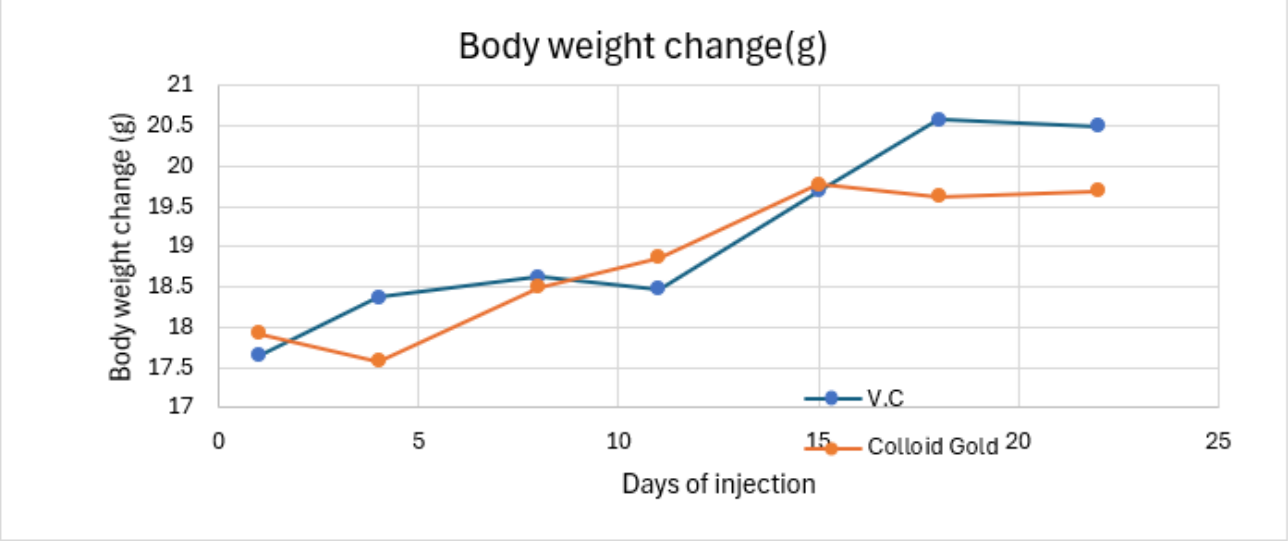


Figure 2: Lung cancer adenocarcinoma. Therapeutic effect of colloid goldal -camostat mesylate against lung cancer xenografts. Initial tumor size, 17.7 g, is = 96% of mice body weight. Typical photo of mice on day 4 and autopsy photos of the control and treated group on day 20

Discussion

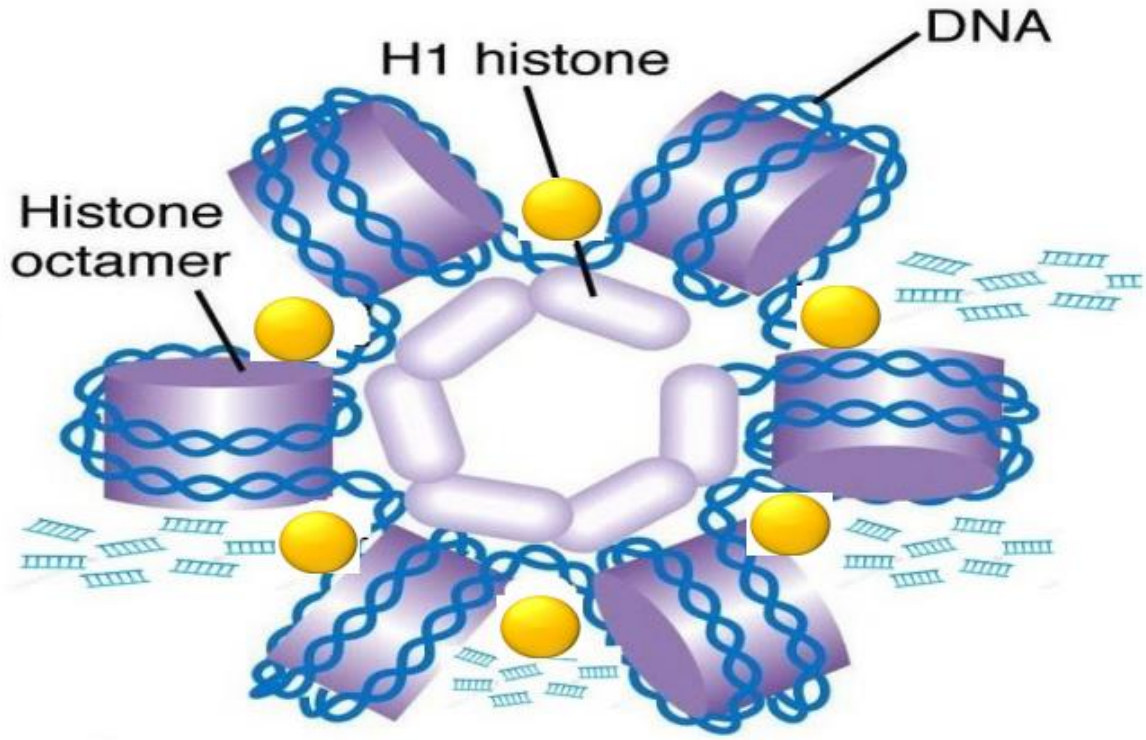
An isolated gene can be engineered at will and transferred back into the germ line of an animal, a functional and heritable part of. Cleavage of DNA at specific sites repair. Plasmid DNA can integrate by restriction nucleases, which greatly facilitates the isolation and manipulation of individual genes. DNA cloning vectors whereby a single DNA molecule can be copied to generate many billions of identical molecules. This foreign DNA is integrated into the host genome during double strand break into host DNA through a process called genetic recombination. Genetic recombination occurs when two different DNA molecules exchange pieces of genetic information. Integration of plasmid DNA into host DNA can occur several mechanisms, including: homologous recombination: This occurs when the plasmid DNA sequence is similar to a region of the host chromosome. The plasmid integrates into the host DNA by recombination with homologous areas, resulting in the transfer of the plasmid DNA to the host chromosome. Site-specific recombination occurs when plasmid DNA contains specific recombination sequences that are recognized by host cell enzymes. These enzymes integration into a specific site on the host chromosome. When plasmid DNA contains transposable elements, which are sequences that can move from one location in the DNA to another, transposition occurs [8]. Transposable elements in the plasmid can cause additional DNA rearrangements into the host chromosome [6].

Mechanism governed by the formation and dissolution of gold–sulfur bonds [7] between the gold nanoparticles and the sulfur group from the camostat mesylate [9]. Colloidal gold represent a promising class of natural product-based antitumor drug candidates. These compound of colloidal gold with camostat mesylate powder as a sulfur donor, operate through a new mechanism of preventing DNA or RNA interfering into the host genome. These compound offers a major potential therapeutic advantage in that they are cheap cost and have no side effect,in difference from the conventional anti-cancer drugs.

Limitation of the study

This study must extend to the diverse tumor mouse models during the considerable time to evaluate throughly. Human phase 2 and 3 clinical trials are also need in the future.

1.In cytoplasm during cell division formation of gold-sulfur bond



2.In the nucleus

Expel DNA-colloid

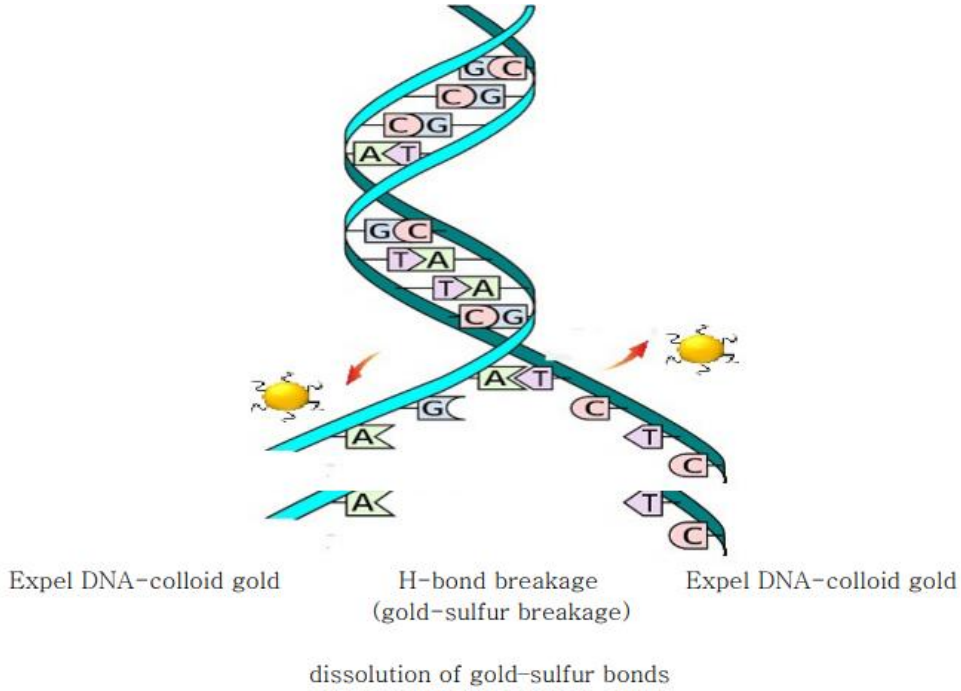


Figure 2: The formation and dissolution of gold–sulfur bonds between the gold nanoparticles and the mesilate can remove foreign genetic materials from living objects.

Conclusion

3.2 nm sized colloid gold can bind 3.4nm DNA pitch between the histone octamers to form gold–sulfur bonds during the anaphase of the cell cycle, which can be dissoluted the bonds to expell the colloidal gold-DNA fragments out of the nucleus.

Institutional Review Board Statement

This study was reviewed and approved by the Institution of Animal Care and Use Committee (IACUC) of Ewha Womans University (approval number: IACUC-21-005).

Conflicts of Interest

There is no conflict of interest.

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