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Short Communication

A Proposal for Preparation of a Unique "Cell-Made Nano-Gold Liposomes"

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Abstract

In the 1987, Gao and Huang jointly published a very special method and created the name-the "Solid core liposomes with encapsulated colloidal gold particles". In 1991, Gao et al. studied phagocytosis of protein coated colloidal-gold-agarose-gelatin microbeads by cultured uterine glandular epithelial and stromal cells. They found that the non-phagocytic type fibroblast cells in the cultural dishes turned to be extremely phagocytic type cells in their experimental condition, i.e., fibroblasts after co-incubated with protein coated nano gold rich agarose microbeads would internalize many microbeads that stuffed the entire cell body with microbeads, which looks like a string of purple grape. Because the electron microscopic image showed that each protein coated nano gold rich agarose microbeads after internalization has got an inverted phase of cell membrane in the process of phagocytosis. It is actually a kind of cell-made liposome. The author suggested that if the microbeads were first introduced a toxin in its core and then use crosslinking agent to coat the toxin loaded beads with a specific antibody against certain cancer cells, a novel kind of cell-made targeting drug can be produced.

Keywords: Fibroblast cells; Phagocytosis; Microbeads; Nano-technology

Thirty years ago, I invented a very special solid core liposomes with encapsulated colloidal gold particles [1]. That work was done when I was a visiting assistant professor in the Department of Biochemistry, worked in Prof. Leaf Huang's lab, at the University of Tennessee, Knoxville, during 1984-1986. The aim of that project was to incorporate colloidal gold into liposomes. It was a nano gold project before the terminology of "nano-technology" was popularly known after mid 1990s. Colloidal gold has a good property that its negatively charged surface can adsorb protein or polypeptide or enzyme on its surface without loss of their biological activities. So, it is an ideal carrier for many drugs. However, the element gold is heavy, while lipids are very light, that caused a problem in the preparation of nano gold particles entrapped liposome, especially when centrifugation is needed to be employed, which will result in the piercing the lipid membrane by the gravity force of the gold particles. I tried about 48 different experiments both were failed, until I invented the solid core liposome method.

The preparation of solid core liposomes with encapsulated colloidal gold particles was rather sophisticated and no one did similar work before me. Thus, Prof. Hayat kindly invited me to contribute a chapter in his new book on colloidal gold [2]. As it was described in my chapter in that book the preparation procedure includes four major steps: 1. Preparation of prevesicles with encapsulated solid cores of agarose-gelatin by emulsification of agarose-gelatin sol in organic solvent containing emulsifiers followed by cooling to form agarose-gelatin microbeads in organic solution 2. Extraction of lipophilic components from prevesicles to obtain microspherules of agarose-gelatin gel. 3. Introducing colloidal gold particles into microspherules and coating with required protein molecules. 4. Encapsulation of colloidal gold-bearing microspherules with the modified organic solvent spherule evaporation method for preparation of liposomes with dioleoylphosphatidylcholine/ colesterol/ dioleoylphosphatidylglycerol/ triolein (molar ratio 4.5:4.5:1:1) or other methods. When I finished that project, I moved to the University of North Carolina at Chapel Hill to do other research work.

After I left UTK and was working at UNC, the UTK patent office filed a patent on "Solid core liposome" in 1987 [3], which was approved one or two years later. Then, I found rather unhappy that my name as the first inventor was deleted away from that patent. Thus, I met with and complained to the provost of UTK at that time. He was very kindly to tell me that it was unfair to me to remove away my name from the inventors of that patent based on the fact that I had left UTK, and he appointed the patent office to treat my claim. However, the patent was already issued with Leaf Huang's name alone, the patent office felt difficult to correct it for an issued patent. So, I stopped to offer any further Know-how knowledge to the patent office thereafter. Due to the difficulty in performing the procedure without Know-how knowledge, that actually caused/turned that patent to be invalid until its expiration date of that patent in a long period of 19 years. I believe that it was not only a financial loss to me but it is also a histological loss to America in the development of such a potential novel method in drug delivery. I believe that perhaps everyone can use an expired patent now.

Since the effective patent period had now been passed over, for the benefit of drug delivery pharmacological industry, I would like to propose an even more useful method based on my historical finding to the research community, which I called it as "Cell-made nano-gold liposomes", that can replace the traditional man-made liposomes, because that cells could made nano-gold rich agarose-gelatin microspherules-cored liposome several times more effective than

man-made agarose-gelatin microspherules-cored nano-gold liposomes. My proposal has good evidence as it is indicated below. I might be very proud to tell you that there might be no any drug delivery tool, that is so effective to let the full cell body stuffed with the protein coated colloidal-gold-agarose-gelatin microbeads that I had invented.

In 1991, Gao et al. had published an article called "Phagocytosis of protein coated colloidal-gold-agarose-gelatin microbeads by cultured uterine glandular epithelial and stromal cells [4]. I was the first author of that article. I found a very interesting phenomenon in my experiment. The fibroblast cells are known as non-phagocytic type of cells. However, in my experimental condition the non-phagocytosis-type of cells in the cultural dishes turned to be extremely phagocytic type in nature. I got many microphotographs that the fibroblasts after co-incubated with protein coated nano gold rich agarose microbeads would internalize so many microbeads that turned the entire cell body stuffed with beads like a string of purple grape. I selected and inserted a photo of non-phagocytic cells in the cultural condition and become very active phagocytic type of cells (Figure 1) in my book,

which entitled as "E=7B2^44 Gao's Equation in relation to three tides of global immigration and strategic longevity" [5]. I indicated the fact that the selfish gene is not a single gene. But, it could be a group of cell membrane biosynthesis related genes. The membrane synthesis genes are very important to all living cells. Without membrane means without me. The ruthless law of natural selection favors to those species contain dominant selfish genes or membrane synthesis genes. But, it does not favour to those individuals that intend to be sacrifice. Selfish genes and greedy genes universally exist in both non-phagocytic type of cells and phagocytic type of cells; and we human being must have membrane synthesis genes or selfish genes. So, don't feel ashamed that you and me have selfish genes. As long as we are composed with cells in our body, we must confess that we have cell membrane synthesis or selfish genes. The human society might have to develop from individualism to familism to nationalism to globalism (Homo sapiensism).

The reason that I showed you that photo is that we could use the ability of cultured cells, which have membrane synthesis ability and we could also use their greediness to internalize as many protein-coated-nanogold rich-agarose-gelatin microbeads as they can. The photo shows that almost entire cell body was stuffed with colloidal-gold-agarose-gelatin microbeads. And the electron microscopy revealed that those internalized microbeads having their outer membranes, which could be reasonably to consider that the outer face of the microbeads is just the inner face of the cell membrane, because they were reversely formed through phagocytosis that inverted its facing. See photos in my chapter in Hayat's Book, Page 418 [2], which was copied here as Figure 2. If we can use a gentle sonication method to breakthrough the cell membrane, it is expected that we can get a lot of "Cell-made nanogold liposomes". The characteristic of those "Cell-made nanogold liposomes" could be that they can be cross-linked with specific antibodies

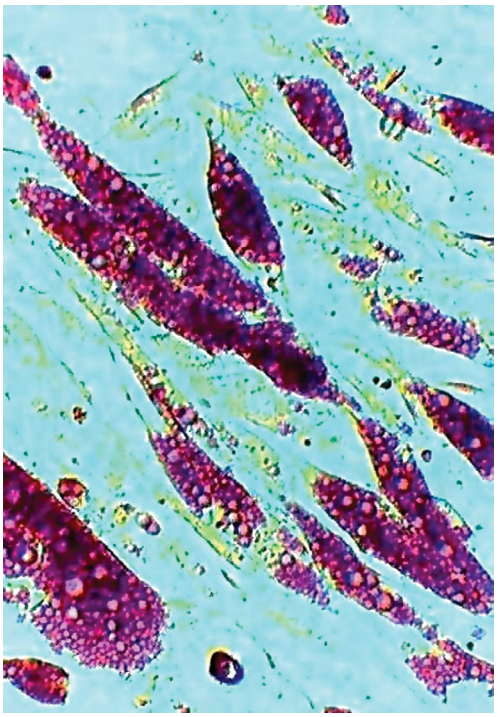

Figure 1: Cultured sheep stromal cell. Showing protein coated nano-gold rich agarose-gelatin microbeads were phagocytosed through overnight incubation with the microbeads, and stuffed whole the cell bodies with internalized microbeads, an unbelievable high rate of drug delivery with Gao's method.

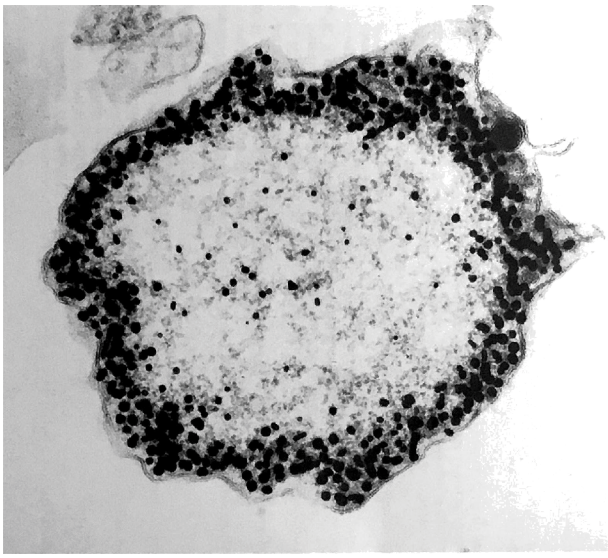

Figure 2: Cell-made liposome, which was composed with protein coated nano-gold rich agarose-gelatin after internalized by cultured cell and leased to the medium. The photo was copied from the same author's chapter in Hayat edited Book, Page 418 [2].

by using cross linking agents, since the original cell inner face of its membrane is abundant in protein and microfilaments. Suppose that the specific antibody can recognize certain cancer cell antigens, and inside the nanogold microbeads we can preloaded with certain toxin, such that ricin or abrin, etc. It is quite promising to use that kind of "Cell-made-nanogold toxic liposome" to kill targeted cancer cells.

If one large dish can raise 1,000 cultured cells, and each cell could make 100 toxic microbeads, then, 1,000 dishes of cultured cells could make 100 million toxic microbeads. The later can be converted to targeting microbead-cored "Cell-made-nanogold toxic liposomes". That could be far enough to be used in clinical curing patients. So that, I made this proposal. I hope that one day scientists can achieve to cure cancer with such a novel "Cell-made nanogold targeting liposomes". And I can offer all my Know-how knowledge to any research groups that they need me.

References

1. Gao K, Huang L (1987) Solid core liposomes with encapsulated colloidal gold particles. Biochim Biophys Acta 897: 377-383.
2. Kuixiong G (1989) Hayat Edited book. Colloidal Gold: Principles, Methods, and Applications. 1st edn. Academic Press.
3. Leaf Huang US Patent 4839111 A: Preparation of solid core liposomes (filed in 1987).
4. Gao KX, Smith SE, Godkin JD (1991) Phagocytosis of protein coated colloidal-gold-agarose-gelatin microbeads by cultured uterine glandular epithelial and stromal cells. Biotech Histochem 1: 1-6.
5. Johnson KG (1985) E=7B2^44 Gao's Equation in relation to three tides of global immigration and strategic longevity.