Journal of Colloid and Interface Science 511 (2018) 325–334

Contents lists available at ScienceDirect

Journal of Colloid and Interface Science

journal homepage: www.elsevier.com/locate/jcis

Regular Article

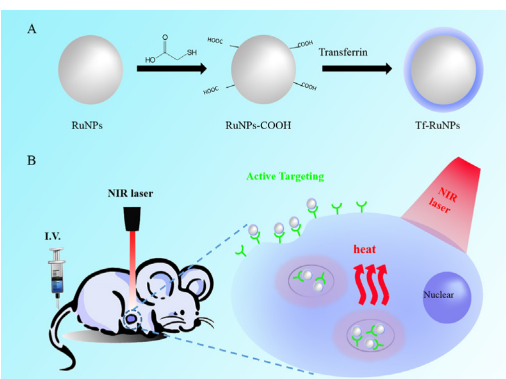
Transferrin modified ruthenium nanoparticles with good biocompatibility for photothermal tumor therapy

Shuang Zhao [1], Xufeng Zhu [1], Chengwen Cao, Jing Sun, Jie Liu *

Department of Chemistry, Jinan University, Guangzhou 510632, China

GRAPHICAL ABSTRACT

Schematic illustration of the preparation of Tf modified RuNPs. Cell uptake of Tf-RuNPs is mediated by Tf receptor-mediated endocytosis. Upon the NIR laser irradiation, the internalized Tf-RuNPs can expeditious convert the absorbed light energy to local heat for PTT.



ARTICLE INFO

Article history:
Received 2 July 2017
Revised 1 October 2017
Accepted 6 October 2017
Available online 7 October 2017

Keywords:
Transferrin
Ru nanoparticles
Tumor target
Photothermal therapy

ABSTRACT

In the past two decades, there were various kinds of photothermal agents being synthesised and investigated for their photothermal effect in antitumor applications. However, it is barely reported that the photothermal effect of Ruthenium (Ru) nanoparticles was researched in depth. In this work, we introduced Ru nanoparticles which possess excellent biocompatibility and metabolize easily to the photothermal therapy field. In addition, to improve the cells capacity of absorbing Ru nanoparticles, these Ru nanoparticles were modified by transferrin (Tf-RuNPs). Subsequently, as is expected, the RuNPs exhibit a remarkably integrated and high-quality photothermal property. On the other hand, it is significantly that Tf modification could also strengthen the cells absorptive ability to uptake Ru nanoparticles through endocytosis., Furthermore, both the *in vitro* cell ablation and *in vivo* tumor treatment verified that the Tf-RuNPs became ideal photothermal agents for photothermal tumor ablation therapy owing to their low toxicity and high cell destruction capability.

1. Introduction

Nowadays, the growing and aging of world population may be responsible for the increasing cancer-causing behaviours. After

* Corresponding author.
E-mail address: tliuliu@jnu.edu.cn (J. Liu).
[1] Both authors contribute equally to this work.

https://doi.org/10.1016/j.jcis.2017.10.023
0021-9797/© 2017 Published by Elsevier Inc.

all, cancer is still a disturbing and global health problem [1–3]. There is one thing that demands our focal attention that cancers were conventionally treated by traditional methods such as chemotherapy, surgery, radiation therapy, *etc* [4]. Unfortunately, these methods are restricted because of the adverse effects. In recent years, a growing number of scientists focus on the exploitation of nanomaterials for photothermal therapy (PTT), a minimally invasive and selective treatment of cancer. In this PTT protocol, photo-absorbing nanomaterials convert photon energy to heat, producing a local hyperthermia to burn cancer cells and tissues. As for the light source, near-infrared (NIR, 700 to 1100 nm) laser is being widely used. Because it can reach several centimetres in biological tissues due to the relatively low absorption of hemoglobin and water as well as less damage to normal tissues [5]. Hence, strong absorption in the NIR region of nanomaterials will be beneficial for the application of PTT.

There are quiet a few, different types of photothermal agents, such as metal nanostructures [6–14], organic compounds [15,16], carbon materials [17–19]. Actually, a multitude of them have been investigated up to now. There are quiet a few different shapes of gold, for typical examples, nanospheres, nanorods, nanoshells, and nanocages, obviously, all of them will bewell-suited to various biomedical applications [20,21]. Even though, almost all the researches pay excessive attention on the narrow range of metal elements like gold, silver, or palladium. On the contrary, studies on the light and heat properties of the precious metal ruthenium (Ru) are rarely reported. According to this, we have studied the photothermal effect of ruthenium nanoparticles with simple spherical morphology. Gold nanomaterials feature the high cost, poor bioassay and thermal stability, while carbon nanomaterials featurepoorly dispersible and may induce oxidative stress as well as immune response, contrarily, the ruthenium nanoparticles have good biocompatibility and exhibit outstanding photothermal effect.

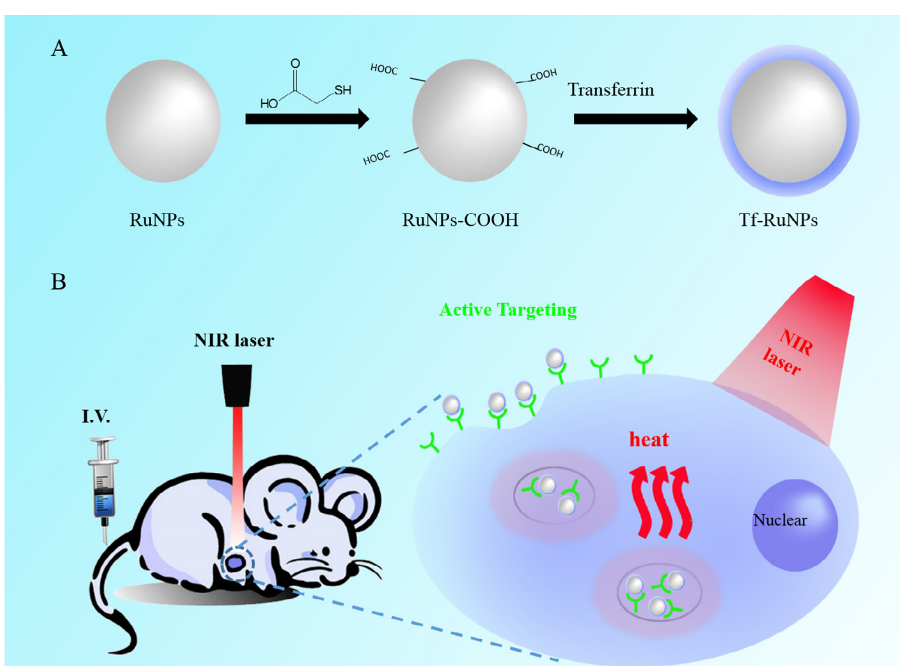
Insufficient intracellular particle delivery may be the main obstacle that prevents the using of metal nanoparticles in the fight against cancerous cells [22]. Considering this, nanoscale modification technology was invented timely. More specifically, it is a promising pathway to enhance the accumulation of nanoparticles. Different ligands have been modified into nanoparticles and significantly enhanced the cellular ability of absorbing via receptor-mediated pathways, such as folic acid [23], hyaluronic acid [24], peptides [25], *etc*. Transferrin (Tf), as a serum protein which is non-toxic, non-immunogenic, and biodegradable: it has been widely studied as a cancer-targeting agent [26]. There is an ocean of Transferrin receptor (TfR) existing on the surface of proliferating and malignant cancer cells [27–29]. Tf/TfR-mediated endocytosis has been proved to be an effective strategy to enhance the nanoparticles accumulation in tumor sites [30]. A host of investigations have indicated that different material modified by Tf extends the blood circulation time and achieves a high selectivity for cancer cells, [32,33].

Collectively, the purpose of this study was to investigate the activity of Ruthenium (Ru) nanoparticles in photothermal therapy against cancer cells. In view of this, we envisage to make Tf modified on the surface of Ru nanoparticles. so that the synthesis of Ru nanoparticles would get prone to be absorbed by cells (Scheme 1). Beyond that, the cellular uptake mechanisms of Tf-RuNPs were detected in cell assays. Also, the photothermal effects of Tf-RuNPs on A549 cells were measured by MTT assay. Furthermore, we observed and assessed the photothermal effects of Tf-RuNPs on tumor-bearing mice. Afterwards, it is demonstrated that Tf-RuNPs exhibit excellent capability to kill cancer cells, with less side effects owing to the use of Tf-RuNPs. Simply put, these new nanoparticles could be successfully used for highly efficient *in vivo* PTT under NIR irradiation.

2. Materials and methods

2.1. Materials

All reagents and solvents were purchased commercially and used without further purification unless specially noted, and Ultrapure MilliQ water (18.2 MW) was used in all experiments. polyvinyl pyrrolidone (PVP), Cetyltrimethylammonium bromide



Scheme 1. Schematic illustration of the preparation of Tf modified RuNPs. Cell uptake of Tf-RuNPs is mediated by Tf receptor-mediated endocytosis. Upon the NIR laser irradiation, the internalized Tf-RuNPs can expeditious convert the absorbed light energy to local heat for PTT.