TOPICAL FORMULATION OF AS1411-GOLD NANOPARTICLES AS CERVICAL CANCER DRUG DELIVERY SYSTEM

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Introduction

AS1411, a G-quadruplex (G4) DNA aptamer, can bind specifically to nucleolin, which is overexpressed in cervical cancer cells.

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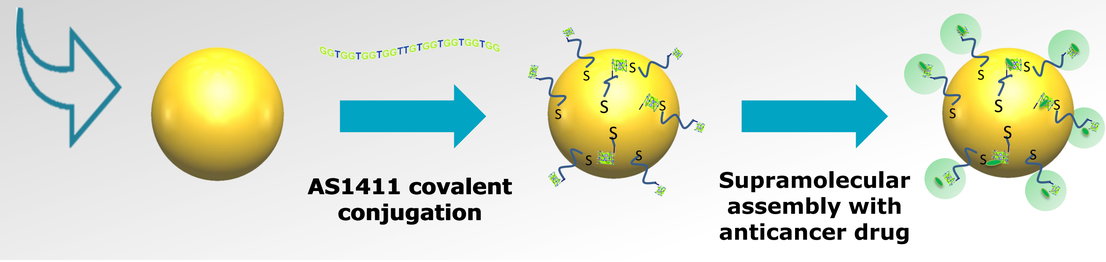
The synthesis of AS1411-based nanoparticles is a potential drug delivery system due to its safety and improvement of aptamer cytotoxicity.

Oncotarget 2015, **6**, 22270-22281

AIM: To develop AS1411-gold nanoparticles (AS1411-AuNPs) to overcome the non-selective toxicity of anticancer drugs (Imiquimod and C_8) and to improve the potency of aptamers for the treatment of HPV-positive cells in precancerous state.

Methodology

Nanoparticles Synthesis › **Nanoparticles Characterization** › **Biological Evaluation**



Results

1. AS1411-AuNPs synthesis and drugs conjugation are homogeneous and led to hydrodynamic diameter increment

A

	Hydrodynamic diameter(nm)
AuNPs	12.00 ± 1.20
AS1411-AuNPs	15.76 ± 1.64
AS1411-AuNPs + IQ	21.16 ± 2.68
AS1411-AuNPs + C_8	18.30 ± 2.53

B

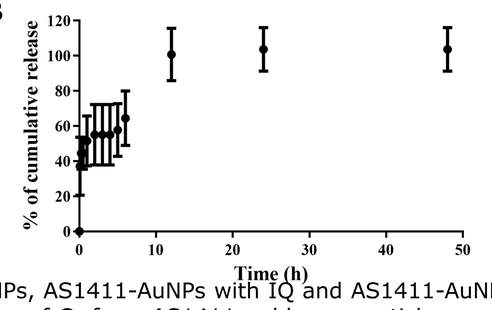
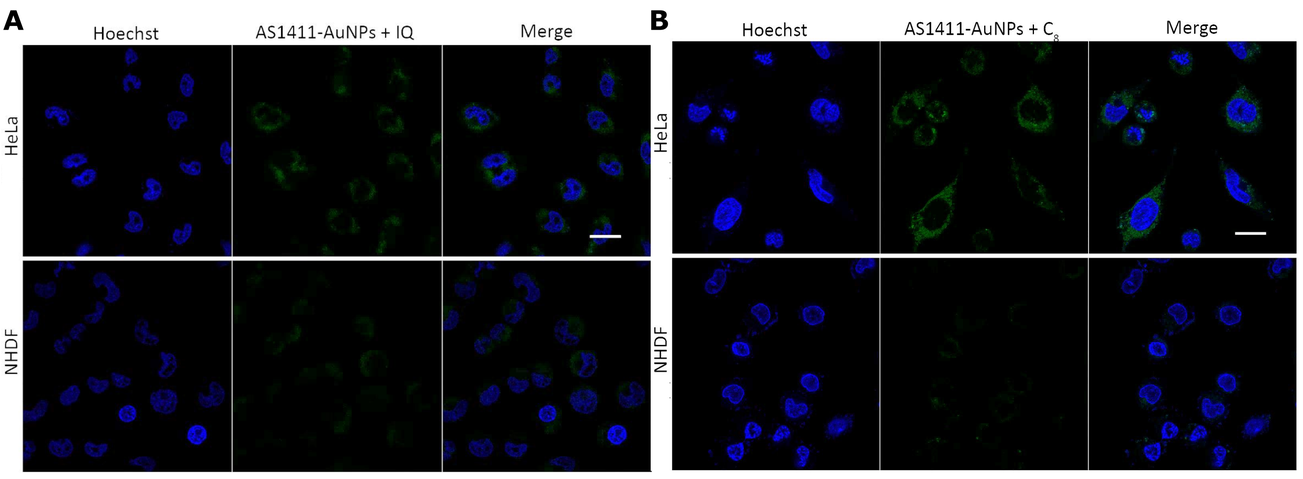


Figure 1. (A) Hydrodynamic size of citrate AuNPs, AS1411-AuNPs, AS1411-AuNPs with IQ and AS1411-AuNPs with C_8 measured by dynamic light scattering. (B) Cumulative release of C_8 from AS1411-gold nanoparticles performed in 20 mM KPi and 100 mM KCl for 48 h (n=3).

2. AS1411-AuNPs improve drugs selectivity to the cancer cell line



C

	IQ	C_8
HeLa	31%	5%
NHDF	49%	9%

D

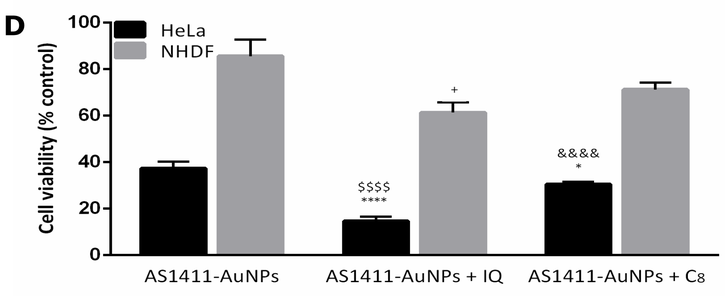


Figure 2. Confocal images after medium replacement in HeLa and NHDF cells treated with (A) AS1411-AuNPs with IQ or (B) AS1411-AuNPs with C_8. (C) IC_{50} of IQ and C_8 in HeLa and NHDF cell lines. (D) Effect of AS1411-AuNPs with or without C_8 or IQ on cell viability in HeLa or NHDF cells for 3 days by MTT assay.

3. AS1411-AuNPs can escape from lysosomes in cancer cells and are internalized by nucleolin positive cells

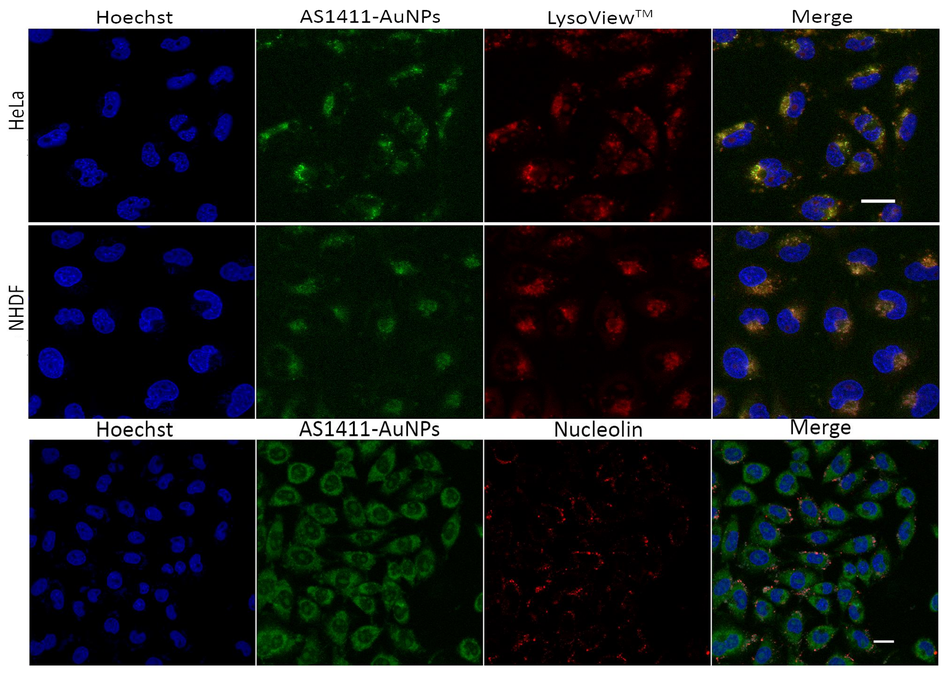
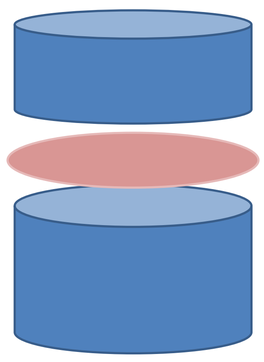


Figure 3. (A) Confocal images of AS1411-AuNPs (green) with LysoView™ 540 in HeLa cancer cells or NHDF non-malignant cells. Lysosomes are stained with LysoView™ 540 (red). (B) Confocal images of AS1411-AuNPs (green) in nucleolin (red)-positive HeLa cells. Cell nuclei are stained with Hoechst 33342 (blue). Scale bar: 20 µm.

4. Topical formulation with AS1411-AuNPs leads to nanoparticle's retention in the vaginal samples

A



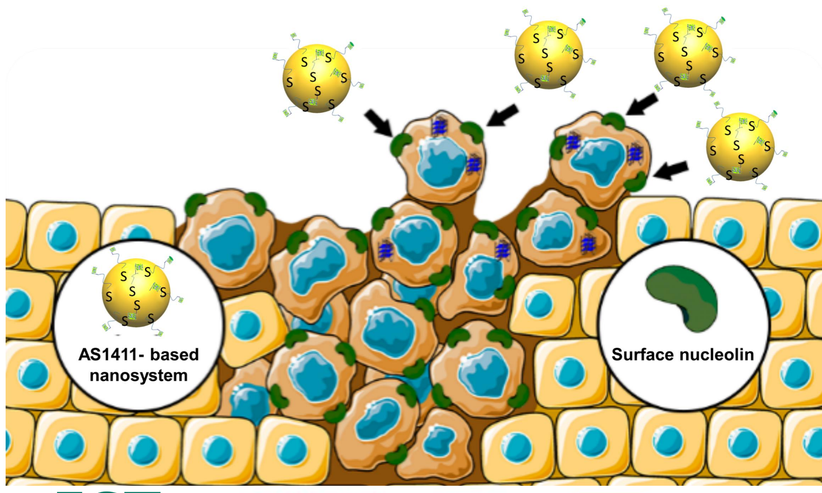
B

	8% Formulation	10% Formulaton
Donor Chamber	3.97 ± 2.81	1.12 ± 0.80
Vaginal Tissue	0.625 ± 0.08	0.78 ± 0.51
Receptor Chamber	n.d.	n.d.

Figure 4. (A) Schematic representation of Franz cells. (B) Drug (C_8) concentration (ng/mL) after application of the topical formulation in the donor chamber for 24h. Drug concentration on the porcine vaginal tissue was measured after 20 minutes of sonication in PBS (2 µL of PBS *per* mg of tissue). n.d.- the compound was not observed in the proper retention time in the HPLC-FLD analysis.

Conclusions

- ✓ **AS1411-AuNPs with drugs were successfully synthesized with a homogeneous size;**
- ✓ **The AS1411-AuNPs confer cancer selectivity to the drugs, being less internalized by normal cells and conferring higher cell cytotoxicity to the cancer cells;**
- ✓ **The formulation with AS1411-AuNPs containing the drugs remain retained in the vaginal samples.**
- ✓ **Overall, AS1411-AuNPs are a promising drug delivery system, that can be loaded in formulations to be applied in cervical pre-cancerous lesions.**



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