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Training for Medical education via innovative
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Training in Brno 2019



Nanotechnology, nanoparticle – basic research at Department of Biophysics

Vladan Bernard
Brno, 2019



Nanotechnology is the applied science dealing with the production and using of materials and particles, whose origin is to be targeted at the manipulation of individual atoms or relatively small groups of atoms.

Nanomedicine can be generally defined as a comprehensive monitoring, management, repair, protection and improvement of all human biological systems, operating at the molecular level - and this purposefully created by using nanodevices and nanostructures, ultimately leading to improved health status of individuals.

Nanomaterials are biomedical devices at the scale 1 – 100 nm at least in one dimension.



Promise of nanomedical devices (why we develop it?):

New methods for prevention, diagnosis, therapy

Daily screening of health (Point Of Care – POC - testing)

Therapy targeted to the individual patient

High sensitivity and specificity

Dynamic evolution

Multidisciplinary issues

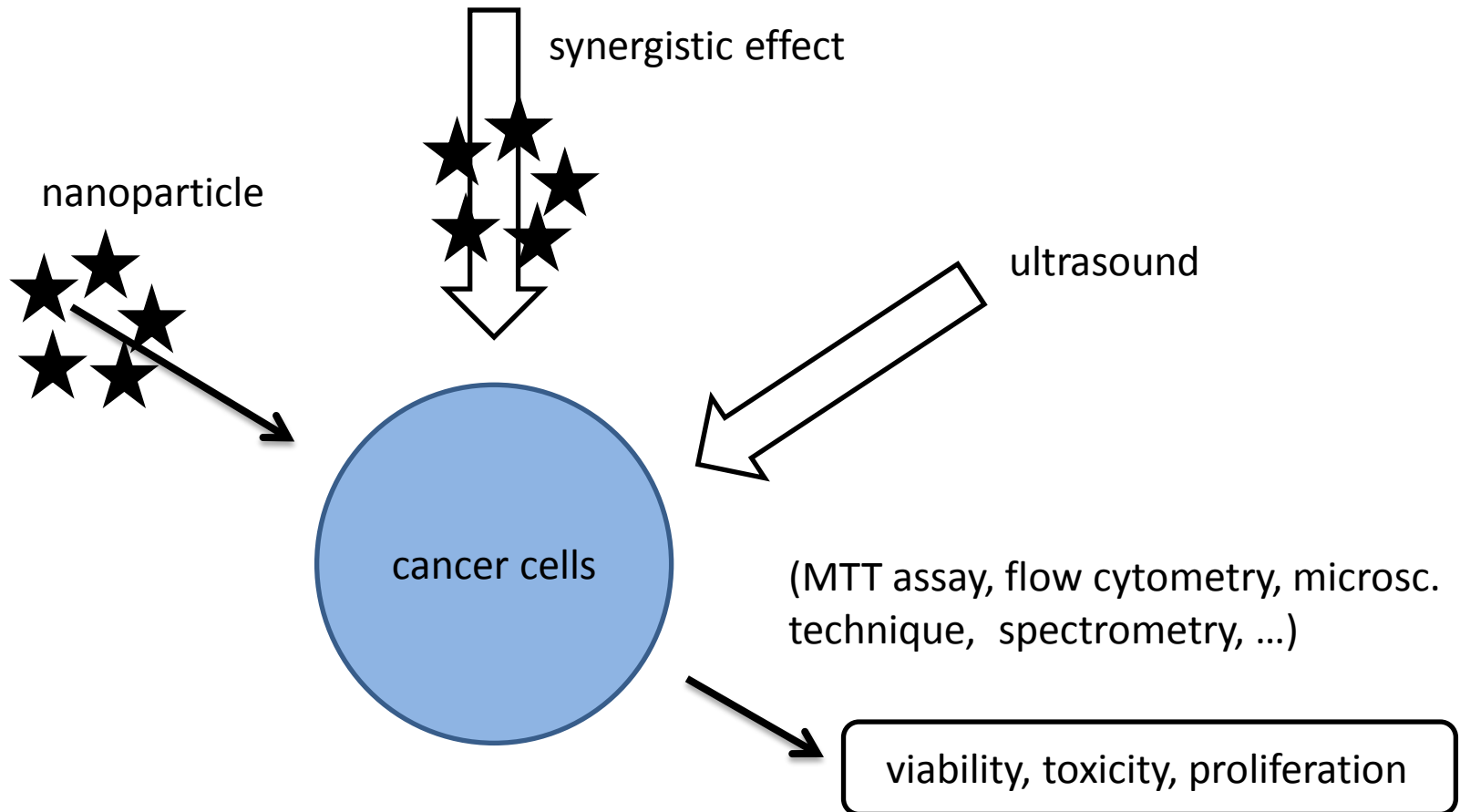
Different criteria and behavior „macro↔nano world“



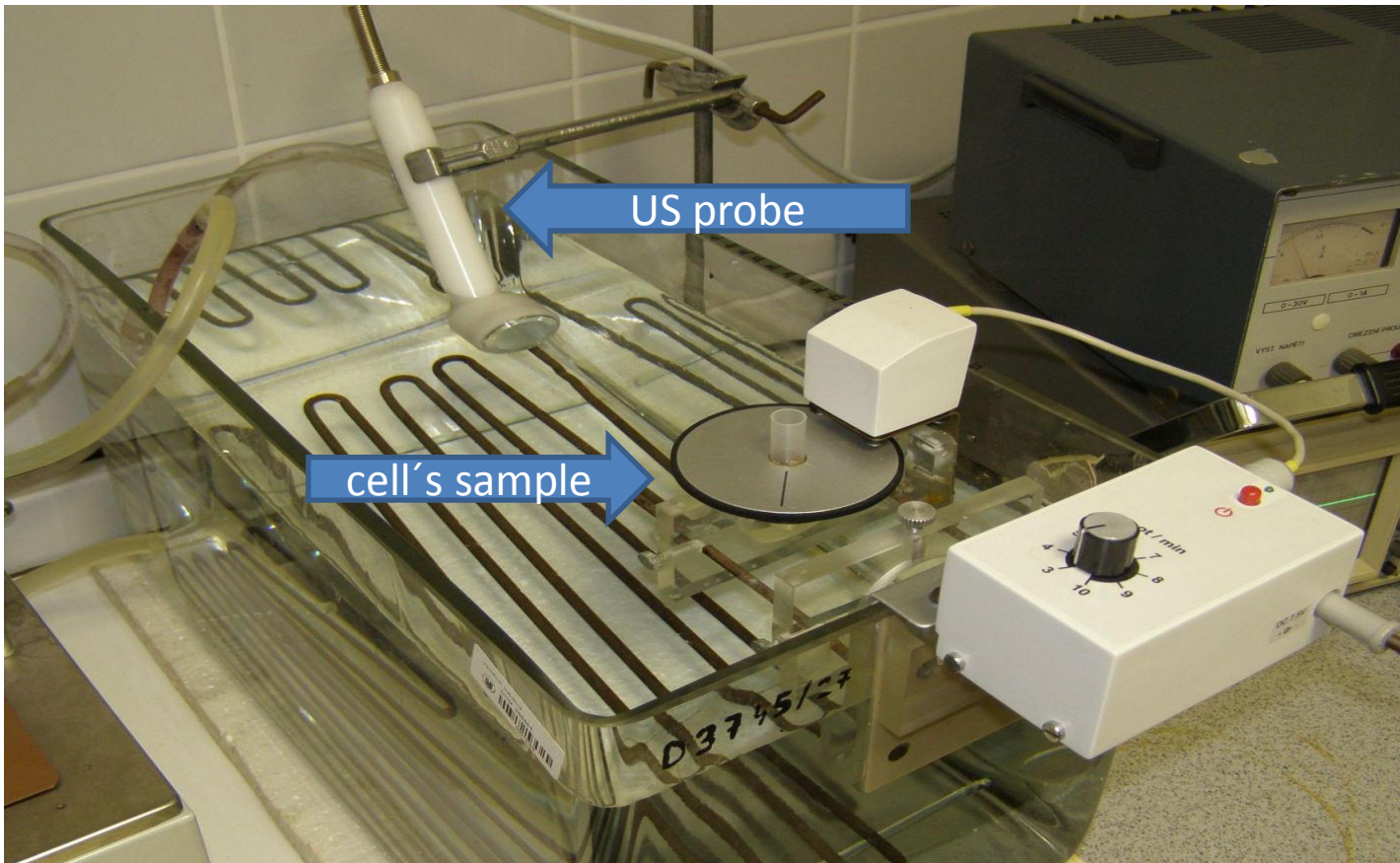
Nanoparticle in research at Department of Biophysics, Masaryk University

- testing of viability, proliferation, toxicity
- metallic nanoparticles (commercial, synthesized)
- in vitro experiments
- carcinoma cell lines
- synergistic effect with therapeutical ultrasound

Design of experiments



Ultrasound application - technical equipment setup



Ultrasound application - technical equipment setup



ORIGINAL RESEARCH

THE VIABILITY OF OVARIAN CARCINOMA CELLS A2780 AFFECTED BY TITANIUM DIOXIDE NANOPARTICLES AND LOW ULTRASOUND INTENSITY

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Abstract

The effect of titanium dioxide nanoparticles and ultrasound was studied on human ovarian carcinoma cells A2780 *in vitro*. The viability of cells has been studied by a standard 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide viability assay in different modes of treatment: application of nanoparticles alone, exposure to ultrasound field alone, application of nanoparticles followed by an exposure to ultrasound, and an exposure to ultrasound followed by addition of nanoparticles. The viability was measured 48 and 72 hours after the exposure. The titanium dioxide nanoparticles used were smaller than 100 nm in diameter, ultrasound was applied at a therapeutical intensity of $1 \text{ W}\cdot\text{cm}^{-2}$ and frequency of 1 MHz; the cells were treated in a 37 °C thermostated water bath in a configuration with far field ultrasound exposure. The final concentration of titanium dioxide nanoparticles was 50 µg/mL. The results showed that a combined effect of titanium dioxide nanoparticles and ultrasound influenced the viability of human carcinoma cells more than the application of titanium dioxide nanoparticles or ultrasound alone. The outcomes showed a significant difference between experimental groups with different sequences of application or exposure of nanoparticles or ultrasound. Maximal decrease of viability was achieved by application of experimental protocol with exposure to ultrasound first, followed by application of nanoparticles. It seems to indicate the possibility to intensify the effect of nanoparticles on cell viability by previous ultrasound exposure.

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2016



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Research Article

**AgCu Bimetallic Nanoparticles under Effect of Low Intensity
Ultrasound: The Cell Viability Study In Vitro**

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The effects of metallic nanoparticles as cytotoxicity or antibacterial activity are widely known. It is also obvious that ultrasound is one of the most widely used therapeutic modalities in medicine. The effect of application of therapeutical ultrasonic field in the presence of metallic nanoparticles AgCu <100 nm modified by phenanthroline or polyvinyl alcohol was examined on human ovarian carcinoma cells A2780. Metallic nanoparticles were characterized by electron microscopy and by measuring of zeta potential. The cell viability was tested by MTT test. The experimental results indicate a significant decrease of cell viability, which was affected by a combined action of ultrasound field and AgCu nanoparticles. The maximum decrease of cells viability was observed for nanoparticles modified by phenanthroline. The effect of metallic nanoparticles on human cell in presence of ultrasound exposure was found—a potential health risk or medical advantage of targeted therapy in the future.

Journal of Cancer Research,
2014

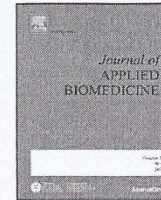


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Original Research Article

Combined effect of silver nanoparticles and therapeutical ultrasound on ovarian carcinoma cells A2780

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Antibacterial activity of silver nanoparticles is widely known and used. The effect of application of therapeutical ultrasonic field in the presence of silver nanoparticles < 100 nm was examined on human ovarian carcinoma cell A2780. The cell's viability was examined by MTT assay and by life-time microscopy. The presence of nanoparticles in the cell was examined by using electron transmission microscopy. Experimental results indicate a significant decrease of viability of cell, which was affected by the combined action of ultrasound field and silver nanoparticles, compared to the separate exposure of silver nanoparticles or ultrasonic field. The experiments showed a significant effect of succession of application of these two factors. The presence of nanoparticles inside cells after incubation was showed. The results show the possibility of using of ultrasonic field as a factor that can significantly affect cell viability in the presence of silver nanoparticles.

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ORIGINAL RESEARCH

**AGCU BIMETALLIC NANOPARTICLES MODIFIED BY POLYVINYL
ALCOHOL – THE CELLS VIABILITY STUDY IN VITRO****Vladan Bernard¹, Ondřej Zobač², Marcela Vlková³, Vojtěch Mornstein¹,
Jiří Sopoušek²**¹Department of Biophysics, Faculty of Medicine, Masaryk University, Brno, Czech Republic²Department of Chemistry, Faculty of Science, Masaryk University, Brno, Czech Republic³Department of Clinical Immunology and Allergy, St Anne's Faculty Hospital and Faculty
of Medicine, Masaryk University, Brno, Czech Republic**Abstract**

The effects of elementary metallic nanoparticles on living objects as cytotoxicity or antibacterial activity are widely known. Ag nanoparticles are a suitable and well known example. Nanoparticles formed by an alloy of Ag and Cu stabilized by polyvinyl alcohol were examined on two human tumor cells - ovarian carcinoma cells A2780 and skin melanoma cells A375. Bimetallic AgCu nanoparticles were synthesized by using a method of chemical co-reduction of silver nitrate and copper (II) nitrate hydrate. The nanoparticles were characterized by electron microscopy and by measurement of zeta potential. Cell viability was tested by using an MTT (tetrazole colorimetric viability assay) test. The effect on cell apoptosis and necrosis was measured by using flow cytometry. The experimental results indicate a differentiated impact of nanoparticles on the cells used. A more significant effect of viability decrease was observed for A2780 cells. The cell death caused by the nanoparticles used was observed particularly in the form of initial and advanced apoptosis for both cells lines, necrosis was observed to a lesser extent. The synthesized bimetallic nanoparticles seem to be a suitable candidate for targeted suppression of cell proliferation.

Clinician and technology,
2018

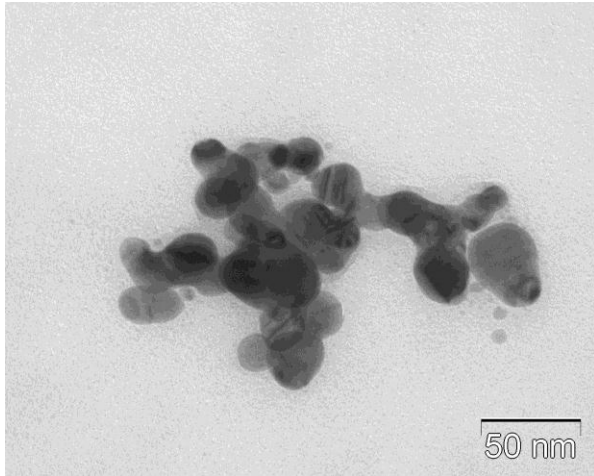


Fig. 1: TEM image of nanoparticles of AgCu/PVA

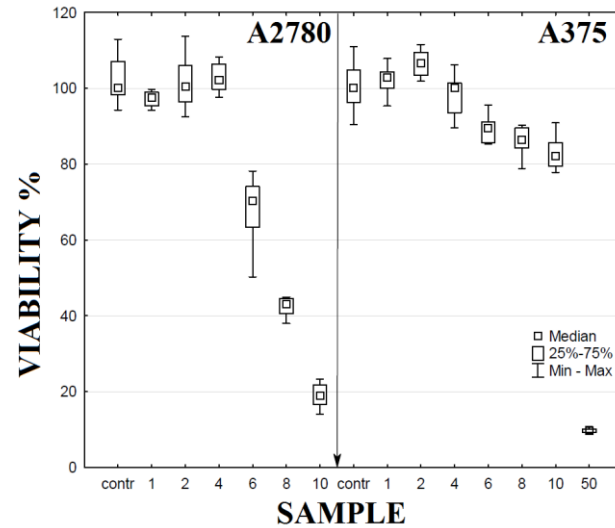
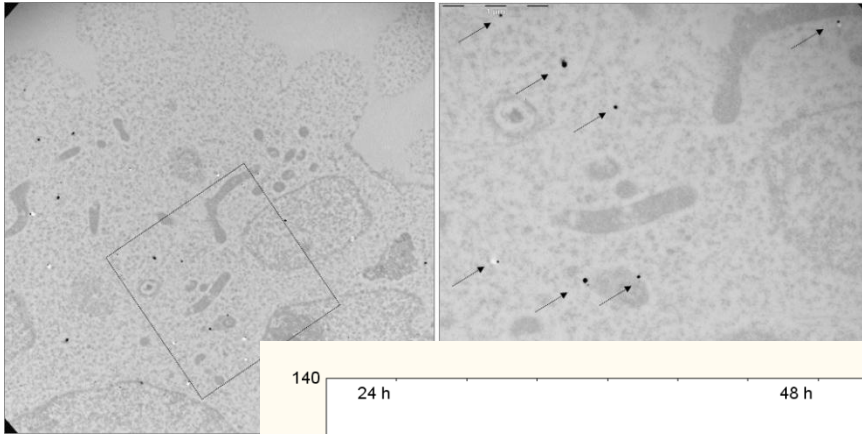
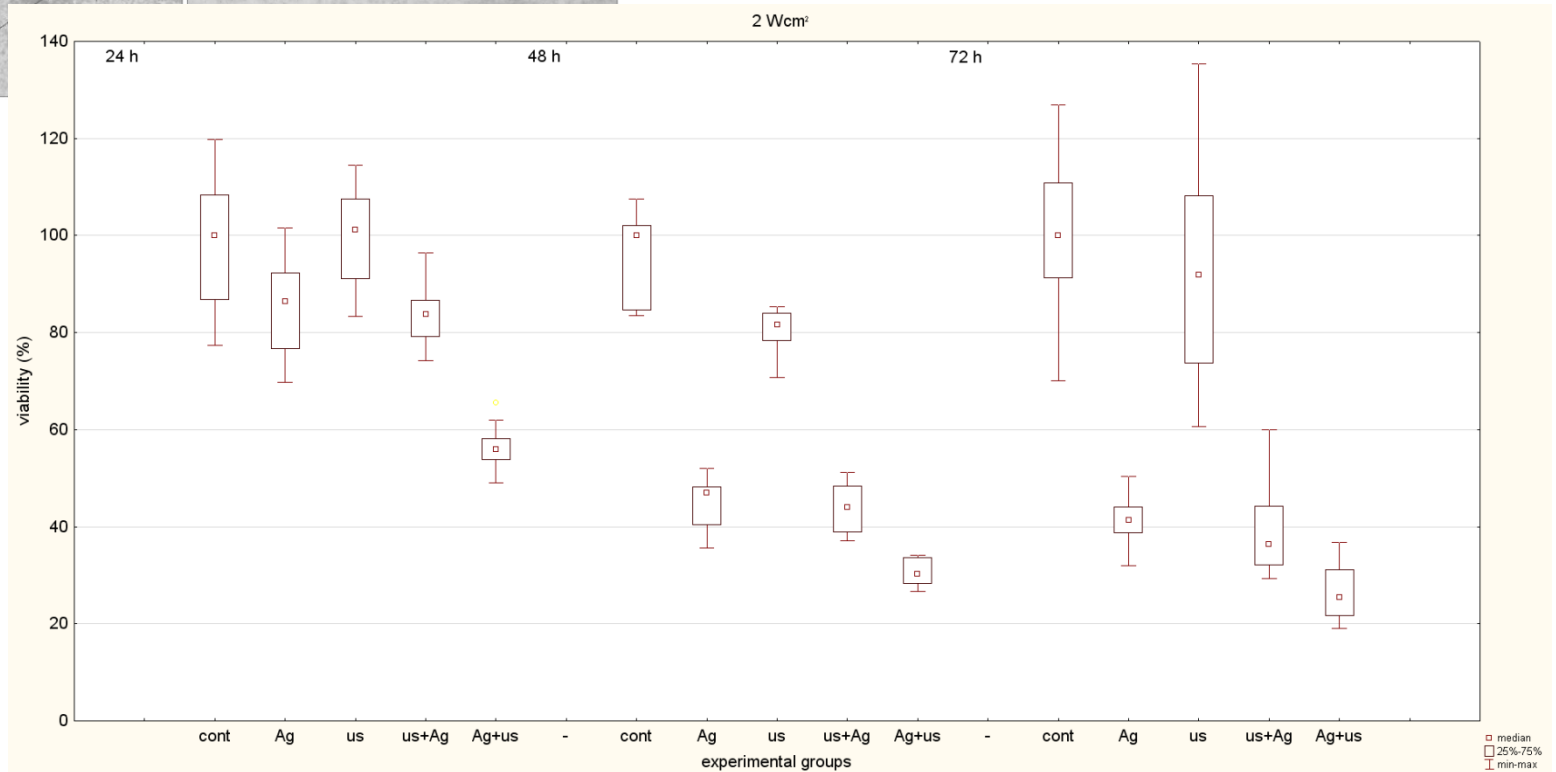


Fig. 2: Cell viability at 48 h of incubation with AgCu NPs modified by PVA. Samples: contr – control sample, 1 – AgCu NPs in concentration $1 \text{ mg}\cdot\text{l}^{-1}$, 2 – AgCu NPs in concentration $2 \text{ mg}\cdot\text{l}^{-1}$, 4 – AgCu NPs in concentration $4 \text{ mg}\cdot\text{l}^{-1}$, 6 – AgCu NPs in concentration $6 \text{ mg}\cdot\text{l}^{-1}$, 8 – AgCu NPs in concentration $8 \text{ mg}\cdot\text{l}^{-1}$, 10 – AgCu NPs in concentration $10 \text{ mg}\cdot\text{l}^{-1}$, 50 – AgCu NPs in concentration $50 \text{ mg}\cdot\text{l}^{-1}$

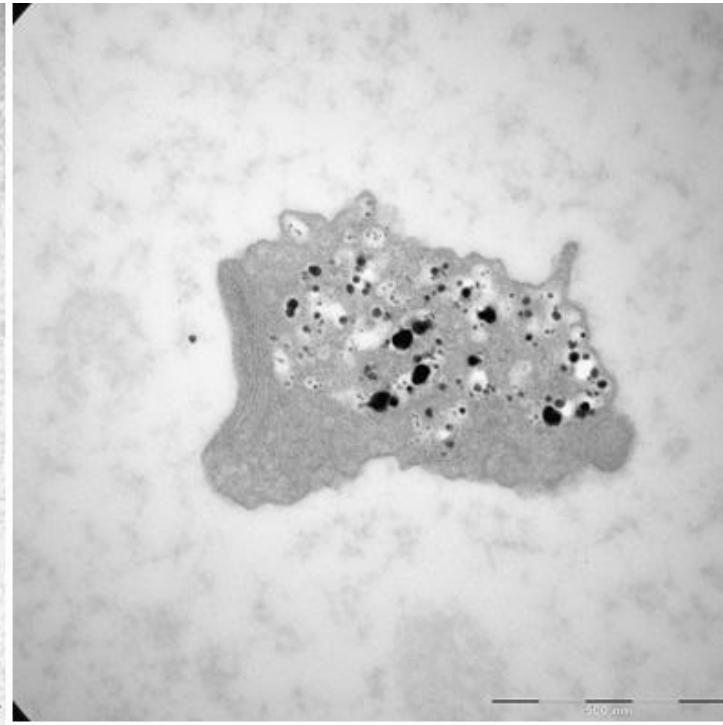
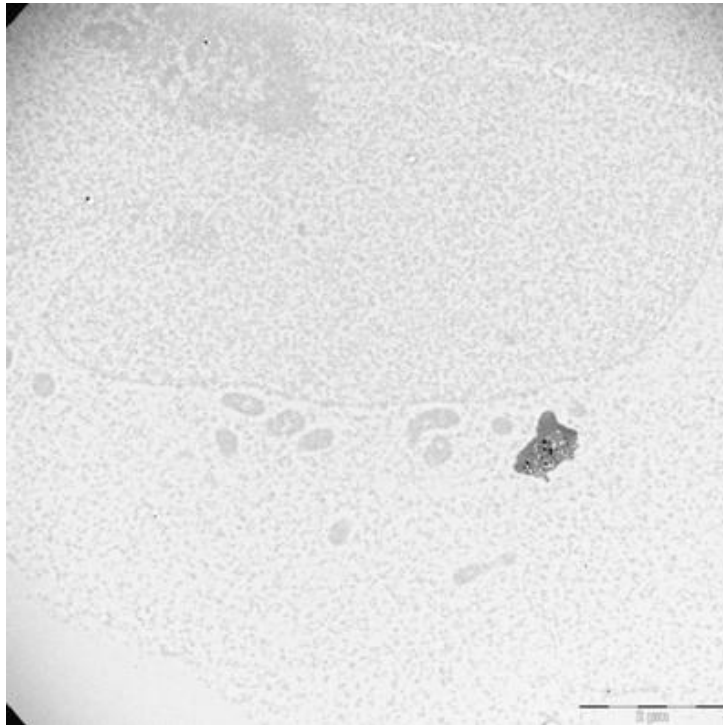
AgCu NPs, effect of PVA stabilization,
concentration effect



Ag NPs – cell penetration, amplification
of NPs effect in case of ultrasound field



Ag NPs- bladder production process ; probable removal of NPs from cells.





The outputs:

Nanoparticle activity

- viability and proliferation – depending on cell type, nanoparticle type and size, on stabilization package, ...
- evidence of cell's membrane penetration
- amplification of synergistic effect of nanoparticle and ultrasound mechanical field

Broader context

- introduction and adoption of new laboratory methods connected with nanotechnology in cell laboratory at the department
- strengthening education in nanotechnology for medical student



Thanks for your attention

