

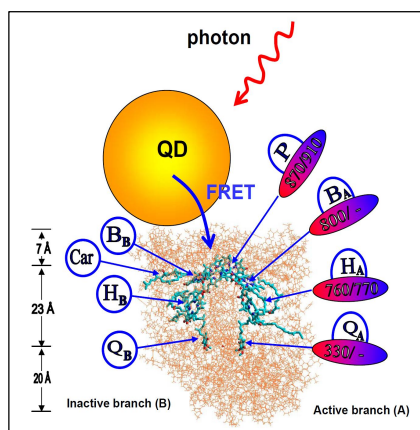
1. PUBLISHABLE SUMMARY

Main achievements in the frames of the accomplished "Energy Conversion within the Hybrid Materials Engineered from the Nanocrystals Quantum Dots and Photochromic Membrane Proteins" project concern:

- (1) development of the nano-bio hybrid materials for enhanced photosynthesis in artificial light harvesting and energy transmitting systems;
- (2) development of the nano-bio hybrid materials for photovoltaic applications;
- (3) energy transfer within hybrid materials and within the immunocomplexes for multiplexed high-through-put detection of rare cancer cells in view of development of advanced diagnostics of a breast cancer micrometastases.

These results are summarized below.

Quantum Dots for Enhanced Photosynthesis

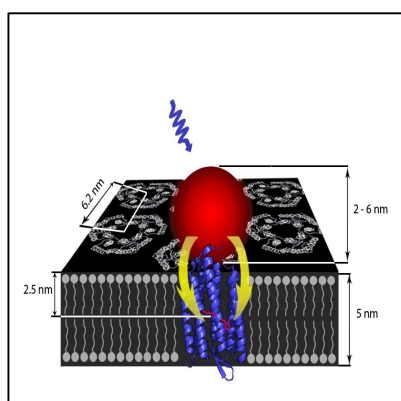


The straightforward way to construct an artificial photosynthetic device for practical solar fuel production for the practical use of solar energy is to mimic the structural and functional organization of the natural photosynthetic machinery. Nanocrystals are able to collect light over a wide spectral window having bigger absorption than natural photosystems. They are also very efficient in excitation energy transfer. We have succeeded to tag the Quantum dots (QD) with photosynthetic reaction centers of *Rb. sphaeroides* (RC) in such a way (see picture) that Förster resonance energy transfer (FRET) from QD to RC produces nearly three-fold increase in the rate of generation of excitons in the RC. Even stronger enhancements are theoretically predicted paving the way to significant increase of efficiency of photosynthesis. This study represents the **first example** of the efficient transfer of excitation energy harvested by

nanoparticles (QDs) to a complex biological photosynthetic system (RC). The results are important because they pave the way for the use of nanocrystals as light-harvesting built-in antennae for artificial photosynthesis. It is worth mentioning that the enhancement of biological functions of natural photosynthetic systems should have a strong impact on energy-related technologies.

Nabiev, I., Rakovich, A., **Sukhanova, A.**, Lukashev, E., Zagidullin, V., Pachenko, V., Rakovich, Y., Donegan, J.F., Rubin, A.B. and Govorov, A.O. (2010) *Fluorescent quantum dots as artificial antennas for enhanced light harvesting and energy transfer to photosynthetic reaction centers*. *Angewandte Chemie Intl Ed.* 49, 7217-7221. **IF=11.829**

Quantum Dots for Enhanced Photovoltaics

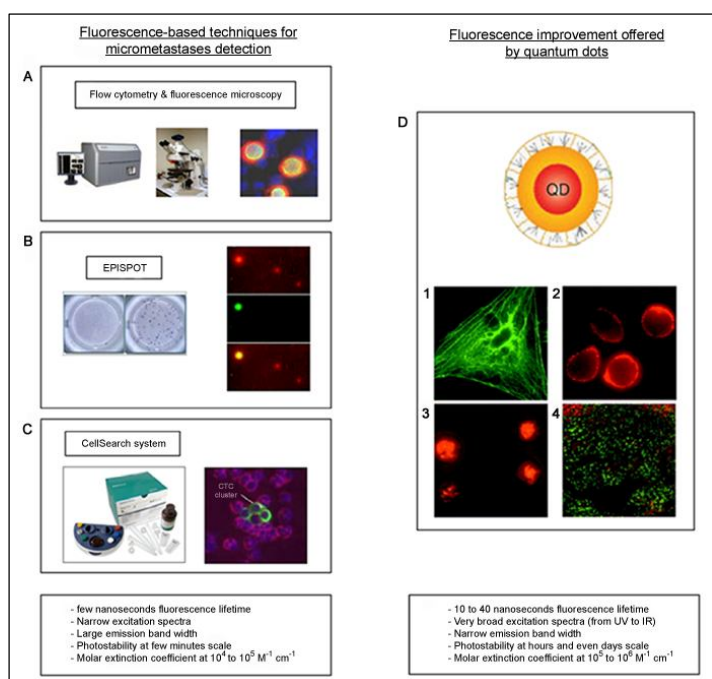


Purple membrane (PM) from bacteria *Halobacterium salinarum* contains a photochromic protein bacteriorhodopsin (bR) arranged in a 2D hexagonal nanocrystalline lattice. Absorption of light by the protein-bound chromophore retinal results in pumping the protons through the PM creating an electrochemical gradient which is then used by the ATPases to energize the cellular processes. We have realized such specific nano-bio optical and spatial coupling of nanoparticles (QDs - donors) and bR retinal (acceptor) which provided a mean to achieve FRET with the efficiency approaching 100%. The integration of QD within the PM containing bR significantly increased the efficiency of light-driven transmembrane proton pumping, which is the main bR biological function. This new QD-bR hybrid material may have numerous optoelectronic, photonic and

photovoltaic applications. The QD-PM nanounits operating in the FRET regime provide a "nanodimension" for application in molecular electronics, optical switching, and photovoltaic elements with the advantages of their size, efficiency of light- and electric field-controlled operation, robust structure, stability, and low cost production.

Rakovich, A., **Sukhanova, A.**, Lukashev, E., Oleinikov, V.A., Artemyev, M., Gaponik, N., Bouchonville, N., Molinari, M., Troyon, M., Rakovich, Y.P., Donegan, J.F. and Nabiev, I. (2010) *Resonance energy transfer improves the biological function of bacteriorhodopsin within a hybrid material built from purple membranes and semiconductor quantum dots*. *Nano Lett.* 10 (7), 2640-2648. **IF= 9.991**

Quantum Dots for Multiplexed Detection of Rare Cancer Cells



We show that multiparametric tool for rare tumour cells detection is likely to be developed and implemented in the emerging area of micrometastases (MMs) detection and early-stage cancer diagnostics. The early multiplexed and fast detection of many biomarkers simultaneously with high sensitivity and specificity made possible through this unique method will lead to improvement of patients' treatment outcomes and also to reduction of health care costs. Multiplexed QD-based diagnostics for MMs detection will make possible to implement high content analysis of antigen expression patterns of primary tumour tissue and MMs in parallel, which can potentially radically increase the informational value of the assays. This will elucidate differences in patterns and reflect individual molecular signatures of microinvasions and corresponding primary tumours. It would also allow for the interrogation of these cells for the

key features related to treatment responses.

Panel A. Micrometastases (MMs) analysed by flow cytometry and observation by fluorescence microscopy.

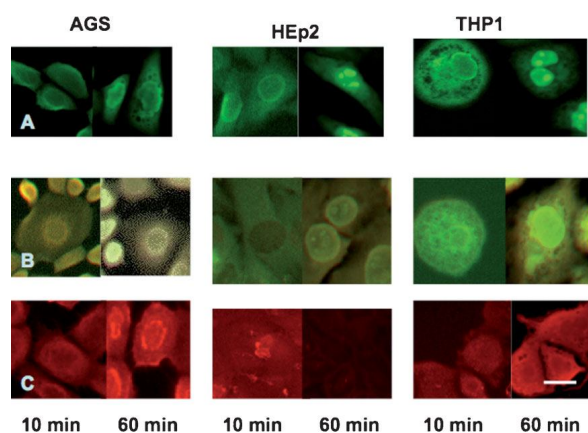
Panel B. Epithelial immunospot – EPISPOT assay showing breast cancer MMs.

Panel C. Cluster of breast cancer MMs detected by the CellSearch system. Anti-CK antibodies (Ab) are labelled with FITC (green).

Panel D. QD structure and fluorescence images corresponding to QD applications for diagnostics: (1) actin staining (green QDs) on fixed fibroblast cells; (2) live MDA-MB-231 breast tumour cells labelled with a red QD-Ab conjugate targeting the urokinase plasminogen receptor; (3) intracellular labelling of live mammalian cells using QD-Tat peptide conjugates; (4) frozen tissue specimens stained with QDs (targeting the CXCR4 receptor, red) and a nuclear dye (green).

Mahmoud, W., **Sukhanova, A.**, Oleinikov, V.A., Rakovich, Y.A., Donegan, J.F., Pluot, M., Cohen, J.H.M., Volkov, Y. and Nabiev, I. (2010) *Emerging applications of fluorescent nanocrystals quantum dots for micrometastases detection*. *Proteomics* 10, 700-716. **IF=4,426**

Quantum Dots for Crossing the Intracellular Barriers



We have demonstrated that the intracellular penetration and distribution of QDs is cell specific. Our data pave the way to targeted delivery of QDs or QD-based products to desired type of the cell. These results give rise to important considerations regarding the differential compartmentalization and susceptibility of organs, tissues, and cells to nanoparticles, and may be of prime importance for biomedical imaging and drug delivery research employing nanoparticle-based probes and systems.

Williams, Y. E., **Sukhanova, A.**, Davies, A. M., Oleinikov, V. A., Nabiev, I. Kelleher, D. and Volkov, Y. (2009) *Probing cell type-specific intracellular nanoscale barriers*

using size-tuned quantum dots. *Small* 5, 2581-2588. **IF=6.171**