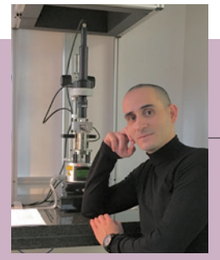

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Please replace [at sign] with @.

Research Interests

Atomic Force Microscopy, Nanomedicine, Nanotechnology, Physiology, Cancer Physiology

Education

2002	Doctor of Pharmacy and Physiology, Pharmacy and Medical Faculties of Münster University, Germany

Professional Career

2002-2006	Postdoc, Medical Faculty of Münster/Germany, and University of Cambridge UK
2006-2015	Associate Prof. and group leader, Inst. of Physiology II, Medical Faculty of Münster Univ.
2015 - present	Prof. for Physiology, Inst. of Physiology II, Medical Faculty of Münster Univ.

Honors

2011	Rolf-Dierichs-Stiftung, 'Innovative Medical Research' award at the Medical Faculty, Münster
2018	Distinguished lecturer of the year award' Medical Faculty, Münster

Publications

1. Liashkovich, I., Rosso, G., Shahin, V., (2019). Nuclear envelope permeability barrier as a fast-response intracellular mechanostat. Advanced Science, 2019 Aug 29;6(21):1900709. doi: 10.1002/advs.201900709.

2. Azzam, I., Liashkovich, I., Luchtefeld, I., Kouzel IU, Shahin, V., (2019). Facilitating plasmid nuclear delivery be interfering with the selective nuclear pore barrier. Bioeng Transl Med. 2019 Jun 22;4(3):e10136. doi: 10.1002/btm2.10136.

3. Kramer, A., Liashkovich, I., Oberleithner, H., Ludwig, S., Mazur, I., Shahin, V. 2008. Apoptosis leads to a degradation of vital components of active nuclear transport and a dissociation of the nuclear lamina. PNAS. 105:11236-41.

Facilitating nuclear delivery of pharmacological nanoparticles by interfering with the selective nuclear pore barrier

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Nuclear pore complexes (NPCs) are elaborate nano-transporters built from diverse proteins termed nucleoporins (Nups). They control all nucleocytoplasmic transport and form a stringent barrier between the cytosol and the nucleus. While selective nucleocytoplasmic transport enables translocation of macromolecules up to striking sizes approaching megadalton-scale, the upper cutoff for unselective diffusion is at 40 kDa. Elevating the cutoff is of particular importance for nuclear delivery of therapeutic nanoparticles that are destined to act inside the nucleus. We study compounds that interfere with the biophysical and functional properties of NPC. The ultimate goal is to raise the upper NPC cutoff for passive nuclear delivery to a substantial degree, relevant for therapeutic nanoparticles. We present two different classes of compounds that significantly lower the stringency of the NPC barrier, by two distinct modes of action, interfering with either the NPC channel barrier or the NPC scaffold. Our ongoing research reveals that former class facilitates nuclear delivery of 5kbp pDNA in up to 10-20% of the tested cells, compared to no delivery at all in control conditions. We envisage that the various tested compounds of this class may serve as lead substances and usher in the design of potent new strategies to increase nuclear delivery of therapeutic nanoparticles.

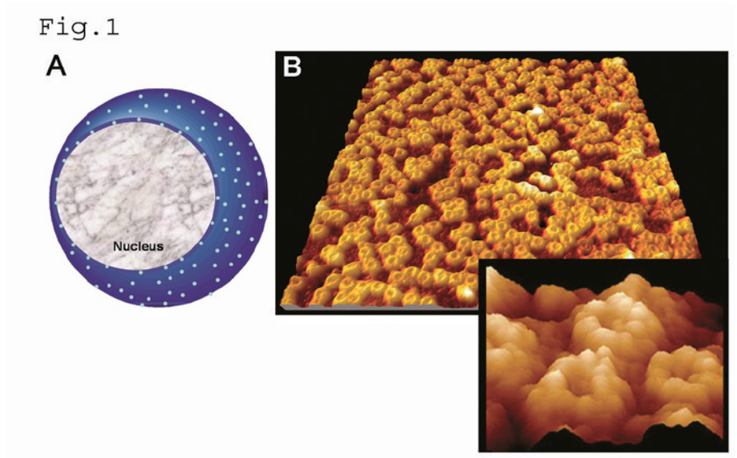

Fig. 1. A: Scheme of the cell nucleus. B: AFM images of the cytoplasmic face of the nuclear envelope (large image, 4 x 4 µm) and selected NPCs (magnification, bottom right, 280 x 280 nm) of Xenopus laevis oocytes.From: Shahin,V. (2006). The nuclear barrier is structurally and functionally highly responsive to glucocorticoids. BioEssays 28, 935-942.