NOVEL STRATEGY TO DISRUPT THE NUCLEAR PORE BARRIER REVERSIBLY: IMPLICATIONS FOR NANOMEDICINE

Victor Shahin, Westfälishe Wilhelms-Universität, Münster, Germany
shahin@uni-muenster.de
Gonzalo Rosso, Institute of Physiology II, Medical Faculty of University of Münster, Germany
Ivan Liashkovich, Institute of Physiology II, Medical Faculty of University of Münster, Germany

Several thousands of nuclear pore complexes (NPCs) perforate the nuclear envelope of each eukaryotic cell. These elaborate proteinaceous assemblies mediate all nucleocytoplasmic transport highly selectively through a central channel residing within a rigid and well-structured NPC scaffold. The selectivity of the NPCs is the major obstacle for non-viral gene therapy due to the prevention of exogenously applied therapeutic macromolecules from nuclear entry. Selectivity is attributed to highly dynamic and disordered Phenylalanine-Glycine rich proteins within the NPC central channel. The NPC scaffold poses an additional barrier-albeit ignored so far. We designed two distinct strategies to reversibly disrupt the NPC channel and scaffold in a separate fashion. Disruption of either is found to result in a significant increase of the NPC permeability and a combination of the two further intensifies the individual effects. The induced breakdown of the NPC permeability barrier may be exploited for gene therapeutic purposes.