

## **Reviewer report of the doctoral thesis**

**Author of the doctoral thesis:** Mariia Uzhytchak

**Title of the thesis:** Influence of functionalized nanoparticles of different sizes, materials, and surface properties on cellular machinery

**Reviewer:** Radek Šachl

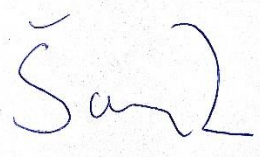
Nanomedicine has rapidly advanced in recent years, offering a growing array of potential applications such as nanoparticle-based drug delivery or non-invasive diagnostic imaging. However, this quick development has occasionally led to issues, including the withdrawal of some drugs from the market. These instances highlight the need for a deeper understanding of the molecular processes involved in nanoparticle-mediated drug delivery. This dissertation thoroughly addresses this need.

Specifically, in the study by Uzhytchak et al. (*Applied Physics Letters*, 2017), the authors demonstrate an efficient method for transporting superparamagnetic iron oxide nanoparticles into cells using strong magnetic pulses, enabling targeted magnetic labeling of cells. In a follow-up publication, O. Lunov, M. Uzhytchak et al (*Cancer*, 2019) employed this method to induce permeabilization of lysosomal membranes in cancer cells, enabling controlled induction of apoptosis. The underlying mechanism of this nanoparticle action was further explored by Uzhytchak et al. (*Cells*, 2020), who found that iron oxide nanoparticles cause lysosomal dysfunction, altering the subcellular localization of pmTOR and p53 proteins. Furthermore, in Levada et al. (*Nano Convergence*, 2020) the authors investigated the cytotoxicity of iron oxide nanocubes in human hepatitis cells, discovering that these nanoparticles induce autophagic flux rather than apoptosis. Finally, in Smolkova et al. (*Applied Materials and Interfaces*, 2021), the authors examined DNA-functionalized nanostructures and observed that cellular uptake is linearly dependent on cell size and can be enhanced by coating with the peptide aurein.

Overall, the dissertation is based on eight publications: five presenting original research and three offering comprehensive reviews of the dissertation topics. Notably, the candidate is listed as an author on a total of 25 publications, which is undoubtedly an exceptional achievement. I believe that all eight publications are pioneering works in the field with significant potential for scientific impact.

After a careful reading of the entire dissertation, I can only conclude that the PhD candidate Mariia Uzhytchak has comprehensively reviewed the literature, contextualized her dissertation within current scientific knowledge, and demonstrated a significant contribution to further development of nanomedicine through her own scientific work. I have no serious comments to make on the present dissertation and look forward to discussing the results of this dissertation in more detail during the defence.

In conclusion, I recommend the present dissertation for defence without any reservations and congratulate Mariia Uzhytchak on this achievement.



Radek Šachl

In Prague, 28th of May 2024