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Referee Report on Doctoral Thesis:

Titanium Dioxide – Phosphonate Assemblies as Medical Nanoprobes
by **Ivan Řehoř**

The PhD Thesis contains a comprehensive introduction to medical probes and related topics, clearly formulated aims, discussion of results related to each step given in the Aims section, and concluding remarks. The results are backed by two papers in impacted journals: J. Mater. Chem. (2009) has 1 citation according to the Web of Science (without autocitations, 1.6. 2011), the second paper has appeared this year in Eur. J. Inorg. Chem. The third paper describing biological results is presented in a submitted version to J. Med. Chem. The fact that I. Řehoř is a first author in all publications indicates his important contribution to the research work.

The goal of the PhD Thesis was to develop a system that combines two functions – a probe function due to the molecules for magnetic resonance and fluorescence imaging, and the photocatalytic function under UV irradiation caused by the carrier. Discussion is supported by experimental results and documents the focus on the main goal. To achieve it, there is a strong impact of synthetic chemistry, NMR analysis, analysis of luminescence properties of the probing molecules, and finally the applicability of the probes is documented by the successful labeling of cells. The presented results are new, performed under defined conditions and can allow to formulate the directions for future development in this area. The overall topic of the research is highly actual and I have no doubt that the presented results and discussion were performed on the high level.

I have the following questions concerning this work:

What is the advantage of a phosphonate group on DOTAPP and rhodamine-PPA? Is it related to the acido-basic properties of a phosphonate group? Sulfonate and carboxyl groups also strongly interact with the surface of TiO_2. Sulfonates deprotonate at low pH values, this might be interesting for binding on TiO_2 at acidic media used in this work.

What is the behavior of the dye on the TiO_2 surface? There are possible effects of aggregation, fluorescence quenching in interaction of the dye with the TiO_2 surface, etc. Were these processes observed? Does adsorption of the probes obey the Langmuir adsorption isotherm?

The photocatalytic effects of TiO_2 appear not very efficient when compared with the effect of UV without TiO_2. It can be due to the localization of nanoparticles in cells, the molecules attached to a nanoparticle surface (what happened with the probes after UV treatment?), etc. Can be the photocatalytic effects improved?

Which results obtained in this work are the most important for future development of these or similar systems?

In conclusion, the present thesis proofs author's capability of an independent scientific work and there is no doubt that this PhD thesis fulfills the criteria for obtaining a PhD degree. I recommend this work to be **accepted**.

Řež, June 2, 2011 Ing. Kamil Lang, CSc.