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## **Review of the PhD thesis: Immunocomplexes of IL-2 and anti-IL-2 mAbs as a novel class of selective and extremely potent immunostimulators**

In his PhD thesis Dr. Jakub Tomala summarizes the experimental data from three independent studies that focus on different aspects of in vivo effects of IL-2 immunocomplexes. Structure of the thesis is logical, well written and is easy to read. In the introduction author reviews current view on the biology and function of the most relevant interleukine immunocomplexes and summarizes previous work done on HPMA copolymer bound drug conjugates. Second part of the thesis is composed of three original articles published in first tier scientific journals. Dr. Tomala is the first author of the papers in the Journal of Immunology and International Journal of Cancer and coauthored a paper in the Cancer Research.

Study in the Cancer Research documents that the progression of BCL1 leukemia is associated by gradual increase of regulatory T cells.

Paper in the Journal of Immunology documents the capacity of IL-2 immunocomplexes to expand activated CD8 T cells and NK cells.

In the paper in the International Journal of Cancer authors further expanded their studies on the role of IL-2 immunocomplexes and show the synergic effect of combined therapy by HPMA copolymer bound doxorubicin and IL-2 immunocomplexes in mice tumor models.

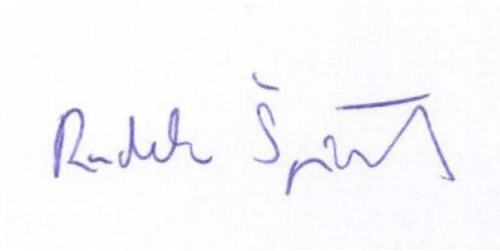
I have the following questions complementing the published reports:

- Given that all the studies reported in your thesis were performed in mice models what is your opinion on the effects of IL-2 immunocomplexes administration in humans?
- What would in your opinion the optimal timing of sequential chemotherapy and therapy with IL-2 immunocomplexes in order to maximize the therapeutic potential?
- Is administration of IL-2 immunocomplexes associated with detectable toxicity?
- Given the complex mode of action of IL-2 immunocomplexes described in your studies, what effector mechanism do you consider to be the most important one for observed anti-tumor effect?

During his PhD studies Dr. Tomala showed a proficiency in the vast number of methods as documented by three original articles in the first tier scientific papers. The results of his scientific projects clearly exceed the average level

of PhD candidates and he meets the requirements set by the Immunology board of PhD studies. I fully recommend that dr. Tomala is awarded the PhD degree in the field of immunology.

Radek Špišek

A handwritten signature in blue ink on a light blue grid background. The signature reads "Radek Špišek" in a cursive style. The first name "Radek" is written in a simple, slightly slanted cursive. The second name "Špišek" is more stylized, with a prominent horizontal stroke above the "š" and a sharp upward stroke at the end.