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**Re: Supervisor's report on Adela Fellnerova's Diploma thesis:
Chimeric antigen receptors in the treatment of hematological malignancies**

The study describes one of the first attempts in the Czech republic to construct a new type of a chimeric antigen receptor (CAR), an artificial molecule expressed on the surface of T cells, which is envisioned to be implicated in the treatment of B-lymphoma malignancies. The project was carried out as a collaborative effort between dr. Otahal, who initiated the development of this emerging and breakthrough technology in CZ, and our laboratory at IMG AS CR. The overarching idea was to link the expression of two CAR constructs targeting B cell surface molecules CD19 and CD20 into one vector (SuperCar) and compare its efficiency with individual CD19 and CD20 constructs. This would prevent "malignant escape B lymphoma mutants" from being undetectable by CAR immunosurveillance. This work provided a very broad platform for Adela to learn a plethora of molecular, recombinant and tissue culture techniques that are essential and indispensable for current translational research.

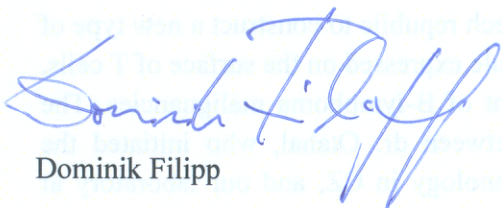
Adela Fellnerova joined my research group in 2014. She quickly adapted to laboratory life and routine. In the very first months she commenced to work on two relatively complicated projects both related to current approaches to modern immunotherapies: one focused on the Adoptive Cell Transfer (ACT) approach for the treatment of prostate cancer, the other on the CAR technology. And even though, only the latter topic is the subject of Adela's present thesis, she was able to master several basic as well as advanced and relatively complicated protocols used in modern immunotherapies.

In her thesis, Adela presents her original data documenting the step-by-step progress in the way to build a functional SuperCar. Her tasks were to identify the malfunctioning parts of originally synthesized SuperCar, find their suitable replacement, test their individual expression and activatory properties, mark them with traceable tags, and then, as a final step, co-ligate these parts into a SuperCar. Except the very last step, all of these sub-goals have been successfully achieved. The construction of the SuperCar has been delayed for several

technical reasons which could be, in the near future, overcome by preparing the whole functional SuperCar construct using synthetic approach. In aggregate, Adela's results document the path of developing new reagents for CAR immunotherapy and illustrate the variability of approaches how to test their properties and efficiencies. Irrespective of whether or not the results described in her thesis will be implicated into CAR research in CZ, Adela's thesis, in my view, represents well-appreciated research activity related to translational onco-research in the Czech Republic.

Adela Fellnerova is dedicated, diligent, accurate, and well organized student. Her work represents an initial step towards implementation of CAR technology into Czech clinics and an attempt to push the development of CAR technology forward. Various experimental approaches, clear presentation of results and a thorough discussion fully attest that Adela is well prepared for the scientific carrier she has chosen.

Based on the above review, I recommend Adela Fellnerova's thesis to be accepted as the fulfilment of the requirements for the degree of Master of Science.



Dominik Filipp