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Supervisor's review of PhD thesis

Author: Jakub Gemperle, Mgr.

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Title of the thesis: **Analyzing the role of the p130Cas SH3 domain in p130Cas-mediated signaling**

Jakub joined our lab in 2009 as a pre-graduate student with exceptional interest in cell biology and biochemistry. Under my supervision he defended his master thesis in 2012 with distinction. During his work in the lab he has worked on 3 projects with Src-p130Cas signaling as common denominator of all 3 projects. He started to work on project focused on regulation of p130Cas SH3 domain binding by Src-mediated tyrosine phosphorylation. Jakub was all the time a leading force in the project. He performed a phage display screen to identify a consensus binding site of p130Cas SH3 domain, helped to describe structure of CAS SH3 domain with bound ligand using NMR and exploiting the newly identified binding requirements of the CAS SH3 domain he predicted and experimentally verified several novel CAS SH3 binding partners, including PKN3. His second project was aimed to unravel the role of PKN3 kinase in Src-p130Cas-dependent cancer cell growth and invasiveness. He showed that PKN3 phosphorylates p130Cas, directly interacts with p130Cas and that PKN3-p130Cas interaction is important for cancer cell growth and invasiveness independently of Src transformation. Besides these two major projects led by him, Jakub was also involved in Src-FRET biosensor project. He helped to test the Src-FRET biosensor in vitro and established acceptor photobleaching method in the lab.

During the 9 years Jakub has adopted a variety of methodological approaches of molecular biology, protein biochemistry, structural biology and protein computer modeling, microscopy and cell cultivation. Among others I would like to point out generation of knock-out cell lines using a CRISPR-CAS9 approach, fluorescence live-cell imaging including FRET, large scale protein purifications and even took part in NMR data analyses.

I write this to the best of my opinion and I believe Jakub has demonstrated that he can successfully pursue his own scientific career and met all requirements to be awarded a PhD degree.

In Prague, 7th of December 2018

Doc. RNDr. Daniel Rösel, Ph.D.