Posudek školitele na diplomovou práci

☒ školitelský posudek	Jméno školitele: Jan Mašek, PhD
	Datum: 18/5/2025

Autor:
Bc. Eliška Trampotová

Funkční testování vlastností variant Jagged1 ligandu asociovaných s jaterními cholestázami
Functional assessment of the Jagged1 ligand variants associated with cholestatic liver disease

Zadané cíle práce, včetně tématu literárního přehledu:
JAGGED1 (JAG1) is one of the five Notch receptor ligands. It plays a crucial role in several developmental processes, such as angio– and vasculo– genesis, or bile duct and heart development. Deregulation of JAG1 signalling, if compatible with life, can result in developmental defects such as the Alagille syndrome (OMIM: 118450). Thorough assessment of JAG1 biological functions was the subject of a literature review.
The candidate's master's thesis project aimed to extend our understanding of the molecular mechanisms regulating JAG1 activity, via its intracellular domain. Project built on two JAG1 variants carrying missense mutations associated with Alagille syndrome and Biliary atresia in humans, but with unknown effects on JAG1 signalling properties. Despite targeting a similar region in the intracellular domain of Jag1, the two mouse mutants show recapitulating the mutations display opposing phenotypes, especially in liver vasculature (unpublished). Eliška's work aimed to test the mutated JAG1 ligand's capacity to interact with different Notch receptors using multiple reporter assays and cell types, and to assess the JAG1 variants' biological properties using WB and microscopy.

Přístup studenta k práci s literaturou:
There were no issues with how to use literature. Eliška can work with original articles very methodically, extracting only the most relevant information.

Přístup studenta k práci v laboratoři (přístup při učení se nových metod, aktivita, samostatnost, systematičnost práce i docházky do laboratoře):
Eliška's work in the lab was highly collegial yet independent. She has the necessary grit, obvious when preparing and testing the (unfortunately unsuccessful) Mib1-expressing cells. Her curiosity and capacity to learn new techniques became clear already when visiting the lab of our collaborator, David Sprinzak, in Tel Aviv in summer 2023.

Přístup studenta při sepisování práce:
Eliška picks up very quickly all the discussed concepts, and I had no issues with her approach to writing the thesis. One hiccup occurred when finalizing the discussion and changing the writing style from „results" to „discussion mode", which took her some time to grasp. Here I need to admit I feel I am to be blamed equally, as I, given Eliška's overall superb performance, assumed she would pick it up by herself on our regular journal clubs, and should have given honing this skill better attention.

Splnění cílů práce a celkové hodnocení:
The topic of Eliška's thesis is complex, focusing on the pathophysiological mechanisms in the setting of development. She approached it responsibly and energetically, generating a solid body of data. Several of her results were unexpected and thus led to follow-ups such as the optimization of new staining, which were beyond the initial plan of the project. The most recent experiments are preliminary and in need of repetition. These were included in the thesis as they represent exciting new avenues of the project, demonstrating Eliška's growing maturity in interpretation of data. Despite the incomplete shape of the evidence caused by technical delays, Eliška, in my view, succeeded in writing a well-balanced thesis, which I am happy to recommend for defense.

Návrh hodnocení školitele: ☒ výborně ☐ velmi dobře ☐ dobře ☐ nevyhověl(a)
Podpis školitele: