

Evaluation Report on the Diploma Thesis:  
**Structural insights into 14-3-3 dependent regulation of ubiquitin ligase Nedd4-2**

The diploma thesis by Bc. Andrej Tekel is written in beautiful English, I would almost say “in a modern Shakespeare-like English”. As such, it was very pleasant to read it. Typos are not present, however, there are few examples where the language contains laboratory slang (which also reads extremely well as I also work in laboratory but should be avoided in scientific publications). One example “In previous studies in our lab, we confirmed with shorter Nedd4-2 constructs that 14-3-3 indeed bind these sites and also found out 14-3-3 isoform specificities for these sites [63].” Should read: “In previous studies in our laboratory, we confirmed with shorter Nedd4-2 constructs that 14-3-3 proteins indeed bind these sites and also found out 14-3-3 isoform specificities for these sites [63].” Nevertheless, probably, language wise, the best diploma thesis I have read.

The thesis is traditionally divided into six chapters: Introduction (here termed Literature review), Aims, Materials, Methods, Results and discussion, Conclusion and has over ninety pages including citations. The Introduction is very well written and provides sufficient information about the background. Methods are well explained and Results well described. The thesis illustrates that Bc. Andrej Tekel has gained extensive experience in various biophysical methods AUC, SAXS and HD exchange. The main result of the thesis is a model of 14-3-3 dimer in complex with the phosphorylated Nedd4-2 ligase based on the SAXS data. **All together the thesis is excellent and I recommend it to be also graded as such.** Finally, I have one question for the discussion. Can you compare your model of the phosphorylated Nedd4-2:14-3-3 complex with one generated by the AlphaFold3? Are there any major differences?

All the Best in future carrier,

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