

Reply on CEC1

Stephan Grzesiek et al.

Author comment on "Imatinib disassembles the regulatory core of Abelson kinase by binding to its ATP site and not by binding to its myristoyl pocket" by Stephan Grzesiek et al., Magn. Reson. Discuss., <https://doi.org/10.5194/mr-2022-6-AC1>, 2022

We thank the chief editor of MR for this comment highlighting the importance of fair and transparent discussion of scientific results. It is clear that errors are inevitable in the scientific process of knowledge creation. While this is annoying, it is not fatal as science corrects itself and wrong results do not persist as they don't pass the tests of others trying to reproduce them.

We want to comment on several statements:

1. We did not write this small note because we are hurt as competitors, but we wrote this note for two reasons:

- We continue to study the activation mechanism of Abl in several directions and will not be able to publish this work, if the erroneous claims in Xie et al. 2022 remain uncorrected.
- We feel very privileged as scientists in academia funded by tax payers' money to pursue our curiosity and create new knowledge without having to worry about our material needs. We believe that this privilege also contains the obligation to keep the process of knowledge creation working properly. If we don't do it, who else should do it? We understand this note as part of this effort and hope that it will help the scientific progress.

2. We always wanted a fair, transparent exchange with the Kalodimos group about our differing results and interpretations.

3. The chief editor comments that the HSQC data presented in this note do not prove that imatinib binding to Abl's ATP site disassembles the core. It is true that the HSQC data by themselves do not prove this. However, we have given multiple evidences in previous publications on the very same Abl core construct that imatinib binding to the ATP site disassembles the Abl core. These data comprise ^{15}N T_1 and T_2 relaxation data, RDC data, ^1H - ^{15}N chemical shifts for 286 residues covering ~80% of the SH3 and SH2 domains and ~60% of the KD of the Abl⁸³⁻⁵³⁴ construct, as well as completely orthogonal SAXS data. The current note shows that the ATP site binding and the disassembly follow the same strong affinity that is expected for imatinib ATP site binding. We are currently preparing a revised manuscript in response to this comment and the comments of the other referees. In the revised version, we will detail the previous findings more clearly in a significantly

enlarged introduction.