BIOLOGICAL CRYSTALLOGRAPHY
ISSN 1399-0047

Responses to *Crystallography and chemistry should always go together: a cautionary tale of protein complexes with cisplatin and carboplatin*

Todd O. Yeates*

Department of Chemistry and Biochemistry, University of California, Box 951569, Los Angeles, CA 90095-1569, USA. *Correspondence e-mail: yeates@mbi.ucla.edu

Received 16 July 2015
Accepted 29 July 2015

Keywords: cisplatin; carboplatin; response.

In this issue of *Acta Cryst. D*, Shabalin *et al.* (2015) critique and re-evaluate dozens of crystal structures in the PDB in which proteins are bound to the platinum compounds cisplatin or carboplatin. Investigators whose structures were critiqued were contacted and several wrote comments in response. Through all those comments there was much agreement with certain sentiments expressed by Shabalin *et al.*, including the idea that identification and refinement of metal ligands (and other unanticipated molecules in a crystal) is often extremely difficult. There was a shared opinion that greater vigilance and further tools for validation are needed. Shabalin *et al.* offer challenges to previous structural interpretations that vary in their severity. One end of the spectrum concerns cases where difficult decisions were required about whether or not to model a ligand into relatively weak features in an electron-density map. For example, in one protein that was re-examined (SOD), Shabalin *et al.* conclude that a missing fourth ligand to one of the Pt atoms should have been included but was not, and that a ligand to another Pt atom was included where the electron density was too weak for accurate modeling. They express similar opinions in their re-examination of RNase. Responses to Shabalin *et al.* in these two cases by A. Merlino, L. Messori, V. Calderone and S. Mangani include concessions on at least one point, that platinum is four-coordinated in the SOD structure; its omission by the original authors was a modeling decision or oversight not intended to convey that platinum was actually three-coordinated. In addressing other challenges such as whether reported ligands to platinum were reliably modeled, the responders maintained that their original assignments reflect plausible interpretations of electron density. At the other end of the critique spectrum, Shabalin *et al.* identify specific errors and arrive at alternate interpretations after re-refining the crystal structures of some other proteins bound to platinum compounds. These include ATOX1 and hen egg-white lysozyme. Here, Shabalin *et al.* offer challenges to the assignment of electron-density features to platinum atoms *versus* other metals, the identification of the ligands to platinum, and the modeling of various buffer constituents in the crystal structures. Owing to the specific re-interpretations offered by Shabalin *et al.* in these two cases, responses from the original investigators are published in this issue (Tanley *et al.*, 2015; Boal & Rosenzweig, 2015). Irrespective of the

particular findings and conclusions in these studies, the take-home lesson is clear that we must be ever more vigilant in protecting and improving the veracity of the structural and chemical information in the PDB so that it will stand as one of the most valuable (and hard-won) repositories in modern science.

References

Shabalin, I., Dauter, Z., Jaskolski, M., Minor, W. & Wlodawer, A. (2015). *Acta Cryst.* D**71**, 1965–1979.

Tanley, S. W. M., Diederichs, K., Kroon-Batenburg, L. M. J., Levy, C., Schreurs, A. M. M. & Helliwell, J. R. (2015). *Acta Cryst.* D**71**, 1982–1983.

Boal, A. K. & Rosenzweig, A. C. (2015). *Acta Cryst.* D**71**, 1984–1986.