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Response from Tanley *et al.* to *Crystallography and chemistry should always go together: a cautionary tale of protein complexes with cisplatin and carboplatin*

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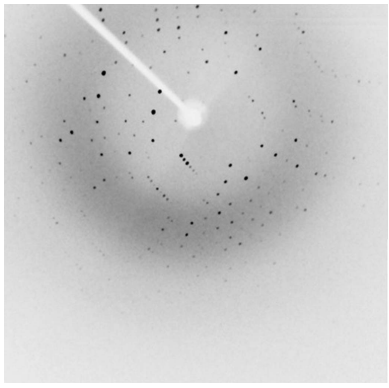
Clearly cisplatin and carboplatin and their interactions with proteins are important as is shown by the various research groups that are actively involved studying these X-ray crystal structures, and which are focused on in the critique article by Shabalin *et al.* (2015). We welcome this detailed interest by Shabalin *et al.* in these various crystal structures in the PDB and for harnessing the processed structure factor and derived atomic coordinates data. We have also made available numerous raw diffraction image data sets as due diligence for researchers in this area. Some of these have been harnessed. We aim to complete the availability of the full suite of raw data sets as soon as possible. The suggestions of Shabalin *et al.* (2015) of the need for improved tools in model validation, especially for metal protein ligand complexes, we also support. Some of the tools that are discussed by Shabalin *et al.* (2015) are not yet available in *e.g* the *CCP*4 suite, which we use predominantly. We also have used the *SHELX* suite for metal occupancy refinements as a complement to *CCP*4.

The predominant criticisms of our publications by Shabalin *et al.* (2015) involve our model refinements of hen egg-white lysozyme with various platin metal ligand types. These model refinements are the work and responsibility of SWMT and JRH. We wish to note that we did not use the incorrect PDB ligand for cisplatin cited by Shabalin *et al.* (2015) and instead used individual atom placements not least for the tendency for the chemical transformation of these two platins that we observed.

Shabalin *et al.* (2015) shared with us their three new refinements, with a brief e-mail commentary, ahead of their publication. These three new model refinements showed differences in approach between our and their methods, namely a larger placement of split occupancy side chains than we had made and placement of a larger number of bound waters. We did not accept the bulk of these changes as there was insufficient, if any, electron-density evidence. However, we do agree with their critical scrutiny of our bound solvent/solute molecules, highlighted in their article, and the need for some assignment changes or deletion. We note that on these the PDB annotators were very thorough and did offer queries in some cases. SWMT and JRH discussed these but thought that the precision of their placement was poor and the rather



rigidly applied clashes checks, *i.e* as if these solute molecules were perfectly known, were in themselves not correct. So, for those electron-density 'blobs' we chose to include molecules in our coordinate files but, as a lesson learnt by us from the studies with our data by Shabalin *et al.* (2015), we would in future prefer not to assign a choice of solute molecule to them where we cannot be certain. Indeed, we already applied this principle in Fig. 2 of Tanley *et al.* (2014) and from which we quote *We have placed atoms where we are confident of their assignment, namely the histidine, the bromines and the platinums. At the extreme left the density is less easily interpretable*. Unfortunately, an attempted assignment of four light atoms to that 'less easily interpretable density' was left in the deposited PDB file. Shabalin *et al.* (2015) highlight this intra-ligand clash.

In conclusion, we agree with the need to revise the three PDB files for which Shabalin *et al.* have deposited their own files with the PDB, namely 4yem, 4yen and 4yeo. However, since we cannot agree with some of the changes made by Shabalin *et al.* we see no option but to revise our own files *i.e.* as distinct from those three of Shabalin *et al.*.

We believe that as a process of realising a 'living PDB', which we support, it would be optimal for such revisions to be made by collaboration in that it would more likely lead to a single revised PDB file rather than ending up with multiple versions. To that end we have offered the PDB suggestions for how this might be approached in future.

References

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