



Response to *Errors in Crystal structure of HINT from Helicobacter pylori*

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A response is published to a Letter to the Editor by Maize [(2016), *Acta Cryst.* **F72**, 336–337].

We appreciate and thank Ms Maize for showing interest in our article (Tarique *et al.*, 2016), for writing such a comprehensive critique in her Letter to the Editor (Maize, 2016), and also for raising this issue in the general interest of the scientific community.

Looking at the previous literature for HINT proteins, the nature of this protein has been the topic of much debate as no direct biological function of the protein was known. There are two different views on this protein. Previously, one group of researchers was of the opinion that HINT and PKCI are very similar but that the latter binds and inhibits protein kinase C, while the former does not. Gradually over a period of time the opinion was formed that they are the same protein and the notion that it binds and interacts with protein kinase C is unproven. However, in the literature the nomenclature for this family of proteins has been found to be repeatedly interchanged. The confusion arises from the annotation of this protein in the respective genomic database of the organism where it is still named as protein kinase C interacting protein, which should also have been annotated as HINT.

The confusion arises again from the various PDB entries where the same protein was named as PKCI in one entry and HINT in another. Even the latest HINT entry from *Entamoeba histolytica* has again used the term PKCI and described it as a separate branch of HINT. Even the link maintained by NCBI classifies the HINT subgroup and PKCI related protein as a separate branch of the HIT family (<http://www.ncbi.nlm.nih.gov/Structure/cdd/cddsrv.cgi?uid=238607>). Interestingly when we first cloned HINT from *Helicobacter pylori* it was annotated as PKCI in the NCBI gene bank (<http://www.ncbi.nlm.nih.gov/gene/898890>). Even the kegg database classifies HINT from *H. pylori* as PKCI (http://www.genome.jp/dbget-bin/www_bget?hpy:HP0404). The ensemble bacterial genome database again classifies HINT from *H. pylori* as PKCI (<http://ensemblgenomes.org/id/AAD07473>).

Lorimer *et al.* (2015) also mentioned that ‘EhHIT is similar in amino-acid sequence to proteins that have been given the designation protein kinase C inhibitor-1 (PKCI-1). This HINT branch has also been identified to contain purine nucleoside- and nucleotide-binding proteins’ (3oxk; Lorimer *et al.*, 2015).

As HINT and PKCI are the same then, in our opinion, we prefer not to use the term PKCI at all, even though it is used continually in other places. In the manuscript by Tarique *et al.* (2016) both old and new references were used and it was inferred that HINT and PKCI are different proteins but with very similar structure. However, we are thankful to Ms Maize who has raised and resolved this issue.

We agree that the substrate for HINT was mistakenly written as phosphoramidite (a typographical error) that should have been written as phosphoramidate.

References

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