平成 20 年 5 月 29 日
独立行政法人理化学研究所
播磨研究所　研究推進部

城生体金属科学研究室　研究業績レビュー（中間レビュー）報告

【対象研究室】
放射光科学総合研究センター　城生体金属科学研究室　城 宜嗣 主任研究員

【実施日】
平成 20 年 1 月 25 日

【レビュアー】

渡辺　芳人	名古屋大学　物質科学国際研究センター
青野　重利	自然科学研究機構　岡崎統合バイオサイエンスセンター
Michael Waterman	Dept. of Biochemistry, Vanderbilt University
齋藤　正男	東北大学　多元物質科学研究所

【レビュー結果の要約】

城研究室は in vitro において多くの生体金属タンパク質の機能と構造の研究において成功している。この仕事が国際的に注目され続けていることは間違いなく、主要な国際会議に研究室メンバーが招待を受けていたり、著名な雑誌に多く掲載されていたりすることからも、革新的で科学的重要性が高いということがうかがえる。

城主任のマネジメント能力は卓越しており、若手研究者のトレーニングにも尽力している。メンバーについても活動的で、准教授レベルが輩出されている。さらに、城研の多くのプロジェクトは豊富なファンドを受けている。

将来計画はよく練られ、困難なものもあるが、城主任のこれまでの成果を鑑みれば成功の可能性は高い。理研や SPring-8 では構造生物学は大きな部分を占めるが、もっと細胞学や分子生物学と融合することがより効果的だろう。

【放射光科学総合研究センター長による指摘事項への対応】

城主任は、非常に一般的なスタイルで研究を進めているので、レビュアーの理解度は高い。今後ともこの方向で進めるか、独自性を出していくかはご本人の選択だろうと考えるが、最終レビューまで現在の研究スタイルで進むことで可である。

【レビュー結果概要】

- The strategy of his research is clear and well designed. He has achieved very good results in his research and contributed to the progress of the research field of bioinorganic chemistry.

- The number of the original papers he has published from 2000 to 2007 is 121. In each of these cases the work has been published in the leading journals, which clearly shows that both of the productivity and quality of his research are top level in world standard. The international recognition of this laboratory is outstanding both in terms of novelty and scientific significance as clearly demonstrated by the number of important meetings around the world in which members are invited to participate. The high quality publications from the laboratory demonstrate both the originality and scientific significance of their work.

- More importantly, many projects of the group have been supported by MEXT Grants, indicating that the originality and novelty of projects conducted by this group are also highly appreciated by peer reviewers.

- Dr. Shiro's work on IDO is the first structural determination of heme-containing dioxygenases in the world, which will be the beginning of the fully understanding of the structure-function relationships of heme-containing dioxygenases.

- His works on cytochrome P450-type nitric oxide reductase (P450nor) and P450 peroxygenase are also very interesting because these P450-type enzymes are very unique compared with other P450s. He has determined the crystal structures of these unique P450-type enzymes and elucidated the reaction mechanisms of them. These results have opened a door for the research of P450s to a new stage.

- The X-ray facilities of the SPring-8 have been serving very much for these research projects. In addition, metalloproteins related to signal transduction are currently getting very important issue, while studies in this area are still pre-mature. Thus, the group is focusing their efforts on this subject. In conclusion, the research objectives as well as the results are very novel and significant. $P450_{BSb}$ is a highly potent heme enzyme as an oxidation catalyst applicable to industrial use, while it still needs more work.

- Following this exciting success, he has solved crystal structures of novel P450 enzymes and this has put him one of the front runners in the field of P450 studies, despite the fact that he started P450 structural biology much later than many other investigators. More important accomplishment is the crystal structural determination of a dioxygenase, indole amine dioxygenase, which is not only one of the central enzymes in tryptophan metabolism but also recognized as one of the important players in clinical cancer biology.

- The future plans are well-thought out based on what has been accomplished. Some might be tricky. But based on his accomplishment, likelihood of success appears to be high. Given the proximity to SPring‐8 and being in Riken, structure biology occupies a fairly large portion in this planned research. I think, however, that his research activity would be benefited by incorporating more “cell and molecular biology”. This will strengthen the structural biology component by clarifying physiological and biological significance of his future projects.

- The background of his group members is chemistry or biochemistry. If there are some scientists with the background of biology and medical science, it will be very beneficial for his group to expand his research. Certainly stronger collaboration with the Cell Biology Program at RIKEN might be desirable as would be recruiting investigators into the Biometal Science Laboratory at a tenured level in hopes of maintaining consistent biological background for the work by the protein chemists.

- The management by Dr. Shiro is really outstanding, i.e., many of the Lab members have been promoted at the associate professor level and junior researchers in the Lab are very active. Young scientists in his group are motivated to do good science.