MS5-P10 Study of metal coordination sphere parameters derived from the open access Crystallography Open Database

Antanas Vaitkus[1], Andrius Merkys[1], Saulius Gražulis[1,2]

1. Vilnius University Institute of Biotechnology, Saulėtekio av. 7, LT-10222 Vilnius, Lithuania
2. Vilnius University Faculty of Mathematics and Informatics, Naugarduko 24, LT-03225 Vilnius, Lithuania

email: antanas.vaitkus90@gmail.com

Metal coordination sites in proteins have been a subject of research for several decades now. Numerous works with the interest in specific chemical elements as well as wider scope databases have been published both on-line and off-line. Usually one of the two approaches is taken when compiling the datasets – the results are either calculated directly from the protein structures or they are derived from the structures of small molecules. In most cases the same data processing algorithms can be applied with minimal modifications; however, it is the data source that plays a far greater role than it appears at first glance.

The most popular protein structure data source for this kind of calculations is the Protein Data Bank (PDB) database. Among the benefits of using the PDB is its open access nature that allows any interested parties to check and reproduce the published results. However, the PDB is not drawback-free either; for example, grouping structures by the type of coordinating metal often results in unsatisfactory sample sizes.

The use of small molecule structure data sources presents an almost mirror image of the pros and cons – the number of high resolution structures containing metal coordination spheres is much greater, but all of the data sources used in this type of research so far are proprietary databases and as a result makes the research unreproducible without acquiring the database license.

To overcome this limitation the open access Crystallography Open Database (COD) was used as the source to automatically compile a set of metal coordination sphere parameters. The entire COD was scanned for structures containing metal coordination spheres and the selected entries were further processed by calculating coordination parameters such as the coordination number, ligand-metal-ligand angles and metal-ligand distances, as well as comparing the configuration of the coordination sphere with a list of idealised geometry templates.

The gathered results are accessible via the MySQL database interface as well as an interactive website where the coordination sphere information can be viewed grouped by a combination of various parameters like the chemical type of the coordinating metal, the chemical type of the coordinated ligands and the best fitting idealised geometry. An option to produce a normal distribution mixture model of the examined interatomic distances and angles is also provided.

Keywords: Metal coordination spheres, database

MS5-P11 Structural and functional studies of the *Mycobacterium tuberculosis* VapBC30 toxin-antitoxin system

Sang Jae Lee[1], In-Gyun Lee[1], Bong-Jin Lee[1]

1. The Research Institute of Pharmaceutical Sciences, College of Pharmacy, Seoul National University

email: sjlee33@snu.ac.kr

Mycobacterium tuberculosis is the causative agent of tuberculosis and contains an unusually high number of VapBC systems. The VapBC system, which is implicated in dormant state formation, virulence, and stress response, is an interesting target for the rational design of an antimicrobial peptide against tuberculosis. Here, we report that the *M. tuberculosis* VapC30 toxin regulates cellular growth through both magnesium and manganese ion-dependent ribonuclease activity and is inhibited by the cognate VapB30 antitoxin. We also determined the 2.7-Å resolution crystal structure of the *M. tuberculosis* VapBC30 complex, which revealed a novel process of inactivation of the VapC30 toxin via swapped blocking by the VapB30 antitoxin. Our study on *M. tuberculosis* VapBC30 leads us to design two kinds of VapB30 and VapC30-based novel peptides which successfully disrupt the toxin-antitoxin complex and thus activate the ribonuclease activity of the VapC30 toxin. Our designed peptides mimic the helical regions of the VapB30 or VapC30 in the heterodimer interface of the VapBC30 complex, and they were capable of disrupting the interactions between VapBC30 complex *in vitro*. Our approach may form a foundation for the design of antimicrobial peptides targeting toxin-antitoxin systems, and the designed peptides may prove to be viable candidates in the development of anti-tuberculosis drugs.

Keywords: Rv0623, Rv0624, toxin-antitoxin systems, VapBC30, antimicrobial peptides, Mycobacterium tuberculosis