Deciphering the Structure of The Condensin Protein Complex

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Short Abstract — **Understanding chromatin organization within the nucleus is a key question in cell biology. Despite recent progress, little is known about the mechanisms underlying chromatin structure and how it can be established. One prominent hypothesis suggested is that loop-extrusion motors bind and translocate segments of chromatin to form structural loops. Such motors are proposed to be Structural Maintenance of Chromosomes (SMC) - Kleisin protein complexes.**

Here, we use Direct Coupling Analysis (DCA) to reveal the full structure of the condensin protein complex. We demonstrate that this methodology predicts coevolved residue-residue interactions between the different components of the complex. These are used to predict the full structure of SMC complexes, for which only limited experimental data exists. This work serves as pioneering study to understand the establishment of chromatin architecture.

***Keywords* — condensin, cohesion, chromosome, cell replication, direct coupling analysis, co-evolution**

I. BACKGROUND

MEMBERS of the structural maintenance of chromosomes (SMC) and kleisin families of proteins are conserved in all domains of life and have key roles in the maintenance of chromosomes [1]. One such protein complex is cohesin, which has several critical biological roles. It has been suggested that cohesin organizes DNAs into chromatids by capturing small loops of DNA and then extruding them in a processive manner [2]. Similar to eukaryotes, the condensin complex in prokaryotes is also part of SMC-kleisin family. Condensin is formed by SMC-kleisin proteins SMC and ScpA, respectively, and a third subunit, ScpB [2]. Despite major progress in recent years, many questions related to the structure and function of SMC-kleisin complexes remain open. Importantly, the complete structure of SMC-kleisin complexes has yet to be established. The two main models of the structure of these complexes are: (1) two rings acting as a pair of molecular "handcuffs" in which each embrace one DNA single, or (2) a single ring that embraces two DNA strands. Although limited structural data exist for each subunit of the condensin protein complex [3-4], these cannot capture the dynamics and reveal interaction surfaces in details, and therefore are limited in their ability to disentangle the various controversies of the complex.

II. RESULTS

Here, an integrative approached was used by combining previously known crystallographic data with evolutionary information in order to study a series of controversial features of the condensin protein complex [5-6]. Combined with molecular dynamics (MD) simulations, we are able to predict the full structure of the previously unknown condensin complex. This allows us to:

A. *Construct the full structure of condensin*

Taking advantage of existing experimental data, we use extract both homologous sequences and experimentally known structures. Direct coupling analysis (DCA) then run predicts a contact map, revealing the interprotein residue contacts between all constituents. To obtain the complete structure of the condensin complex, we use the subcomponents and dock them guided by the DCA top contact predictions.

B. Examine the plausibility of higher-order stoichiometries

Having established a full DCA contact map, we examine whether our DCA contact predictions remain preserved in higher order stoichiometries of condensing while comparing their stability with the previously obtained structure.

C. Reveal alternative configurations

Specific domains in the complex are suggested to serve as entry and exit gates for DNA, respectively. Our results manage to predict the rearrangement of these domains, which may lead to the opening of the ring in the presence of DNA. Moreover, the flexibility of ScpA subunit projects on the overall structure of the condensin complex, allowing possible interaction with the DNA strand and its release from the ring.

III. CONCLUSION

In this project the full all-atom structure of the condensing protein complex is revealed. Using our integrated methodology of existing experimental data with co-evolution information, we are able to study a series of controversial features of the condensin protein complex. Hence, this study serves as key foundation for the system-level study of the various SMC-kleisin protein complexes.

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