Characterization of the Cohesin Complex in Neurospora crassa

Chaney Hart[1], Vincent Bicocca[1,2], Eric Selker[1,2]

University of Oregon[1], Institute of Molecular Biology[2]

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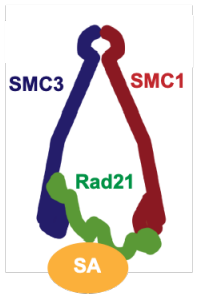
Introduction

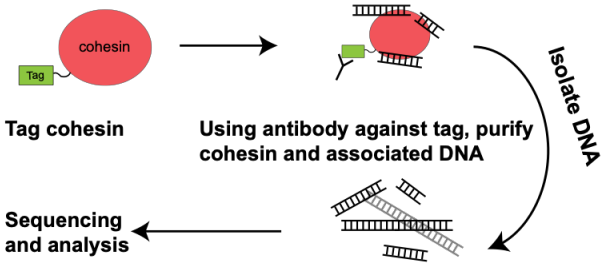
The protein complex cohesin (left) is able to manipulate the stru cture of the genome due to its ring-like shape[1]. While not fully understood, cohesin impacts diverse genomic functions such as genomic structure and gene expression. It is thought that this underlies the prevalence of cohesin mutations in various forms of cancer[2]. One of the challenges limiting our fundamental understanding of cohesin is that the patterns of how and where it interacts with the genome vary widely between organisms.



Aim

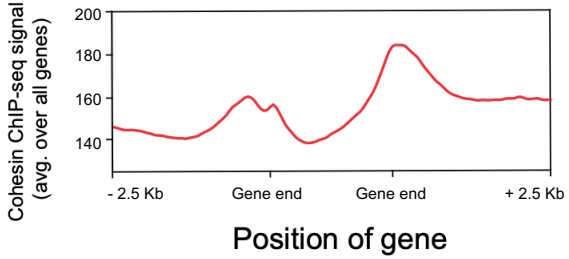
In order to learn more about the factors that influence cohesin's positioning and function, I took the first steps in characterizing the complex in an important model organism of genomic function in which cohesin has not been studied - the filamentous fungus *Neurospora crassa* (right).

ChIP-seq



Cohesin's genomic localization was characterized by chromatin immunprecipitation of cohesin tagged with a FLAG epitope followed by whole genome sequencing (ChIP-seq).

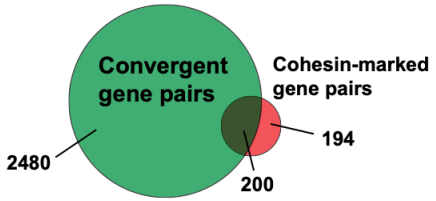
Cohesin associates near the end of genes



ChIP-seq data averaged over all genes in the N. crassa genome shows that cohesin preferentially associates with the transcription start site and the trancription end site of genes. It' s enrichment is particularly strong in the latter case.

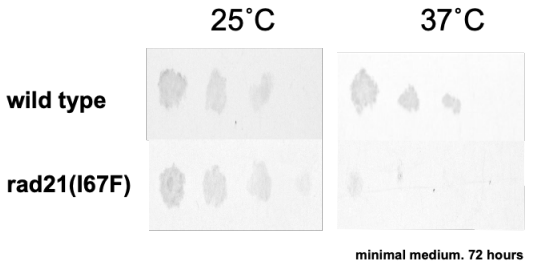
Cohesin is enriched at convergent genes

A pair of convergently transcribed genes



Cohesin is detected at 200 of the 2480 convergent gene pairs in N. crassa which is significantly more more than expected by chance.

Temperature-sensitve cohesin mutation



Due to its essential function, deletion of cohesin is lethal. However, cohesin can be abrogated in Neurospora crassa by subsituting isoleucine (I) 67 of cohesin subunit RAD21 with phenylalanine (F). The resultant strain is viable at room temperature but does not survive cohesin impairment at 37˚C.

Discussion

My findings that cohesin is enriched at the end of genes and at convergent genes is consistent with what has been observed in another widely studied organism, fission yeast[3]. Additional studies are needed to determine the implications of this pattern on important functions of the cohesin complex such as gene regulation and genomic organization. The temperature-sensitive cohesin mutant I developed will be invaluable in future investigations of cohesin in *N. crassa.*

References

1. Gligoris, T., Lowe, J., *Cell*, 2016.
2. Viny, A.; Levine, R., *Current Opinion in Hematology*: 2018.
3. Schmidt, C. K. *et al.*, *Genome Biol.* 2009.

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