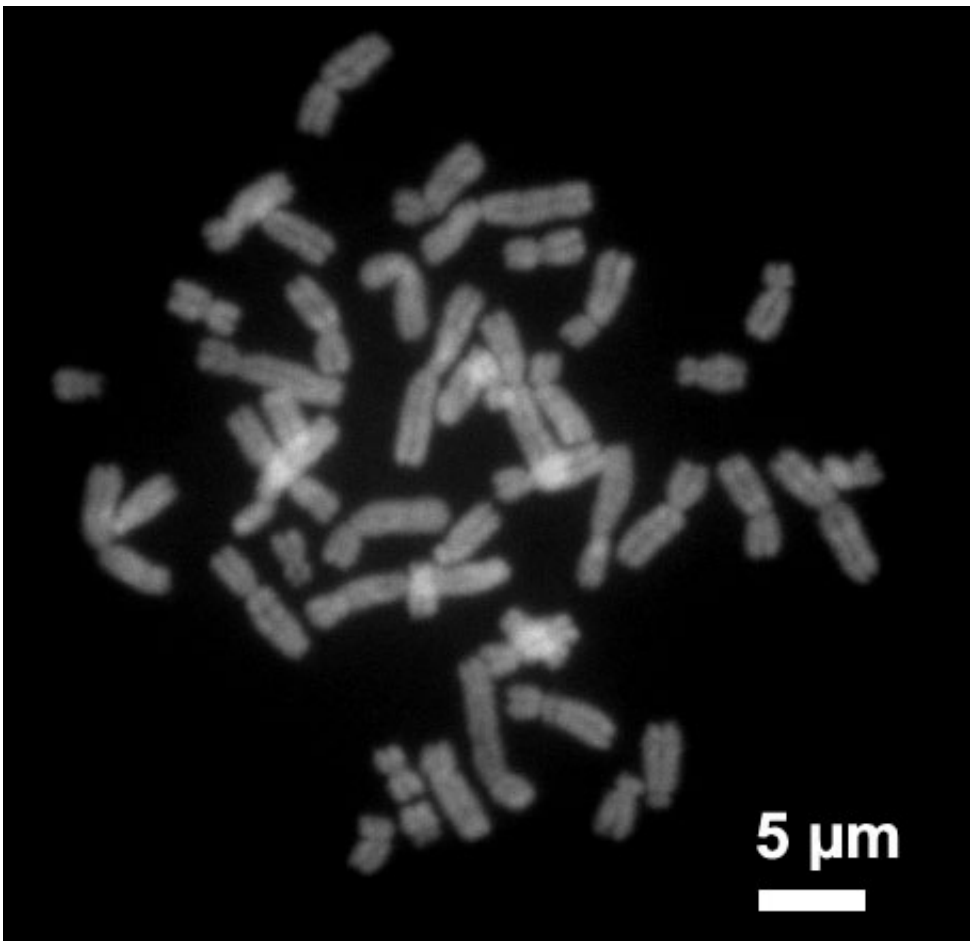
Scientists discover how key proteins segregate vital genetic information during mitosis

August 6 2015



Human chromosomes during metaphase. Credit: Steffen Dietzel/Wikipedia

Chromosomes are responsible for carrying our genes and essentially

protecting the information that helps ensure normal, healthy growth, with vital instructions being passed on from cell to cell by a process known as mitosis. While this copying mechanism has been well understood for decades, scientists have been unable to describe exactly how genetic information is protected and properly segregated as mitosis is happening.

Now, new research from The Wistar Institute has identified an interaction between proteins that provides a pivotal role in organizing chromosomes so that vital genetic information gets passed on safely.

The results of the study were published online by the journal *Molecular Cell*.

To understand how dividing cells protect and faithfully segregate genes that have been transcribed, researchers focused on a protein complex found in human cells called condensin. This set of proteins helps compact more than 20,000 protein-coding genes in the human genome into something that can fit inside the nucleus of each of our cells. Recent studies have found that condensin genes are heavily mutated in various cancers. These mutations promote cancer-causing processes through dysregulation of gene expression as well as chromosomal instability.

Ken-ichi Noma, Ph.D., associate professor in Wistar's Gene Expression and Regulation program, studies how disorganization of a cell's nucleus can lead to cancer. Identifying the relationships between proteins that are responsible for protecting chromosomes is a crucial step in learning more about some of the first disruptions of our genes that result in disease.

"How condensin is able to assemble the specific structure of mitotic chromosomes and how this organization promotes segregation during mitosis are two significant questions that have faced those of us working

in genome biology," Noma said. "We believe this study provides a molecular basis for these important questions."

Previously, Noma's lab showed that many genes are connected to centromeres. Centromeres are sites where two chromatids - copies of newly replicated chromosomes - are positioned to be properly split up during mitosis. Condensin mediates the clustering of RNA polymerase III-transcribed genes (abbreviated Pol III genes) and Pol II-transcribed "housekeeping" genes that are necessary for every cell to function properly. However, scientists did not know exactly how the condensin was being recruited to aid in this process.

In this study, Noma and his colleagues identified the interactions of proteins that link condensin and mitosis. By studying mitosis in yeast, they were able to identify a subunit of condensin called Cnd2 that binds directly to a protein called the TATA box-binding protein (TBP). TBP is a general transcription factor required for every type of transcription. When Cnd2 binds to TBP, it recruits condensin onto Pol III genes and Pol II-transcribed housekeeping genes. When this happens, condensin tethers these genes to the centromeres so that when mitosis occurs, the genetic information remains protected and intact as the chromatins are split apart.

"This genome-organizing mechanism contributes to effective transmission of important genetic materials during mitosis," Noma said. "By gaining a better understanding of this essential process, we can now study the origins of diseases that arise when this phenomenon is disrupted."

"This is a very elegant example of how Wistar science can broaden our understanding of basic mechanisms of important biologic processes, in this particular case, chromosomal segregation during cell division," said Dario C. Altieri, M.D., president and CEO of The Wistar Institute and

director of The Wistar Institute's Cancer Center. "The information obtained from this type of work is pivotal for a better understanding of human diseases and potential new therapies."

Provided by The Wistar Institute

Citation: Scientists discover how key proteins segregate vital genetic information during mitosis (2015, August 6) retrieved 27 June 2024 from https://phys.org/news/2015-08-scientists-key-proteins-segregate-vital.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.