Study explores role of mediator protein complex in transcription and gene expression

September 10 2019

PhD student Alejandro Saettone. Credit: Ryerson University

Did you know that the DNA in any cell of the human body—or any organism for that matter—contains the genetic information required to develop every possible type of cell within that organism? Yet cell types differ markedly from each other both structurally and functionally. This

is manifest through the production of different proteins encoded in the genetic information of the cell.

How is the information in DNA expressed as different proteins in diverse cells, such as those in a human liver, brain, heart or, maybe more pressing to ask, in a cancerous tumour?

This kind of fundamental question is the focus of molecular biologists, particularly those with an evolutionary bent, who seek to understand how life evolved and how gene expression and cell development occur.

Dr. Jeffrey Fillingham, an associate professor in the Department of Chemistry and Biology at Ryerson University, and Dr. Ronald Pearlman, University Professor Emeritus in the Department of Biology at York University, are just the sort of molecular biologists who ask these basic questions. Among their areas of interest, the two researchers study transcription and gene expression.

"Transcription is the process by which the information contained in DNA is turned into RNA, which carries the messages that direct the synthesis of proteins involved in making a particular cell," says Pearlman. "The question is, 'how, when, why and where are genes activated so they can be transcribed into cell-specific proteins?'"

Recently, a team based at Fillingham's Ryerson research lab in the MaRS Discovery District explored this question, working with researchers in Pearlman's group at York University and supported by others in Dr. Jack Greenblatt's research group at the University of Toronto, as well as contributions from the SciNet HPC Consortium at the University of Toronto, along with Université Laval.

The team studied protein complexes involved in transcription using two experimental techniques: affinity purification and mass spectrometry. To

do so, they looked at transcription in a single-cell eukaryotic (contains organelles such as the nucleus bounded by a membrane) model organism called Tetrahymena, which is an ideal system to study because it is easy to work with and manipulate molecularly, biochemically, and genetically, and grows quickly. Its genome has more evolutionary similarity to humans than other non-mammalian model research organisms.

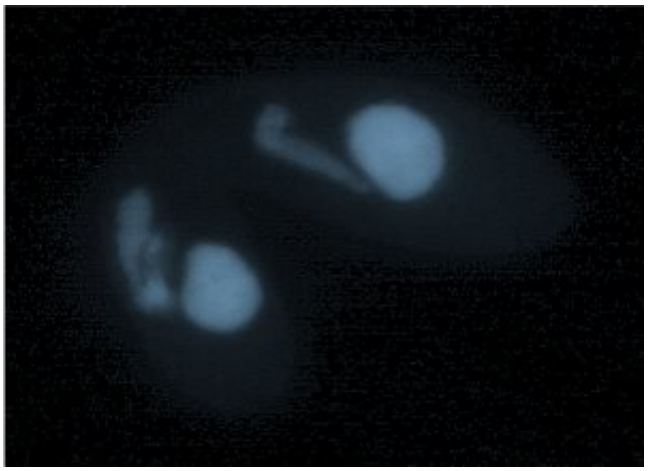

Image of 2 mating Tetrahymena going through meiosis - nuclei are stained with DAPI. Credit: Alejandro Saettone

The objective of the study was to better understand the function of a protein complex called Mediator, which plays a central role in gene expression through transcription, with particular focus on a protein called Med31, a subunit of the Mediator complex.

Med31 is interesting to molecular biologists because it has been conserved through millennia of evolutionary change, which means that highly similar versions of the protein are found in organisms as divergent as Tetrahymena and human beings. (Tetrahymena Med31 has

approximately 42% sequence identity with human Med31.) Previous studies have demonstrated Med31 has ancient roots, is present in almost all organisms alive today, and plays a central role in cell development regulation in mammals.

These aspects of Med31—and Mediator—lead to some interesting questions.

"The fact that Med31 is so conserved in evolution indicates that it plays some key fundamental role in transcription," says Fillingham. "What is it doing? What is its role? Those are questions the answers to which nobody has really got at yet."

The team's investigation shed some light on the functioning of Mediator and Med31 in Tetrahymena by suggesting some ways that Mediator may function in developmental regulation for organisms. The findings were published in an article called "The Med31 Conserved Component of the Divergent Mediator Complex in Tetrahymena thermophila Participates in Developmental Regulation" in the highly-regarded journal *Current Biology*, one of several in the prestigious Cell Press stable of journals.

Current Biology's decision to publish the article is notable because it focuses on publication of research with a broad general interest, which means the journal editors and reviewers believe the findings of the Fillingham-led team are of interest and value to the wide biology community. What's also interesting is that another paper using the same Tetrahymena model system published in the same journal issue reached similar conclusions to this study by asking different research questions, which amplifies the veracity of the team's findings.

"In the field of transcription and gene expression, our findings are very interesting," says Fillingham. "People will be interested to know how Tetrahymena Mediator is functioning in gene regulation and what this

tells us more generally about transcription and regulation of gene expression."

More information: Jyoti Garg et al, The Med31 Conserved Component of the Divergent Mediator Complex in Tetrahymena thermophila Participates in Developmental Regulation, *Current Biology* (2019). DOI: 10.1016/j.cub.2019.06.052

Provided by Ryerson University