



Calico Cats Inspire X Chromosome Research

Researchers Work to Unlock the Mysteries Behind X Chromosome Inactivation or 'Silencing,' a Trait Famously Evident in Calico Cats

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WASHINGTON D.C. Feb. 18, 2014 -- Calico cats, renowned and beloved for their funky orange and black patchwork or "tortoiseshell" fur, can thank X chromosome inactivation or "silencing" for their unique look.

A team of University of California San Francisco (UCSF) researchers is striving to unlock the mystery of how one X chromosome can be rendered nearly completely inactive. They will present their latest results at the 58th Annual Biophysical Society Meeting, which takes place Feb. 15-19, 2014, in San Francisco, Calif.

The cells of female mammals contain two copies of the X chromosome, one each from mom and dad, but because cells only need one active X, the other one is "turned off". Calico cats have an orange fur color gene on one of their X chromosomes and a black fur color gene on the other, so that the random silencing of one of the X's in each cell creates their distinctive patchwork coats. But while such manifestations of X chromosome inactivation have long been observed, researchers are still unclear of exactly how a cell silences a chromosome.

The UCSF researchers approached this mystery by first finding a way to image the X chromosome in its natural position within an intact cell. "A cell's nucleus contains the genetic code, its DNA. But while the structure of the DNA was determined more than 50 years ago, and we're rapidly determining the position of specific genes on chromosomes, no one had visualized the DNA within an intact nucleus -- an unfixed, hydrated whole cell," explained Elizabeth Smith. "We decided to try."

Smith is a postdoctoral fellow working in Carolyn Larabell's lab in the Anatomy Department at UCSF. Larabell is the director of the National Center for X-Ray Tomography, which is where the instrument development is taking place.

The work could eventually help researchers better understand how many different kinds of genes can be turned on or off without altering the underlying DNA sequence. "The inactivation of one out of two X

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chromosomes in females is an enormously important epigenetic process," said Smith. "Uncovering how only one X chromosome is inactivated will help explain the whole process of epigenetic control, meaning the way changes in gene activity can be inherited without changing the DNA code. It can help answer other questions such as if and how traits like obesity can be passed down through generations."

To visualize the DNA within an intact nucleus, Smith and colleagues turned to a novel imaging technology, soft x-ray tomography. "We obtained high-resolution, 3-dimensional views of the intact nucleus and, by using a prototype cryo fluorescence microscope along with the x-ray microscope, we were able to identify one specific chromosome, the inactive X chromosome of female cells," Smith said.

The team imaged and analyzed the inactive X chromosome in a number of different cells and was surprised by the wide variation in the structural organization adopted by the chromosome. "We were able to show a remarkable substructural organization of this chromosome, which consists of three distinct domains of differing amounts of chromatin," said Smith.

To obtain their results the researchers developed a new "correlated imaging" technique. This new form of microscopy has a wide range of possible future applications, particularly to identify the position of specific molecules within the densely packed environment of the nucleus. "With new fluorescent probes, we can start identifying the position of specific genes in context -- inside the tangled network of DNA within the intact nucleus," Smith explained.

While this work is still at the basic research stage, it shows potential to have a significant impact on understanding, diagnosing, and treating X-chromosome-linked diseases in the future.

Link to NIH X chromosome information: ghr.nlm.nih.gov/chromosome/X

The presentation "The Topological Organization of the Inactive X Chromosome in its Native State" by Elizabeth A. Smith, Gerry McDermott, Karen Leung, Barbara Panning, Carolyn A. Larabell and Mark A. Le Gros will be at 11:00 a.m. on Tuesday, February 18, 2014 in Room 130/131 in San Francisco's Moscone Convention Center.

ABSTRACT: <http://tinyurl.com/neqyrpo>

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ABOUT THE MEETING

The Biophysical Society Annual Meeting is the largest meeting of biophysicists in the world, and each year, it brings together thousands of researchers working in many different multidisciplinary fields. Some 4,513 abstracts were submitted for the 2014 meeting, and more than 7,000 attendees will attend from all 50 U.S. states and another 58 countries. The meeting will feature 500 speakers, more than 850 poster presentations per day, 23 symposia and five workshops. There will also be 211 exhibits from 162 different companies. Despite its size, the meeting retains its small-meeting flavor through its subgroup symposia, platform sessions, social activities, and committee programs.

QUICK LINKS

Main Meeting Page: <http://tinyurl.com/mfjh37p>

Abstracts Search: <http://tinyurl.com/lbrearu>

MEETING HIGHLIGHTS

Future of Biophysics Symposium: <http://tinyurl.com/ponx4ck>

New and Notable Symposium: <http://tinyurl.com/klv3jht>

ABOUT THE SOCIETY

The Biophysical Society, founded in 1958, is a professional, scientific Society established to encourage development and dissemination of knowledge in biophysics. The Society promotes growth in this expanding field through its annual meeting, monthly journal, and committee and outreach activities. Its 9000 members are located throughout the U.S. and the world, where they teach and conduct research in colleges, universities, laboratories, government agencies, and industry. For more information on the Society, or the 2014 Annual Meeting, visit www.biophysics.org

