4D Nucleome Program

It is estimated that each human cell contains approximately 2 meters (6.5 feet) of DNA, squeezed inside the cell's microscopic nucleus. We now know that DNA is not randomly arranged within the nucleus; instead, the organization of the nucleus is tightly controlled. However, the functional consequences of this organization are not well understood. What are the principles that govern the three-dimensional architecture of the nucleus, and how does this architecture contribute to gene expression regulation? How does nuclear architecture change over time (the fourth dimension) in the course of normal development? Do dysfunctional alterations in nuclear organization lead to disease, and/or could they be used to diagnose diseases?

The Common Fund's 4D Nucleome program (http://commonfund.nih.gov/4Dnucleome/index) aims to understand the principles underlying nuclear organization in space and time, the role nuclear organization plays in gene expression and cellular function, and how changes in nuclear organization affect both normal development and various diseases. This program will develop technologies, resources, and data to enable the study of the 4D Nucleome, including novel tools to explore the dynamic nuclear architecture and its role in gene expression programs, models to examine the relationship between nuclear organization and function in both normal development and disease, and reference maps of nuclear architecture in a variety of cells and tissues.

Program Initiatives

› **Nuclear Organization and Function Interdisciplinary Consortium (NOFIC):** The NOFIC is composed of multidisciplinary teams that will develop and validate novel approaches and genome-wide mapping technologies that will lead to a deeper understanding of nuclear organization in time and space, and the role of this organization in regulating gene expression programs.

› **Nucleomics Tools:** This initiative stimulates development and validation of chemical and biochemical technologies for measuring three-dimensional interactions between specific places in the genome (genomic loci), or between genomic loci and regulators of genome organization and function, in mammalian cells.

› **Study of Nuclear Bodies and Compartments:** This initiative supports the development of tools and strategies to study the three-dimensional architecture of the nucleus in relationship to the spatial arrangement of nuclear bodies and molecular machinery regulating gene expression, the structure and function of poorly characterized nuclear structures and compartments, and the role of specialized proteins and RNAs in nuclear organization and function.

- **4D Nucleome Imaging Tools:** This initiative stimulates the development of higher throughput, higher resolution, and higher content imaging approaches that can measure changes in nuclear organization in live single cells.

- **4D Nucleome Network Organizational Hub (4DN-OH):** The 4DN-OH will develop a community website to facilitate sharing of data, reagents, standards, and protocols; foster collaborations; organize yearly scientific meetings; and oversee administrative aspects of the program. 4DN-OH will also administer the Opportunity Pool, a fund to support new projects and initiatives that address identified needs arising throughout the lifetime of the program.

- **4D Nucleome Network Data Coordination and Integration Center (4DN-DCIC):** 4DN-DCIC will track, store, and display all data generated by 4D Nucleome investigators; provide a Data Analysis Center to assist with integrated analyses; develop metrics and standards to be adopted by the community at large; and provide visualization tools to facilitate access and understanding of complex data sets.

To find out more about future 4D Nucleome funding opportunities, please visit: http://commonfund.nih.gov/ 4Dnucleome/index.

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