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Functional complementation of a genetic deficiency with human artificial chromosomes (HACs)

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Abstract

Since their description in late nineties, Human Artificial Chromosomes (HACs) carrying a functional kinetochore was considered as a promising system for gene delivery and expression with a potential to overcome many problems caused by the use of viral-based gene transfer systems. Indeed, HACs avoid the limited cloning capacity, lack of copy number control and insertional mutagenesis due to integration into host chromosomes that plague viral vectors. In my talk, I will summarize a recent progress made in the HAC technology and concentrate in details on one of the most advanced HACs, alphoid^{tetO}-HAC, and generated de novo using a synthetic tetO-alphoid DNA array that allows a regulated expression of full-length human genes. In addition, I will update TAR cloning strategy for rapid and selective isolation of any desirable genomic fragment or gene with its own regulatory elements up to 250 kb in size from complex genomes. Combination of HAC-based and TAR techniques can make a major breakthrough in functional and structural genomics, in diagnostic and gene therapy.

Biography

Natalay Kouprina received her M.Sc. in physical chemistry from the St. Petersburg State University, Russia, and her Ph.D. and Dr.Sc. in cell biology from the Institute of Cytology, Russian Academy of Sciences. While in Russia, she worked on the identification of genes that control the replication and segregation of chromosomes in budding yeast. In 1991 she moved to the United States and focused her interests on genomics. At present she is a staff scientist at the National Cancer Institute, USA. Her current interest is to combine a transformation-associated recombination (TAR) cloning technology that allows selective isolation of a gene of interest up to 300 kb in size from complex genomes, including humans, with the human artificial chromosome or HAC-based gene delivery vector to develop a novel system for the delivery and expression of full-length mammalian genes. Such a novel approach has a potential for gene functional studies and gene therapy. She has 83 publications in many leading journals.