Functional Annotation of the Mammalian Genome (FANTOM)

Abstract

Functional Annotation of the Mammalian Genome (FANTOM) is an international research consortium established in 2000 to assign functional annotations to the full-length complementary deoxyribonucleic acids (cDNAs) that were collected during the Mouse Encyclopedia Project at RIKEN. FANTOM has since developed and expanded over time to encompass the fields of transcriptome analysis. FANTOM’s object is to move steadily up the layers in the system of life, progressing from an understanding of the “elements” — the transcripts — to an understanding of the “system” — the transcriptional regulatory network, in other words, the “system” of an individual life form.

Consortium History

FANTOM1 developed an effective system for functional gene annotation by designing appropriate rules and methods. The result was mainly published in Nature in 2001 (Kawai et al. 2001). The paper was followed by the draft sequence of human genome (Lander et al. 2001) a week later because they used FANTOM1’s cDNA for gene number prediction.

During FANTOM2, the base sequences were determined and assigned functional annotations to a set of 60,770 full-length mouse cDNAs. This was the first project worldwide to standardize full-length
mammalian cDNAs. The research was published in a special issue of Nature on the decoding of the mouse genome in 2002 (Okazaki et al. 2002).

FANTOM3 utilized a new technology, CAGE, to reveal that more than 63 percent of the genome — instead of the known approximately 1.5 percent fraction of protein-coding exons — is transcribed as ribonucleic acid (RNA). The project confirmed the existence of more than 23,000 noncoding RNAs (ncRNAs) and that greater than 73 percent of the transcriptional units show sense-antisense transcription. This work was published in two papers in the “RNA special issue” of Science in 2005 (Carninci et al. 2005; Katayama et al. 2005).

FANTOM4 used deepCAGE to monitor the dynamics of transcription start site (TSS) usage during a time course of monocytic differentiation. The expression levels from each promoter and transcription factor (TF) binding site predictions were then used to build a transcriptional regulatory network model (Suzuki et al. 2009). Additionally, transcription initiation RNAs, the expression of the “repeatome,” and an atlas of combinatorial TF regulation were published in FANTOM4.

FANTOM5 (in progress) is expanding the efforts made in FANTOM3 and 4 and aims to generate a map of the majority of human promoters and comparative transcriptional regulatory network models of each cellular state. To achieve this, the project is using deepCAGE sequencing on the Heliscope true single molecule sequencer on RNA isolated from every major human organ, more than 200 cancer cell lines, 30 time courses of cellular differentiation, mouse developmental time courses, and more than 200 primary cell types.

FANTOM6 (in planning stages) is a worldwide collaborative project aiming at identifying all functional elements in mammalian genomes. FANTOM6’s goal is to systematically elucidate the function of long ncRNAs in the human genome.

Data Sharing

FANTOM data resources are available on the website.

Impact/Accomplishment
Simultaneously with producing data, FANTOM established the FANTOM database and the FANTOM full-length cDNA clone bank, which are available worldwide. The FANTOM resources have been used in several important research projects. For instance, the full-length cDNA database was used in a computer prediction of the genomic position (transcriptional unit) of genes by the International Human Genome Sequencing Consortium. Also they have been used by a research group led by Shinya Yamanaka at Kyoto University, Japan, for establishing induced pluripotent stem (iPS) cells. In the study, 24 transcription factors were selected from the FANTOM database as candidate initiation factors. Furthermore, the Allen Institute for Brain Science in the United States has created a digital atlas that encompasses the whole brain and has made it publicly available. The atlas graphically illustrates the expression of genes within the mouse brain using Informatix software. This project has also made use of the FANTOM database.

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