

European large-scale functional genomics in the rat for translational research (EURATRANS)

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Research Areas



Tool Development



Biomarker Research

Genomic Biomarker



Data-Sharing Enabler

At a Glance

- Status: **Completed Consortium**
- Year Launched: **2010**
- Initiating Organization: **European Commission Sixth Framework Programme (FP6)**
- Initiator Type: **Government**

Abstract

The European large-scale functional genomics in the rat for translational research (EURATRANS) consortium brings together investigators who will use next-generation sequencing technologies to generate genomic, transcriptomic and epigenomic datasets. The goal is to create quantitative metabolomic and proteomic datasets to give significant depth of coverage, at multiple levels, across pathophysiological phenotypes. The aim is to enable insights into disease mechanisms, through an integrative, cross-disciplinary approach to understanding large-scale functional genomic datasets in rats and humans.

Mission

The European large-scale functional genomics in the rat for translational research (EURATRANS) consortium brings together investigators who will use next-generation sequencing technologies to generate genomic, transcriptomic and epigenomic datasets. These datasets will be gathered, annotated and integrated in relational and dynamic models that will be used in comparative analyses to understand human gene function at the level of the molecule, cell, tissue and organism.



The specific objectives of EURATRANS includes:

Large scale data generation using functional genomics technologies through the generation of the complete genome sequence for 9 key model rat strains (parental progenitors for crosses used). Based on the existing Brown Norway (BN) reference genome and building on the collective experience in sequencing the Spontaneously Hypertensive Rat (SHR) genome at >10x coverage using the Illumina/Solexa platform to sequence the parental progenitor rat strains for the experimental crosses used in this project (RI strains and HS) using next-generation sequencing technology to identify genetic and structural variation at the genome-scale level.

Generation of a genome-wide transcriptional catalogue of coding, microRNAs and other non-coding RNAs using next-generation sequencing (RNA-seq) in selected cells and tissues of the key model strains, in RI panels and in rat ES cells. In addition, the consortium aims to determine the transcriptional initiation complexes in a subset of cells and tissues by ChIP-Seq.

Identification of the differential methylation state of genomic DNA by methyl-sequencing in the BXH/HXB and LEXF/FXLE RI strains by characterizing genome-wide chromatin state maps in defined cells and developmental stages in the progenitors of the BXH/HXB, LEXF/FXLE and HS panel.

The consortium will use in vivo stable isotope labeling with amino acids (SILAC) to quantify the proteome in key cells and tissues of the progenitor strains of the RI and HS lines and in RI strains and map differential protein expression across the RI strains. The consortium has access to key cells and tissues to generate metabolomic profiles in the key parental strains and two sets of rat recombinant inbred strain panels and map the genetic determinants of the metabolome.

Consistent data processing such as read mapping, feature identification, and visualisation.

Establishment of a bioinformatic research framework integrating multilevel datasets from molecular to physiological. The deliverable will be a bioinformatic and analytical research framework for annotating and integrating the generated multilevel DNA variation (genetic & structural), transcription, micro-RNA, metabolomic, proteomic, and epigenomic datasets, using the extensive sets of physiological data generated in the two RI panels and the HS by Euratools and the Japanese Phenome Project.

Building and validating models by identifying the genetic determinants of new molecular phenotypes using existing high resolution SNP maps in RI and HS animals that were generated through the Euratools and STAR consortia.



Building molecular gene regulatory networks and identifying the most prominent hubs and nodes by applying techniques for QTL and quantitative trait transcript (QTT) network building using correlational and Bayesian models.

Projection of regulatory networks on (patho-)physiological data to identify molecular pathways underlying specific physiological and disease phenotypes.

Validation of the key components in disease-related networks through perturbation and manipulation of gene function by loss and gain of function experiments in vivo and in vitro. By using established techniques including ENU mutagenesis, transposon mediated mutagenesis in rat spermatogonial stem cells, transgenesis, antisense approaches, and emerging ES cell technologies, the consortium will create tools that allow for the manipulation of network components in perturbation experiments to validate findings.

Comparative informatics and translation to human by identifying the regulatory expression networks, and epigenomic, metabonomic and proteomic signatures that are conserved between rats, mice and humans. By integrating human GWAS data in the consortium's three focus disease areas with all models generated, the aim of this effort is to identify biological pathways and processes that are important for these common human diseases (cardiovascular/metabolic, inflammation, psychiatric).

Validation of biological insights from the discovery of pathways for the three focus disease areas in human disease tissues. The aim will be to use the collective tissue banks and patient cohorts to validate the consortium's findings in the human disease process.

Financing

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Homepage

<http://www.euratrans.eu/>

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