In **WP 1.1 (Genome sequencing)**, complete genetic inventories of the rat BN-Lx and SHR strains (founders of the recombinant inbred panel) were published in the open access journal Genome Biology. In addition, the effects of this variation on transcriptional characteristics were described. Complete inventories of the founder strains of the rat heterogeneous stock (8 strains) were compiled and used to identify the genetic basis of a wide range of phenotypic traits measured in more than 1,600 derived HS panel animals. This work was published online by May 26th (doi:10.1038/ng.2644). Genome sequencing has been extended to an additional 24 inbred rat strains and substrains. A manuscript describing the genome analysis of 27 rat strains as well as the selective processes underlying shared phentoypic traits is currently under review.

In **WP 1.2 (Transcriptome)**, alternative splicing was quantified on the exon level in liver and left ventricle tissue in the RI strains and parental strains. Expression levels of microRNA were quantified in liver and left ventricle tissue in the RI strains and parental strains. Transcriptome data on exon and gene level were integrated with genetic data and suggests that 30% of RNA-seq eQTL which not only affect the global gene expression level, but also cause differential alternative transcript events in their target genes, preferentially in the last exon. Transcriptome data of microRNA and mRNA were integrated with genetic data and suggests that only a small proportion of mRNA eQTL are regulated directly by microRNA

In **WP 1.3 (Epigenetics)**, new human antibodies against transcription factors showing reactivities in rat were obtained, some showing immunoreactivity to highly specific cell types. Some of these factors shuttle between the cytoplasm and the nucleus, potentially regulating gene expression. The genome-wide maps for hisotne methylation were completed for the parental strains and the RI lines in the liver and left ventricles and in the liver for Pol II. Computational pipelines have been devised for their analysis and to characterize chromatin signatures at regulatory elements and to identify what could be the determinants for their distribution. Using the ChIp-seq maps for modified histones and Pol II, allele-specific distribution of the marks or the enzyme were identified. One remarkable finding was the mapping of a single trans-acting QTL that co-localized with nearly 900 H3K4me3 traits.

In **WP 1.4 (Proteomics)**, differential protein expression between RI liver lines and parental rat was identified. All data related to this milestone has been acquired and further data analysis and processing is ongoing. Quantitative tissue analysis for 30 RI strains (liver proteome comparison) was performed and 10 different tissue samples analyzed derived from the BN-Lx strain. Collectively these analyses have identified >12,000 rat proteins. Data analysis is still ongoing and a collective list of the rat proteome to a depth of >10,000 proteins can soon be provided to the consortia.

In **WP 1.5 (Metabonomics)**, a pipeline for in vitro validation of the biological effects of metabolites in cell lines was developed. ShRNA was applied for the analysis of the biological effects of enzyme dowregulation in vitro in 3T3 adipocytes. A UPLC-MS based tissue metabolite phenotyping pipeline for BHX/HXB RI strains was developed. Preliminary heritability estimates for MS-based metabotypes for heart ranging from 0.08 to 0.7. mQTL mapping for RI heart was achieved.

In **WPs 1.6/2.1 (Regulatory networking and computational infrastructure)**, the immunological disease portal is online. We built new SNP tracks within the Rat Genome Database to display are EURATRANS data. Data mining tools for mapping discovered variations to network components and the Pinball algorithm as a mechanism for direct integration free of alignment bias and also largely free of artefacts caused by errors or incomplete sections of the reference genome assembly were developed.

In **WP 2.2 (Functional validation)**, four novel shRNA transgenic rat lines have been developed and all show inducibility of the knockdown effect and interesting phenotypes and may become valuable novel rat models for diseases. We have demonstrated germ line transmission of a targeted mutation generated by homologous recombination in two independent rat ES cell lines. Furthermore, the generation of transgenic rats by transposon technology is now well established and very efficient, a result which was prominently published by several consortium members (Katter et al., FASEB J 2013).

In **WP 3.1 (Comparatie analysis)**, a large number of eQTLs can be mapped in the HS and biologically meaningful gene networks have been identified.

In **WP 3.2 (Integration with GWAS)**, we significantly augmented the annotation, visualisation and underlying data resources for the human GWAS positive regions.

In **WP 3.3 (Validation)**, all tissues/cells have been collected.

(31.03.2013)