

**Monday November, 3
10.30am – 12.00pm
Poster Session 1
Immunity/Infection/Epigenetics and Comparative Genomics/
Computational Biology
Posters P1- P44**

- P1 IFN-INDEPENDENT ACTIVATION OF IFN-DEPENDENT GENES IN MOUSE EMBRYONIC FIBROBLASTS INFECTED BY THE RIFT VALLEY FEVER VIRUS**
Tania Zaverucha Do Valle¹, Agnes Billecocq², Laurent Guillemot¹, Robert Geffers³, Klaus Schughart⁴, Michele Bouloy², Xavier Montagutelli¹, Jean-Jacques Panthier¹
¹*Mouse Functional Genetics Unit, CNRS URA 2578, Institut Pasteur, Paris, France*, ²*Molecular Genetics of Bunyaviruses, Institut Pasteur, Paris, France*, ³*Array Facility/Cell Biology, Helmholtz Centre for Infection Research, Braunschweig, Germany*, ⁴*Experimental Mouse Genetics, Helmholtz Centre for Infection Research, Braunschweig, Germany*
- P2 GENETIC DISSECTION OF POLYGENIC SUSCEPTIBILITY/RESISTANCE TO YERSINIA PESTIS IN MOUSE INTERSPECIFIC CROSSES**
Charlène Blanchet¹, Elisabeth Carniel², Jean Jaubert¹, Jean-Jacques Panthier¹, Xavier Montagutelli¹
¹*Mouse Functional Genetics Unit, CNRS URA 2578, Institut Pasteur, Paris, France*, ²*Yersinia Unit, Institut Pasteur, Paris, France*
- S15/P3 THE GENETICS OF SUSCEPTIBILITY TO SYSTEMIC PNEUMOCOCCAL INFECTION**
Laura Boubbane¹, Aras Kadioglu², Pete Underhill¹, Andrew Haynes¹, Ayo Toyee², Chris Holmes¹, Peter W Andrew², Steve Brown¹, Paul Denny¹
¹*MRC Mammalian Genetics Unit, Harwell, Oxfordshire, United Kingdom*, ²*Department of Infection, Immunity and Inflammation, University of Leicester, Leicester, United Kingdom*
- P4 THE COLLABORATIVE CROSS MOUSE POPULATION FOR DISSECTING THE COMPLEXITY OF HOST GENETIC FACTORS INFLUENCING IMMUNE RESPONSE CELL LINEAGES IN PERIPHERAL BLOOD**
Hana Sandovsky-Losica, Israel Zan-Bar, Richard Mott, Fuad Iraqi
¹*Tel-Aviv University, Tel-Aviv, Israel*, ²*Oxford University, Oxford, United Kingdom*
- P5 THE COLLABORATIVE CROSS MOUSE POPULATION FOR DISSECTING THE COMPLEXITY OF HOST SUSCEPTIBILITY TO *PEROPHYROMONAS GINGIVALIS*-INDUCED ALVEOLAR BONE LOSS**
Ariel Shusterman¹, Yael Houry-Haddad¹, Ervin Weiss¹, Richard Mott², Fuad Iraqi³
¹*Department of Prosthodontics Hadassah Medical Center, Jerusalem, Israel*, ²*University of Oxford, Oxford, United Kingdom*, ³*Tel-Aviv University, Tel-Aviv, Israel*
- P6 THE COLLABORATIVE CROSS MOUSE POPULATION FOR DISSECTING THE COMPLEXITY OF HOST SUSCEPTIBILITY MECHANISMS TO ASPERGILLUS FUMIGATUS INFECTION**
Hanna Tayyim¹, Nir Oshero¹, Richard Mott², Fuad Iraqi¹
¹*Tel-Aviv University, Tel-Aviv, Israel*, ²*University of Oxford, Oxford, United Kingdom*
- P7 THE COLLABORATIVE CROSS MOUSE POPULATION FOR DISSECTING THE COMPLEXITY OF HOST SUSCEPTIBILITY MECHANISMS TO KLEBSIELLA PNEUMONIAE INFECTION**
Karin Vered¹, Itzhak Ofek¹, Richard Mott², Fuad Iraqi¹
¹*Tel-Aviv University, Tel-Aviv, Israel*, ²*University of Oxford, Oxford, United Kingdom*
- P8 GENETIC DETERMINANTS OF THRIFTY METABOLISM AND ENHANCED BONE DENSITY IN PWD/PHJ MICE – A WILD-DERIVED STRAIN**
Karen L Svenson, Kevin Flurkey, Luanne L Peters
The Jackson Laboratory, Bar Harbor, Maine, United States
- P9 SCREENING FOR IMMUNOLOGICAL DISORDER IN MICE GENERATED BY THE RIKEN RCAI ENU MUTAGENESIS PROJECT**
Takuwa Yasuda, Ayako Kobayashi, Michiko Kawabata, Hitomi Fukiage, Mikiko Ochi, Akimi Sano, Hisahiro Yoshida
Laboratory for Immunogenetics, Research Center for Allergy and Immunology (RCAI), RIKEN Yokohama Institute, Yokohama, Kanagawa, Japan
- P10 CHARACTERIZATION OF NEW SLA-DQB1 ALLELES FROM SEVEN PIG BREEDS USING THE GENOMIC SEQUENCE-BASED GENOTYPING METHOD**
Chankyu Park
Konkuk University, Seoul, Korea, Republic of
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Claude Libert
Ghent University, Ghent, Belgium

- P12** **CONDITIONAL GP130 DEFICIENT MOUSE MUTANTS, 10 YEARS LATER**
Werner Muller
University of Manchester, Manchester, United Kingdom
- P13** **CLINICAL CHEMISTRY OF MICE CONGENIC FOR QTL FOR SURVIVAL TIME AFTER *TRYPANOSOMA CONGOLENSE* INFECTION DOES NOT REVEAL MAJOR DIFFERENCES IN RESPONSE TO THE PARASITE BETWEEN SHORT AND LONG SURVIVORS**
Birgit Rathkolb¹, Andy Brass², Paul Dark³, Valérie Gailus-Durner¹, John Gibson⁴, Helmut Fuchs¹, Martin Hrabé de Angelis¹, Fuad Iraqi⁵, Steve Kemp⁶, Jan Naessens⁵, Matt Pope⁵, Eckhard Wolf⁷, Harry Noyes¹, Morris Agaba¹
¹*Institute of Experimental Genetics, Helmholtz Zentrum München, Germany*, ²*School of Computer Science, University of Manchester, Manchester, United Kingdom*, ³*Intensive Care Medicine, Salford Royal NHS Foundation Trust, The University of Manchester, Manchester, United Kingdom*, ⁴*University of New England, Armidale, Australia*, ⁵*International Livestock Research Institute (ILRI), Nairobi, Kenya*, ⁶*School of Biological Sciences, University of Liverpool, Liverpool, United Kingdom*, ⁷*Institute of Molecular Animal Breeding and Biotechnology, Ludwig Maximilian Universität, München, Germany*
- P14** **GENETIC VARIATION IN INTESTINAL GENE EXPRESSION IN PROGENITORS OF THE COLLABORATIVE CROSS**
Elissa J. Chesler, Cymbeline T. Cuiat, A.V. Palumbo, Vivek M. Philip, M. Podar, Brynn H. Voy
Biosciences Division, Oak Ridge National Laboratory, Oak Ridge TN, United States
- P15** **MICRORNAS PLAY A LIMITED ROLE IN MATERNAL MRNA DEGRADATION**
Mathyas Flenr¹, Ma Jun², Paula Stein², Richard M. Schultz², Petr Svoboda¹
¹*Institute of Molecular Genetics, Prague, Czech Republic*, ²*Department of Biology, University of Pennsylvania, Philadelphia, United States*
- P16** **PROMOTER EVOLUTION OF MCM8 ORTHOLOGOUS GENES IN MAMMALIAN GENOME**
Kenichi Yoshida
Meiji University, Kawasaki, Japan
- S11/P17** **MAPPING OF OBESITY AND FAT DEPOT-SPECIFIC QTLs USING HAPLOTYPE ASSOCIATION AND OTHER RECENTLY DEVELOPED BIOINFORMATICS METHODS**
Zala Prevorsek¹, Shirng-Wern Tsaih², Ioannis M. Stylianou³, Beverly Paigen², Simon Horvat¹
¹*University of Ljubljana, Biotechnical faculty, Ljubljana, Slovenia, Slovenia*, ²*The Jackson Laboratory, Bar Harbor, Maine, United States*, ³*University of Pennsylvania, School of Medicine Institute for Translational Medicine and Therapeutics, Philadelphia, Pennsylvania, United States*
- P18** **CHARACTERIZATION OF DIVERSITY IN BLOOD ETHANOL CLEARANCE RATES IN PRECC MICE**
Christine Powell¹, Jill Steigerwalt¹, Fernando Pardo-Manuel de Villena¹, Daniel Pomp¹, Elissa Chesler², David Threadgill¹
¹*University of North Carolina, Chapel Hill, NC, United States*, ²*Oak Ridge National Laboratory, Oak Ridge, TN, United States*
- S13/P19** **THE PHENOME INTERDEPENDENCY AND SIMILARITY HIERARCHY: A TOOL FOR GENOME-SCALE PHENOTYPIC ANALYSIS**
Jeremy Jay¹, Vivek Philip⁴, Yun Zhang¹, Michael A Langston¹, Erich Baker³, Elissa Chesler²
¹*Department of Electrical Engineering and Computer Science, University of Tennessee, Knoxville, TN, United States*, ²*Life Sciences Division, Oak Ridge National Laboratory, Oak Ridge, TN, United States*, ³*Baylor University, Waco, TX, United States*, ⁴*Graduate School of Genome Science and Technology, University of Tennessee, Knoxville, TN, United States*
- P20** **USING ONTOLOGIES TO ANNOTATE LARGE-SCALE MOUSE PHENOTYPE DATA**
Tim Beck, Ann-Marie Mallon, Andrew Blake, Hugh Morgan, John Hancock
MRC Harwell, Didcot, Oxfordshire, United Kingdom
- P21** **EUROPHENOME: A MOUSE PHENOTYPING RESOURCE**
Ann-Marie Mallon, Hugh Morgan, Tim Beck, Andrew Blake, John Hancock
MRC Harwell, Oxfordshire, United Kingdom
- P22** **THE TRANSCRIPTIONAL NETWORK THAT CONTROLS GROWTH ARREST AND DIFFERENTIATION IN A HUMAN MYELOID LEUKEMIA CELL LINE**
Harukazu Suzuki, Yoshihide Hayashizaki
RIKEN Omics Science Center, Yokohama, Japan

- P23 A RESOURCE FOR COMMUNITY ANNOTATION OF THE MOUSE GENOME**
Deanna Church¹, Carol Bult²
¹National Center for Biotechnology Information, Bethesda, Maryland, United States, ²The Jackson Laboratory, Bar Harbor, Maine, United States
- P24 MOUSECYC: A DATABASE OF CURATED BIOCHEMICAL PATHWAYS FOR THE LABORATORY MOUSE**
Alexei Evsikov, Mary Dolan, Carol Bult
The Jackson Laboratory, Bar Harbor, Maine, United States
- P25 MOUSENET: A PREDICTIVE FUNCTIONAL NETWORK RESOURCE FOR THE LABORATORY MOUSE**
Yuanfang Guan¹, Chad Myers², Carol Bult³, Olga Troyanskaya¹
¹Lewis-Sigler Institute for Integrative Genomics, Carl Icahn Laboratory, Princeton, New Jersey, United States, ²Department of Computer Science, Princeton, New Jersey, United States, ³The Jackson Laboratory, Bar Harbor, Maine, United States
- P26 UNIPROT KNOWLEDGEBASE: LINKING PROTEIN SEQUENCE AND FUNCTION**
Michele Magrane, UniProt Consortium
¹EMBL-EBI, Hinxton, Cambridge, United Kingdom, ²Swiss Institute of Bioinformatics, Geneva, Switzerland, ³Protein Information Resource, Washington DC, United States
- P27 MAUSDB: THE GERMAN MOUSE CLINIC OPEN SOURCE PHENOTYPE- AND MOUSE MANAGEMENT SYSTEM**
Holger Maier, Christoph Lengger, Ralph Steinkamp, Karlheinz F. Schäble, Helmut Fuchs, Valerie Gailus-Durner, Martin Hrabe de Angelis
Helmholtz Zentrum München - German Research Center for Environmental Health (GmbH), Neuherberg, Germany
- P28 MOUSEBOOK: ONLINE INTEGRATED MOUSE INFORMATION SYSTEM**
Andrew Blake, Ann-Marie Mallon, Simon Greenaway, Tim Beck, John Hancock
MRC Harwell, Harwell, Oxfordshire, United Kingdom
- P29 INTEGRATION OF GENE TRAP RESOURCES WITH MOUSE GENOME INFORMATICS (MGI)**
Sophia Zhu, Richard Baldarelli, Sharon Cousins, Howard Dene, Cynthia Smith, Robert Sinclair, Jill Lewis, James Kadin, Joel Richardson, Judith Blake, Martin Ringwald, Janan Eppig, Carol Bult
The Jackson Laboratory, Bar Harbor, ME, United States
- P30 GENOME BUILD 37: CURRENT PRIORITIES AND ISSUES IN MOUSE GENE NOMENCLATURE**
Lois J Maltais, Judith A Blake, Carol J Bult, Janan T Eppig, MGI Staff
The Jackson Laboratory, Bar Harbor, ME, United States
- P31 GENE ONTOLOGY RESOURCES FOR COMPARATIVE GENOMICS: MOUSE AND THE GO REFERENCE GENOME PROJECT**
Judith A. Blake, David P. Hill, Mary E. Dolan, Alexander D. Diehl, Li Ni, Harold J. Drabkin, Dmitry M. Sitnikov
The Jackson Laboratory, Bar Harbor, ME, United States
- P32 THE NEW MGI WEB SITE AND SEARCH TOOL**
Lois J Maltais, James A Kadin, Joel E Richardson, Kim Forthofer, Jill Lewis, Pete Frost, Matt Hall, Jon Beal, Martin Ringwald, Judith A Blake, Carol J Bult, Janan T Eppig
The Jackson Laboratory, Bar Harbor, ME, United States
- P33 TRANS-REGULATION OF MEIOTIC RECOMBINATION HOTSPOTS BY RCR1**
Emil Parvanov, Siemon Ng, Petko Petkov, Kenneth Paigen
The Jackson Laboratory, Bar Harbor, United States
- P34 THE GENOME REFERENCE CONSORTIUM**
Valerie Schneider, on behalf of the GRC
National Center for Biotechnology Information, NIH, Bethesda, MD, United States

- P35 DEVELOPMENT OF A SEMANTIC FRAMEWORK FOR THE INTEGRATION OF MOUSE PHENOME INFORMATION**
Hiroshi Masuya¹, Nobuhiko Tanaka¹, Kazunori Waki¹, Norio Kobayashi², Tetsuro Toyoda², Toshihiko Shiroishi³, Shigeharu Wakana¹, Riichiro Mizoguchi⁴
¹RIKEN BRC, Tsukuba, Ibaraki, Japan, ²RIKEN, Yokohama, Kanagawa, Japan, ³Nat. Inst. Genet., Mishima, Shizuoka, Japan, ⁴Osaka Univ., Ibaraki, Osaka, Japan
- P36 STATISTICAL INFERENCE FOR MAMMALIAN OMIC DATA INTEGRATION ON THE SEMANTIC WEB**
N Kobayashi¹, Y Yoshida¹, Y Mochizuki¹, M Ishii¹, A Matsushima¹, Y Makita¹, N Heida¹, S Asano¹, H Masuya², S Wakana², T Toyoda¹
¹Bioinformatics And Systems Engineering division (BASE), RIKEN, Yokohama, Kanagawa, Japan, ²BioResource Center, RIKEN, Tsukuba, Ibaraki, Japan
- P37 DEVELOPMENT OF INTERIGENT INFRASTRUCTURE FOR DESCRIPTION OF EXPERIMENTAL PROTOCOLS WITH SEMANTIC WEB TECHNOLOGY**
Nobuhiko Tanaka¹, Kazunori Wali¹, Riichiro Mizoguchi³, Norio Kobayashi², Tetsuro Toyoda², Yoko Shibukawa¹, Tomoko Kushida¹, Ikuko Yamada¹, Tamio Furuse¹, Shigeharu Wakana¹, Hiroshi Masuya¹
¹RIKEN BioResource Center, Tsukuba, Ibaraki, Japan, ²RIKEN Bioinformatics and Systems Engineering, Yokohama, Kanagawa, Japan, ³University of Osaka, Suita, Osaka, Japan
- P38 SNP DATABASE AMONG C57BL-RELATED STRAINS AND THEIR CONGENIC STRAINS**
Kazuyuki Mekada, Kuniya Abe, Ayumi Murakami, Kazuo Moriwaki, Yuichi Obata, Atsushi Yoshiki
 RIKEN BioResource Center, Tsukuba, Japan
- P39 SOLUTIONS FOR DATABASE INTEROPERABILITY: A REPORT FROM THE CASIMIR CONSORTIUM**
Damian Smedley¹, Morris Swertz², Katy Wolstencroft³, Glenn Proctor¹, Michael Zouberakis⁴, Jonathan Bard⁵, John Hancock⁶, Paul Schofield⁷
¹EBI, Cambridge, United Kingdom, ²University of Groningen, Groningen, Netherlands, ³University of Manchester, Manchester, United Kingdom, ⁴BSRC Alexander Fleming, Athens, Greece, ⁵John Radcliffe Hospital, Oxford, United Kingdom, ⁶MRC Harwell, Harwell, United Kingdom, ⁷University of Cambridge, Cambridge, United Kingdom
- P40 MOUSE GENOME RESOURCES AT NCBI**
Deanna Church, on behalf of NCBI genomes group
 DHHS/NIH/NLM/NIH, Bethesda, MD, United States
- P41 SIMULATION OF HAPLOTYPE LENGTH OVER MULTIPLE GENERATIONS SUGGESTS A SIMPLE LINEAR RELATIONSHIP BETWEEN NUMBERS OF HAPLOTYPES, NUMBER OF GENERATIONS AND MEAN HAPLOTYPE LENGTH**
Harry Noyes, Steve Kemp
¹University of Liverpool, Liverpool, United Kingdom, ²International Livestock Research Institute (IRLI), Nairobi, Kenya
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Xiting Li, Simon Lovell, Kathryn Hentges
 University of Manchester, Manchester, United Kingdom
- P43 CONSISTENCY OF LINKAGE DISEQUILIBRIUM ACROSS MOUSE POPULATIONS**
 Yun Zhan¹, Vivek M. Philip², Cymbeline T. Cuiat², Gary A. Churchill⁴, Michael A. Langston¹, Elissa J. Chesler²
¹Electrical Engineering and Computer Science, Knoxville TN, United States, ²Genome Science and Technology Program University of Tennessee and Oak Ridge National Laboratory, Knoxville / Oak Ridge TN, United States, ³System Genetics Group, Biosciences Division, Oak Ridge National Laboratory, Oak Ridge TN, United States, ⁴The Jackson Laboratory, Bar Harbor ME, United States
- P44 MOUSE PHENOME DATABASE (MPD)**
Molly Bogue, Stephen Grubb, Carol Bult, Terry Maddatu
 The Jackson Laboratory, Bar Harbor ME, United States

P1

IFN-INDEPENDENT ACTIVATION OF IFN-DEPENDENT GENES IN MOUSE EMBRYONIC FIBROBLASTS INFECTED BY THE RIFT VALLEY FEVER VIRUS

Tania Zaverucha Do Valle¹, Agnes Billecocq², Laurent Guillemot¹, Robert Geffers³, Klaus Schughart⁴, Michele Bouloy², Xavier Montagutelli¹, Jean-Jacques Panthier¹

¹Mouse Functional Genetics Unit, CNRS URA 2578, Institut Pasteur, Paris, France, ²Molecular Genetics of Bunyaviruses, Institut Pasteur, Paris, France, ³Array Facility/Cell Biology, Helmholtz Centre for Infection Research, Braunschweig, Germany, ⁴Experimental Mouse Genetics, Helmholtz Centre for Infection Research, Braunschweig, Germany

Rift Valley fever is an enzootic or epizootic disease caused by a Bunyavirus that affects mostly ruminants in various parts of the African continent, causing substantial economic losses. During outbreaks, it can also affect humans, when it is mostly benign, although it can cause fatal hepatitis and encephalitis. In 2000, it arrived in the Arabian Peninsula, proving its spreading capacity. We have shown that MBT/Pas mice are extremely susceptible to experimental infection by the ZH508 strain of the virus. All mice die within 3 or 4 days after infection (mean mortality of 3.5 days), whereas BALB/cByJ mice have a later mortality (mean of 7.3 days) and a survival rate of 21%. This difference could be reproduced in a mouse embryonic fibroblast (MEF) culture coming from either of these strains. MBT/Pas fibroblasts produced higher virus titres than BALB/cBYJ cells after infection. Therefore, we analyzed the expression profile of infected and non-infected MEFs from both strains using Affymetrix Mouse430.2 chip. We have demonstrated a difference in the regulation of some genes when we compare infected fibroblasts from each mouse strain. Mainly, several IFN-inducible genes are up regulated in BALB/cByJ fibroblasts after infection but are unchanged in MBT/Pas cells. Since the virus has the ability to block IFN type I expression we believe that an IFN-independent mechanism is responsible for the activation of these genes, which can be linked to the lower virus production in BALB/cByJ MEFs and, perhaps to the later mortality of mice from that strain.

P2

GENETIC DISSECTION OF POLYGENIC SUSCEPTIBILITY/RESISTANCE TO YERSINIA PESTIS IN MOUSE INTERSPECIFIC CROSSES

Charlène Blanchet¹, Elisabeth Carniel², Jean Jaubert¹, Jean-Jacques Panthier¹, Xavier Montagutelli¹

¹Mouse Functional Genetics Unit, CNRS URA 2578, Institut Pasteur, Paris, France, ²Yersinia Unit, Institut Pasteur, Paris, France

The plague is a zoonotic disease affecting mainly rodents and accidentally humans. The etiologic agent of bubonic and pneumonic plague is *Yersinia pestis*, a Gram-negative bacterium with an extraordinary pathogenic power. The mechanisms specifically used by *Y. pestis* to kill its host so efficiently and the reasons why some individuals can survive the infection remain largely unknown.

We have identified mouse strains that are either susceptible or resistant to an infection with a fully virulent *Y. pestis*. For example, after subcutaneous injection of 100 *Y. pestis* bacteria, 90-100% C57BL/6 mice die within 5-6 days, while 85-100% SEG/Pas mice survive. A large interspecific backcross led to the identification of four putative QTLs controlling either the survival rate, or the time-to-death in susceptible individuals. Three chromosomal regions involved in the survival rate appear to act in an additive manner.

In parallel, the susceptibility of a set of over 50 Interspecific Recombinant Congenic Strains between SEG/Pas and C57BL/6 has been measured. Several strains were found to differ from C57BL/6, providing a complementary approach for the identification of host genes involved in the response to this infection.

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P4**THE COLLABORATIVE CROSS MOUSE POPULATION FOR DISSECTING THE COMPLEXITY OF HOST GENETIC FACTORS INFLUENCING IMMUNE RESPONSE CELL LINEAGES IN PERIPHERAL BLOOD**

Hana Sandovsky-Losica, Israel Zan-Bar, Richard Mott, [Fuad Iraqi](#)

¹Tel-Aviv University, Tel-Aviv, Israel, ²Oxford University, Oxford, United Kingdom

Mapping quantitative trait loci (QTLs) effecting the immune response cells lineages in the peripheral blood and subsequently identifying the genes underlying these QTL can lead to better understanding of the host response to these different infectious diseases. For this purpose we initiated a study aimed of mapping the genes which control the production of various subsets of cells that are participating in the host defense. The work was carried out by using the Collaborative cross (CC) population. Here, we present the immune profiles data on 22 CC mouse lines by quantified the amount of peripheral blood T, B, and Macrophages cells of mature mice (3-5 mice per line of 10 weeks old). The Immunophenotyping was performed using flow cytometry analysis. Blood samples were collected from the orbital venous plexus of mice. Blood samples from individual mice were incubated with specific antibodies including anti CD3e (T cells), anti CD19 (B cells), and anti CD11b (macrophages) labeled with FITC, PE-Cy5 and PE, respectively. Our study revealed marked differences in the relative proportions of different cells in the different CC mouse lines. The relative proportions varied between 13.5 – 43% for B lymphocytes and between 6.5 – 36% for T lymphocytes. As for macrophages their proportion value range was 10.6 – 39% in the different CC lines. Our results are compatible with the results which already published for different commercially available inbred mouse strains. Thus, these results form the basis for extending the study of the remaining 80 CC lines which are underdevelopment at Tel-Aviv University.

P5**THE COLLABORATIVE CROSS MOUSE POPULATION FOR DISSECTING THE COMPLEXITY OF HOST SUSCEPTIBILITY TO *PERPHYROMONAS GINGIVALIS*-INDUCED ALVEOLAR BONE LOSS**

Ariel Shusterman¹, Yael Hour-Haddad¹, Ervin Weiss¹, Richard Mott², [Fuad Iraqi](#)³

¹Department of Prosthodontics Hadassah Medical Center, Jerusalem, Israel, ²University of Oxford, Oxford, United Kingdom, ³Tel-Aviv University, Tel-Aviv, Israel

Periodontal diseases are chronic inflammatory diseases, which result in the breakdown of the supporting tissues of the teeth, including resorption of the alveolar bone of the jaw. Previous Epidemiological studies have suggested that susceptibility to chronic periodontitis is controlled by genetic factors of the host. Initially, we studied age matched male and female mice of different inbred strains (BALB/CJ, DBA/2J, C57BL/6J and A/J), which were orally infected with *Porphyromonas gingivalis* and *Fusobacterium Nucleatum*, gram negative bacteria associated with human adult periodontal disease. The infection was repeated three times at 2 day intervals. Six weeks following the final infection, the maxillary jaws were harvested and analyzed for alveolar bone loss using microCT technique. Our results have shown that there is no significant difference on alveolar bone loss between male and female of all tested strains. BALB/CJ mice were highly susceptible while DBA/2J, C57BL/6J and A/J were much more resistant. Following the initial study we have applied the same protocol on 5 lines (6 infected and 6 uninfected mice per line) from the Collaborative Cross (CC) mouse population aimed to determine the phenotypic response of these lines to the challenge. At the time of writing this abstract, analysis of the bone loss using microCT is ongoing. Results of the study will be presented at the meeting. In total, 100 CC lines will be analyzed with the infection. Genomic DNA source was collected for future genotyping with single nucleotide polymorphic markers for mapping quantitative trait loci associated with host susceptibility to the infection.

P6

THE COLLABORATIVE CROSS MOUSE POPULATION FOR DISSECTING THE COMPLEXITY OF HOST SUSCEPTIBILITY MECHANISMS TO ASPERGILLUS FUMIGATUS INFECTION

Hanna Tayyim¹, Nir Osherov¹, Richard Mott², [Fuad Iraqi](#)¹

¹Tel-Aviv University, Tel-Aviv, Israel, ²University of Oxford, Oxford, United Kingdom

Aspergillus fumigatus is an opportunistic filamentous fungal pathogen that presents itself in a wide range of allergic and invasive clinical manifestations depending on the immune status of the host and it has become an important cause of morbidity and mortality in immunocompromised hosts. The initial aim of this research is to define the phenotypic response of about 100 different lines of the collaborative cross (CC) mouse population to *Aspergillus fumigatus* AF 293. Subsequently, these results will provide a base for mapping of quantitative trait loci (QTL) associated with host susceptibility to the disease. Currently, on average, four males and four females of 45 immunocompetent CC lines were challenged with 10⁷ conidia/mouse IV inoculation of conidia of *Aspergillus fumigatus* 293. Mortality and morbidity expressed by changes in the mouse body weight, body temperature and packed cell volume (PCV) was recorded during 28 days of the infection. The survival rate of infected mice varied between the different CC lines, and mortality was due to mainly neurological damages (Cerebral Aspergillosis). Decrease in the body weight, body temperature and PCV in highly susceptible mice was observed. Body weight was a good indicator for disease progress status. More results and details will be presented at the meeting. High molecular weight genomic DNA will be extracted from the mouse tails and genotyped with single nucleotide polymorphic (SNPs) markers to be used for performing QTL mapping analysis. Finally, this is the first report of using immunocompetent inbred mouse strains to determine susceptibility to *Aspergillus fumigatus*.

P7

THE COLLABORATIVE CROSS MOUSE POPULATION FOR DISSECTING THE COMPLEXITY OF HOST SUSCEPTIBILITY MECHANISMS TO KLEBSIELLA PNEUMONIAE INFECTION

Karin Vered¹, Itzhak Ofek¹, Richard Mott², [Fuad Iraqi](#)¹

¹Tel-Aviv University, Tel-Aviv, Israel, ²University Of Oxford, Oxford, United Kingdom

Klebsiella pneumoniae (Kp) is a common pulmonary pathogen causing severe pneumonia often associated with sepsis. Here, we initiated a study aimed of mapping quantitative trait loci (QTL) and subsequently identifying the host genes involved in the susceptibility to the disease using the Collaborative cross (CC) population. Our initial aim is to define the phenotypic response of about 100 different lines of CC mice challenged with *klebsiella*. Here we report our initial results on four well defined different inbred mouse strains (C57BL/6, C3H/HEJ, BALB/C and DBA/2) challenged intraperitoneally with 10⁴ cfu of K2 *Klebsiella*. Furthermore, at the time of writing the abstracts we have results from 46 different lines of the CC population challenged with the same dose and serotype of the *klebsiella* with the same procedure carried out for the four different inbred lines. During 15 days after challenge the body weight and temperature (twice a week) and mortality were recorded. The results show that survival rate of infected mice varied between the four different inbred lines as well between the lines of the CC population. The susceptible mice also have higher body temperature and lost considerable weight as compared to the other strains after Kp challenge. Tail clips from all CC mice have been saved as a DNA source for future genetic studies and for mapping QTL. Currently, more lines are being challenged and full phenotypic results of the different four inbred mouse strains and the all tested lines of the CC population will be presented at the meeting.

P8

GENETIC DETERMINANTS OF THRIFTY METABOLISM AND ENHANCED BONE DENSITY IN PWD/PHJ MICE – A WILD-DERIVED STRAIN

Karen L Svenson, Kevin Flurkey, Luanne L Peters
The Jackson Laboratory, Bar Harbor, Maine, United States

Wild-derived mice represent *mus* subspecies that are genetically quite different from standard inbred strains and offer an opportunity to identify novel genetic influences on phenotype. We compared body composition and bone density in the wild-derived strain PWD/PhJ (PWD) to that of C57BL/6J (B6). PWD mice were smaller than B6 mice; total body weight and lean body mass (LBM) were 35–42% lower in female and male PWD mice ($P < 0.0001$). Surprisingly, despite their smaller size, percent body fat (%BF) was 38% and 35% greater in female and male PWD mice ($P < 0.0001$), although they are not obese. Analysis of LBM and %BF in the C57BL/6J-Chr^{#PWD/PhJ/J} chromosome substitution strain (CSS) set identified a potential locus on chromosome 2 (C57BL/6J-Chr2^{PWD/PhJ/J}) in females for which the PWD allele lowered LBM by 14%. No single CSS reflected a significant PWD influence on LBM in males. These results suggest that the lower LBM in PWD are determined by multiple genes, each with a relatively small effect. In contrast, both females and males of strain C57BL/6J-Chr13^{PWD/PhJ/J} had greater %BF than B6 controls (47%, females; 46%, males). Additionally, males of strain C57BL/6J-Chr11.2^{PWD/PhJ/J}, carrying the distal portion of PWD Chr11, and strain C57BL/6J-Chr5^{PWD/PhJ/J} were 51% and 53% fatter than B6 controls, suggesting that multiple loci determine the “thrifty” phenotype, as determined by %BF, in PWD mice. These loci may act in the same genetic pathway, or modifying loci exist in PWD males that attenuate obesity. Analysis of bone density is also presented.

P9

SCREENING FOR IMMUNOLOGICAL DISORDER IN MICE GENERATED BY THE RIKEN RCAI ENU MUTAGENESIS PROJECT

Takuwa Yasuda, Ayako Kobayashi, Michiko Kawabata, Hitomi Fukiage, Mikiko Ochi, Akimi Sano, Hisahiro Yoshida
Laboratory for Immunogenetics, Research Center for Allergy and Immunology (RCAI), RIKEN Yokohama Institute, Yokohama, Kanagawa, Japan

To establish allergic and immune disease model animals, we conducted *N*-ethyl-*N*-nitrosourea (ENU) random mutagenesis into mice together with various immunological screens. To produce the recessive mutant pool, we mutagenized C57BL/6J male mice and obtained the third generation, then performed phenotype screenings about morphological and behavioral anomalies, hematological alterations and immunological defects in 12 and 16 weeks of age mice. By this screening procedure, we have screened 46 G3 pedigrees and found 9 mutant lines that inherited immunological disorder phenotype by the G4 or later generation. For these mutant candidates, linkage mappings using SNPs markers through intercross with C3H/HeJ animals were performed. To date, 3 mutant candidates (each 1 line for decreased rate of T cells, increased rate of NK T cells and atopic dermatitis phenotype) have been narrowed the each causative gene down to the one region, and are at sequencing stage to identify a point mutation. In contrast, 4 mutant candidates (3 lines for increased levels of IgE and/or IgG1, 1 line for increased rate of T cells) were failed to found a linkage to one region, suggesting that there are two or more responsible regions which may cause their phenotypes. Linkage mappings of the rest 2 lines (increased rate of T cells or NK1.1⁺ cells) are now underway. In this presentation, we would like to discuss the potency to apply ENU mutagenesis to investigation for immunological disorder and the possibility to identify multiple causative genes.

P10

CHARACTERIZATION OF NEW SLA-DQB1 ALLELES FROM SEVEN PIG BREEDS USING THE GENOMIC SEQUENCE-BASED GENOTYPING METHOD

Hojun Choi, Nameun Kim, Kwangha Park, Minh Thong Le, Chankyu Park
Konkuk University, Seoul, Korea, Republic of

Identification of new alleles of MHC genes has significant meaning due to their functional importance. The characterization of SLA molecules is also important for developing suitable pig breeds as basic research models for biomedical research such as xenotransplantation. However, there have been few reports on allelic variations of MHC class II loci in pigs. To evaluate the genetic diversity of SLA-DQB1, we designed the locus specific primers and amplified SLA-DQB1 from 114 pigs using genomic PCR and analyzed their nucleotide sequence differences using direct sequencing and multiple sequence alignment. All 114 animals showed a clear single band with the expected size. Animals used for this study consisted of 9 NIH miniature pigs, 10 Duroc, 10 Landrace, 10 Yorkshire, 10 Berkshire and 65 Korean native pigs. The accuracy of genotyping results was validated by confirming the correct family segregation of the alleles and comparing the genotyping results from our new method to the those from previous cDNA based typing method. In this study, a total of 25 different alleles including 14 previously unreported alleles were classified. All new alleles were identified from the NIH miniature and Berkshire breed pigs. Since there exists no simple method to analyze the MHC loci in pigs using genomic DNA without any allelic bias, our study report the first results from efforts to establish the method for a routine genotyping of pig MHC genes using genomic DNA. This study will provide new information for understanding the breed difference or genetic diversity of pig MHC.

P11

THE DETAILED STUDY OF THE MOUSE SPRET/EI, SHOULD REVEAL NEW ANTI-INFLAMMATORY MOLECULES

Claude Libert
Ghent University, Ghent, Belgium

The mouse strain SPRET/Ei, derived from the species *Mus spretus*, displays an extreme resistance to the lethal effects of several notorious inflammatory triggers, such as TNF or LPS. Whereas control C57BL6 (B) mice succumb from 25 µg of TNF, SPRET/Ei (S) mice resist up to 1000 µg of TNF, a trait closely linked to the gene encoding the major TNF receptor *Tnfrsf1a* on chromosome 6, but also dependent on other loci which interact in an epistatic fashion. The hypo-responsiveness to TNF of S mice is also clear in models of arthritis and asthma. Also against LPS, S mice display a huge and dominant resistance, this time linked to completely other chromosomes, which, however, also in this case, interact by epistasis. Some signaling pathways are normal in S macrophages, but others are not. Hence, several genes are only slightly induced by LPS in S mice and the functions of some of these genes (e.g. encoding type I-IFNs or matrix metalloproteinases, MMPs) in endotoxemia are now under investigation. We are currently studying the gene expression patterns in S and B macrophages in detail and are concentrating on several signaling molecules of the IRF family, their sequence, activation etc. After generating the necessary tools to manipulate the genome of S mice, we are also following a reverse genetic way to identify the critical anti-inflammatory genes of SPRET/Ei.

P12**CONDITIONAL GP130 DEFICIENT MOUSE MUTANTS, 10 YEARS LATER**Werner Muller*University of Manchester, Manchester, United Kingdom*

Gp130 is the common signal transducing receptor for the Interleukin-6 cytokine family. The complete gp130 deficiency leads to early lethality in mice. The conditional gp130 deficient mouse mutant was first published in 1988 (J. exp. Med, 188, 1955-1965, 1988). In this first description, using the type I Interferon inducible Mx1cre transgene, we could show that gp130 is required for the acute phase response. We could also demonstrate that gp130 has functions in many different cell types.

10 years later, the conditional mutation was combined with a number of different cre transgenic mouse lines resulting in phenotypes in all cre lines analysed so far. Gp130 plays an important role for heart muscle cells, for neurons, for T lymphocyte, for hepatocytes, just to name some of the cell types analysed up to now. In one case we could even demonstrate that deleting the gp130 gene in one cell type in one organ has an enormous impact on another structure of the body in which the gp130 gene is still intact (J exp. Med, 204, 1935-1944, 2007). This latter experiment nicely demonstrates the power of conditional gene targeting and the interaction we identified would not have been found in any other experimental system.

An update of the conditional gp130 mouse mutant will be given following previous presentations on the IMGS Meetings in Garmisch-Partenkirchen (1988) and Braunschweig (2003).

P13**CLINICAL CHEMISTRY OF MICE CONGENIC FOR QTL FOR SURVIVAL TIME AFTER *TRYPANOSOMA CONGOLENSE* INFECTION DOES NOT REVEAL MAJOR DIFFERENCES IN RESPON TO THE PARASITE BETWEEN SHORT AND LONG SURVIVORS**

Birgit Rathkolb¹, Andy Brass², Paul Dark³, Valérie Gailus-Durner¹, John Gibson⁴, Helmut Fuchs¹, Martin Hrabé de Angelis¹, Fuad Iraqi⁵, Steve Kemp⁶, Jan Naessens⁵, Matt Pope⁵, Eckhard Wolf⁷, Harry Noyes¹, Morris Agaba¹

¹*Institute of Experimental Genetics, Helmholtz Zentrum München, Germany*, ²*School of Computer Science, University of Manchester, Manchester, United Kingdom*, ³*Intensive Care Medicine, Salford Royal NHS Foundation Trust, The University of Manchester, Manchester, United Kingdom*, ⁴*University of New England, Armidale, Australia*, ⁵*International Livestock Research Institute (IRLI), Nairobi, Kenya*, ⁶*School of Biological Sciences, University of Liverpool, Liverpool, United Kingdom*, ⁷*Institute of Molecular Animal Breeding and Biotechnology, Ludwig Maximilian Universität, München, Germany*

Trypanosoma congolense are protozoan parasites that cause severe diseases in livestock in Africa and also infect mice. Three regions on mouse chromosomes 17, 5 and 1 designated *Tir1*, *Tir2* and *Tir3* respectively control the survival time of mice after infection with *T. congolense*. Three lines of congenic mice were developed to define the boundaries of these regions. Survival times and the degree of parasitaemia and anaemia were obtained, and additionally 16 clinical chemical parameters were measured by the clinical chemistry laboratory of the German Mouse Clinic for the congenic mice and the parental strains from which they were bred. The survival time of the parental inbred mice appeared to correlate with both parasitaemia and liver enzyme activities that might indicate a higher degree of inflammation in the liver; suggesting that inflammation had a beneficial effect possibly associated with reduced parasitaemia. However there was no difference in parasitaemia or liver enzyme activities of *Tir1* and *Tir2* congenic mice relative to their respective controls showing that differences in survival, parasitaemia and degree of inflammation are not associated with each other despite the correlation in the parental lines. This suggested that differences in survival are due to different abilities to control the symptoms of disease rather than different ability to resist the parasite.

P14

GENETIC VARIATION IN INTESTINAL GENE EXPRESSION IN PROGENITORS OF THE COLLABORATIVE CROSS

Elissa J. Chesler, Cymbeline T. Culiati, A.V. Palumbo, Vivek M. Philip, M. Podar, Brynn H. Voy
Biosciences Division, Oak Ridge National Laboratory, Oak Ridge TN, United States

Genetic variation influences the composition of the intestinal microflora population. This variation is both a cause and effect of metabolic variation and disease susceptibility in the mouse. In the present study we have examined the heritability of molecular variation in the gut intestine in replicate male and female mice from the progenitors of the Collaborative Cross. Mouse caecae were dissected, contents were extruded for microbiota sequencing, and intestinal epithelial samples were obtained for gene expression analysis using the Illumina mouse sentrix 6 array. Genetic variation in transcript abundance was high with a median heritability of $> .2$ based on strain intraclass correlation. An analysis of Gene Ontology category over-representation was performed using WebGestalt. This analysis revealed statistically significant over-expression of many categories representing metabolizing enzymes, glycolysis and gluconeogenesis related genes, programmed cell death and intestinal immune processes. While SNP effects are a likely source of upward bias in the heritability statistic, this source of bias is expected to be uniform across biological pathways in this population. In a second experiment, acute metabolic effects were examined in a balanced sample of fasted vs. non-fasted mice matched for sex and strain. Many differentially expressed genes were detected in this comparison. However, there was only limited similarity in transcripts subject to both population variation and fasting manipulation.

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P15

MICRORNAS PLAY A LIMITED ROLE IN MATERNAL MRNA DEGRADATION

Mathyas Flemer¹, Ma Jun², Paula Stein², Richard M. Schultz², Petr Svoboda¹
¹Institute of Molecular Genetics, Prague, Czech Republic, ²Department of Biology, University of Pennsylvania, Philadelphia, United States

MicroRNAs are small endogenous RNA molecules, which typically imperfectly basepair with 3'UTR sequences and repress translation in animal cells. Repressed mRNAs are translocated into p-bodies, cytoplasmic foci associated with mRNA degradation. In the zebrafish embryo, AAGUGC motif-containing miRNAs of the zygotically expressed miR-430 family down-regulate a large fraction of maternal mRNAs. We studied maternal mRNA degradation and the miRNA pathway in mouse oocytes and early embryos by using bioinformatic approaches and immunohistology techniques. Microarray analysis of maternal mRNA degradation suggests that maternal miRNAs play a limited role and do not generate any detectable signature in the 3'UTR composition of the down-regulated maternal transcripts. This is consistent with immunohistological analysis of p-body components in oocytes. However, analysis of *Dicer*^{-/-} ES cells reveals that about 20% of putative targets of the miR-290 family (zygotically expressed, closely related to the miR-430 in the zebrafish) exhibit high expression in the oocyte when compared to the blastocyst stage and somatic tissues. As transcripts targeted by the miR-290 cluster in ES cells are not maternal, we propose that the miR-290 cluster has a role in restricting zygotic expression of genes, which were highly expressed in the oocyte while degradation of true maternal transcripts would be less important.

P16
PROMOTER EVOLUTION OF MCM8 ORTHOLOGOUS GENES IN MAMMALIAN GENOME

Kenichi Yoshida
Meiji University, Kawasaki, Japan

Mini-chromosome maintenance genes (MCMs) are essential for eukaryotic DNA replication initiation. Here we aimed to gain more insight into the evolutionary conserved gene regulatory mechanism of a novel member of MCMs, MCM8, by using bioinformatics and functional assay. Comparative genomic approach for higher eukaryotes orthologous gene could help to understand common gene regulatory mechanism for MCM8 gene. Human, mouse, rat, dog, and chicken MCM8 gene, consisting of 19, 18, 17, 18, and 18 exons, respectively, indicating MCM8 gene structure is well conserved in higher eukaryotes. We searched the proximal region of the transcription start site for potential transcription factor-binding elements using Transfac. Although the NF-Y- and E2F-binding sites within 5'-flanking promoter region were conserved among mammalian MCM8 promoters, transcriptional regulation of the chicken MCM8 ortholog was predicted to be distinct from that of mammalian MCM8 based on the divergence within the 5'-flanking promoter region. Interestingly, putative promoter region harboring E2F-binding motif of human, rat, and chicken MCM8 were up-regulated by exogenous co-expression of E2F1 in transient luciferase reporter assay. Therefore, cell-cycle-dependent transcriptional regulation of higher eukaryotes MCM8 could be partially-conserved during promoter evolution. This study was partly supported by KAKENHI.

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P18
CHARACTERIZATION OF DIVERSITY IN BLOOD ETHANOL CLEARANCE RATES IN PRECC MICE

Christine Powell¹, Jill Steigerwalt¹, Fernando Pardo-Manuel de Villena¹, Daniel Pomp¹, Elissa Chesler², David Threadgill¹
¹University of North Carolina, Chapel Hill, NC, United States, ²Oak Ridge National Laboratory, Oak Ridge, TN, United States

Extensive evidence from human and animal studies supports the hypothesis that ethanol metabolism is a complex trait with both hereditary and environmental influences. Heritable factors underlying ethanol metabolism are of considerable interest as they most likely attribute to inter-individual variations in its toxicity, sensitivity, and preference. The majority of genetic mapping studies in rodents for ethanol metabolism have been limited to the BXD (C57BL/6J x DBA/2J) recombinant inbred lines or F2 crosses in rats. However, results from these studies have not lead to the identification of candidate genes for the detected QTLs or physiological characteristics that may be associated with differential ethanol metabolism. We have analyzed pre-Collaborative Cross (preCC) mice, a large panel of recombinant inbred mouse lines designed specifically for complex trait analysis, to characterize the phenotypic diversity of blood ethanol clearance (BEC) rates, perform phenotype:phenotype correlations to identify interactions between BEC and other metabolic parameters being collected as part of a larger preCC experiment, and lastly to perform genotype:haplotype mapping to identify candidate genes underlying ethanol metabolism. Male preCC mice and founder strains were administered a 3 g/kg dose of ethanol via intraperitoneal injection and tail vein blood draws taken 30 min post-dosing followed every hour for the next 3 hours. Serum was used to measure blood ethanol concentrations over time from which BEC rates were determined. Preliminary analysis of 60 preCC lines tested thus far have shown delta blood alcohol concentrations (mg/dl) between 40 and 350 demonstrating an abundance of phenotypic diversity already captured in a small sub-set of lines. Correlation analyses with physiological characteristics will be presented that reveals inter-phenotypic associations that may contribute to differential ethanol toxicity.

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P20

USING ONTOLOGIES TO ANNOTATE LARGE-SCALE MOUSE PHENOTYPE DATA

Tim Beck, Ann-Marie Mallon, Andrew Blake, Hugh Morgan, John Hancock
MRC Harwell, Didcot, Oxfordshire, United Kingdom

Ontologies are increasingly being used to standardise the annotation of phenotypic instances. Within the domain of mammalian phenotypes two differing approaches can be adopted: the use of a single dedicated phenotype ontology; or the combination of concepts from a range of different ontologies to derive an annotation. Here we present the use of both approaches in an annotation framework which utilizes the flexible and descriptive combinatorial approach to annotate large numbers of mouse phenotypes at the database level, and the use of a more intuitive dedicated phenotype ontology for data access at the points of data entry and querying.

As part of the EUMODIC project mouse baseline and mutant strains are undergoing Standard Operating Procedures (SOPs) to discover phenotypes of interest. This wealth of data will be made available from the EuroPhenome database. In order to ensure precise data definition and facilitate data comparison, individual qualitative parameters captured in each SOP, and the subsequently derived phenotype data, are both annotated in terms of entities and qualities (EQ) utilising a range of OBO ontologies, including the Mouse Anatomy (MA) ontology and phenotypic qualities ontology (PATO).

Previously the work of ontology annotation has largely been carried out post data entry by database curators. Within large-scale phenotyping projects this can be impractical and so a desirable alternative is to have phenotyping scientists working seamlessly with ontologies at the point of data entry. To assist this aim, intuitive compound terms from the Mammalian Phenotype (MP) ontology can be used to input and query data, exploiting current efforts to map MP to the PATO EQ structure.

P21

EUROPHENOME: A MOUSE PHENOTYPING RESOURCE

Ann-Marie Mallon, Hugh Morgan, Tim Beck, Andrew Blake, John Hancock
MRC Harwell, Oxfordshire, United Kingdom

The broad aim of biomedical science in the postgenomic era is to link genomic and phenotype information systematically to allow deeper understanding of the processes leading from genomic changes to altered phenotype and disease. Essential to developing such a linkage are databases which contain information on both normal phenotypes of inbred mouse strains and mutant phenotypes. EuroPhenome (<http://www.europhenome.org>) is an online mouse phenotyping resource that allows access to data generated by the EUMODIC (<http://www.eumodic.org>) project. This aims to gather data from a collection of standardised procedures (SOPs) called EMPReSSlim (<http://empress.har.mrc.ac.uk>) performed on inbred mouse strains and 500 knock-out lines from the EUCOMM project. EMPReSS is the European Mouse Phenotyping Resource of Standardised Screens and was developed by groups of expert scientists to enable rapid, easy and reproducible assessment of phenotype in all major body systems. The EuroPhenome interface allows the user to access the data via the phenotype or genotype. It also allows the user to access the data in a variety of ways, including graphical display, statistical analysis and access to the raw data via web services. To assist with data definition and cross-database comparisons, phenotype data within EuroPhenome will be annotated using combinations of terms from OBO ontologies. Principally the phenotypic quality ontology (PATO) will be used to assign traits to biological entities.

P22

THE TRANSCRIPTIONAL NETWORK THAT CONTROLS GROWTH ARREST AND DIFFERENTIATION IN A HUMAN MYELOID LEUKEMIA CELL LINE

Harukazu Suzuki, Yoshihide Hayashizaki
RIKEN Omics Science Center, Yokohama, Japan

We analyzed transcriptional control in the human monocytic cell line THP-1 throughout a time course of phorbol myristate acetate (PMA)-induced differentiation. Using deepCAGE (a new deep sequencing application of the Cap Analysis of Gene Expression) we have for the first time measured the dynamics of genome-wide transcription start site usage over time. We then used comparative genomic regulatory site predictions in the regions identified by CAGE and modeling of the activities of regulatory motifs through time to identify the key transcription factors (TFs) regulating/driving differentiation, their time-dependent activities, and their target genes. Systematic siRNA knockdown of 52 key TFs confirmed the role of individual factors in the differentiation process. Our analysis of growth arrest and differentiation in THP-1 cells indicates that cellular states are constrained by complex networks involving substantial numbers of both positive and negative regulators. (HS and YH present this work on behalf of The FANTOM consortium and RIKEN Omics Science Center.)

P23

A RESOURCE FOR COMMUNITY ANNOTATION OF THE MOUSE GENOME

Deanna Church¹, Carol Bult²
¹*National Center for Biotechnology Information, Bethesda, Maryland, United States*, ²*The Jackson Laboratory, Bar Harbor, Maine, United States*

Since its initial public release in 2002, the genome assembly and annotation for the reference genome sequence of the C57BL/6J strain of laboratory mouse has undergone multiple rounds of improvement facilitated by both manual and computational analyses. The refinement of existing annotations and prediction of new functional elements in the genome is a long term project that is beyond the scope of any one annotation team. Many regions of the genome are sufficiently complex that most automatic annotation schemes will fail. We present here a Web-based resource for registering issues and suggestions to improve mouse genome annotation. Any member of the research community can create a record in the system to document an annotation issue or suggestion. These records are managed in a central annotation issue tracking repository that is monitored by curators from NCBI, MGI, Ensembl, UCSC, and HAVANA (VEGA). The mouse genome annotation tracking system is modeled after a similar resource that is in use by the Genome Reference Consortium for managing and tracking issues related to the mouse and human genome assemblies. We hope that members of the community will contribute to this resource in an effort to continually improve the annotation of the mouse genome.

P24

MOUSECYC: A DATABASE OF CURATED BIOCHEMICAL PATHWAYS FOR THE LABORATORY MOUSE

Alexei Evsikov, Mary Dolan, Carol Bult
The Jackson Laboratory, Bar Harbor, Maine, United States

The complete genome sequence for the laboratory mouse has served as a valuable resource for generating a comprehensive catalog of genes, as well as other genome features in the mouse genome. To derive new insights into biological processes using the reference genome sequence will require moving beyond a catalog of genome features to representations of how genome features interact in pathways and networks and how perturbations of these interactions contribute to disease processes. Toward this goal, we have implemented a new database of curated biochemical pathways for the laboratory mouse called MouseCyc. The MouseCyc database was implemented using the Pathway Tools software development tool kit and is accessible at <http://mousecyc.jax.org/>. The initial focus for the curation of MouseCyc includes such cell-level biochemical processes as biosynthesis, degradation, energy production, and detoxification. The database currently contains 1,656 enzymatic reactions and 231 curated pathways. MouseCyc is unique among existing pathway databases due to the extent to which the pathway information is integrated with the wealth of biological knowledge for the laboratory mouse that is available from the Mouse Genome Informatics (MGI) database. Moreover, MouseCyc supports comparative analysis of biochemical pathways between mouse and human. In-depth curation to date has revealed a number of key differences in the roles that mouse-human gene orthologs play in basic metabolic pathways.

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P25

MOUSENET: A PREDICTIVE FUNCTIONAL NETWORK RESOURCE FOR THE LABORATORY MOUSE

Yuanfang Guan¹, Chad Myers², Carol Bult³, Olga Troyanskaya¹

¹*Lewis-Sigler Institute for Integrative Genomics, Carl Icahn Laboratory, Princeton, New Jersey, United States,*
²*Department of Computer Science, Princeton, New Jersey, United States,* ³*The Jackson Laboratory, Bar Harbor, Maine, United States*

We have implemented a web-based predictive functional network resource (MouseNet) for the laboratory mouse based on a Bayesian integration of diverse genetic and functional genomic data. The network includes probabilistic functional associations among 20,581 protein-coding genes. An analysis of the global topology of the mouse functional network reveals multiple biologically relevant systems-level features of the mouse proteome. Specifically, we identified distinct novel topological characteristics of central modulators that affect diverse pathways, and also demonstrate that local network topology is informative about the phenotypic traits and disease associations of a gene. MouseNet provides the community with a resource for discovering novel pathway components and phenotype and disease relationships, as well as a tool for exploring systems-level topological and evolutionary features of cellular interactomes. We used MouseNet to predict novel functional associations and network components related to the embryonic stem cell pluripotency gene, *Nanog*. These MouseNet predictions were further supported by subsequent experimental data. The MouseNet resource is currently publicly available at <http://mouseNET.princeton.edu>.

P26

UNIPROT KNOWLEDGEBASE: LINKING PROTEIN SEQUENCE AND FUNCTION

Michele Magrane, UniProt Consortium

¹*EMBL-EBI, Hinxton, Cambridge, United Kingdom,* ²*Swiss Institute of Bioinformatics, Geneva, Switzerland,* ³*Protein Information Resource, Washington DC, United States*

With the ever-growing amounts of sequence and functional data available, resources which collect and curate this information are becoming increasingly important in providing a summary of current knowledge to researchers and facilitating further investigation. The UniProt Knowledgebase (UniProtKB) provides the scientific community with a comprehensive collection of protein sequence records containing extensive curated information including functional and sequence annotation, literature citations and cross-references to more than a hundred databases. The knowledgebase consists of two sections: UniProtKB/Swiss-Prot is manually curated to ensure high-quality information content while UniProtKB/TrEMBL is a preliminary section enriched with automated annotation. The manual curation process involves extracting experimentally validated results from scientific literature and combining these with the output of sequence analysis programs to provide a complete overview of available data. UniProtKB is a universal resource covering more than 160,000 species with a particular focus on mammalian proteins. The complete manually curated human proteome is now available from UniProtKB/Swiss-Prot based on an estimate of just over 20,000 protein-coding genes in the human genome. Processes such as alternative splicing, initiation and promoter usage as well as post-translational modifications vastly increase protein diversity. The human proteome will continue to be regularly revisited and updated as new information becomes available and we are now working towards curation of the complete mouse proteome. The current status of mammalian proteomes in the database will be presented along with future plans.

P27**MAUSDB: THE GERMAN MOUSE CLINIC OPEN SOURCE PHENOTYPE- AND MOUSE MANAGEMENT SYSTEM**

Holger Maier, Christoph Lengger, Ralph Steinkamp, Karlheinz F. Schäble, Helmut Fuchs, Valerie Gailus-Durner, Martin Hrade de Angelis

Helmholtz Zentrum München - German Research Center for Environmental Health (GmbH), Neuherberg, Germany

Mutant mouse lines are important tools to elucidate gene function as observed phenotypes can mostly be attributed to a known genotype. The German Mouse Clinic (GMC, <http://www.mouseclinic.de>) as an open-access platform offers standardized and comprehensive phenotype analysis of mutant mouse lines and screens for potential new mouse models of human diseases. In the GMC, mouse cohorts pass through 14 different screening modules in a strictly defined workflow in the course of primary screen where up to 240 physiological parameters per mouse are measured. Screening many mouse cohorts in multi-parallel workflows is a logistical challenge and requires appropriate IT support and well-defined data infrastructure. Therefore, we developed a web-based database application – MausDB – for the GMC that serves as a central data platform accessible by all GMC users. MausDB supports scheduling of mouse lines to the phenotyping pipelines by work list management functions. Phenotyping data upload to MausDB and re-export is done via spreadsheet files. MausDB also offers standard mouse management functions (breeding support, cage management, etc.) and integrates phenotype data with line/genotype data and other metadata on the individual mouse level. For the GMC, this is a prerequisite for inter-line data analysis, data mining and data exchange in a cross-European phenotyping effort (EUMODIC). Although primarily developed for the GMC, MausDB also proved to be useful for other mouse facilities due to its general purpose design and intuitive user interface. Hence, we offer MausDB to the mouse community as open source software under the terms of the GNU General Public License.

P28**MOUSEBOOK: ONLINE INTEGRATED MOUSE INFORMATION SYSTEM**

Andrew Blake, Ann-Marie Mallon, Simon Greenaway, Tim Beck, John Hancock
MRC Harwell, Harwell, Oxfordshire, United Kingdom

A new database integration system and web search interface called Mousebook (www.mousebook.org) has been created that helps scientists to source information on MRC mouse models at Harwell. MouseBook was conceived and developed by staff at the Mammalian Genetics Unit and is a resource for integrating and sharing the wealth of primary data generated onsite with genetic, genomic and phenotypic data from a number of other databases. MouseBook allows users to browse through the complete lists of primary data as well as search using Google style search techniques for a specific query.

The results interface shows the primary data with integrated links to information from MGD (Mouse Genome Database), Uniprot (Universal Protein Resource), Ensembl and OMIM (Online Mendelian Inheritance in Man) where relevant. Mousebook can also be searched using the Mammalian Phenotype Ontology (MP) by selecting a term from an instance of the MP tree. Mousebook enables users to register and login to receive additional functionality such as an update service which will inform them when new data enters the database matching their search e.g a new stock.

MouseBook aims in the future to expand the searchable data, primarily to include data from EUMODIC, a project which aims to perform a primary phenotype assessment of up to 650 mouse mutant lines derived from ES cells developed in the EUComm project.

P29

INTEGRATION OF GENE TRAP RESOURCES WITH MOUSE GENOME INFORMATICS (MGI)

Sophia Zhu, Richard Baldarelli, Sharon Cousins, Howard Dene, Cynthia Smith, Robert Sinclair, Jill Lewis, James Kadin, Joel Richardson, Judith Blake, Martin Ringwald, Janan Eppig, Carol Bult
The Jackson Laboratory, Bar Harbor, ME, United States

The Mouse Genome Informatics (MGI) database (<http://www.informatics.jax.org>) has expanded its allele representation to include gene trap cell lines present as sequence tags in the dbGSS division of GenBank. In the first phase of implementation, gene trap IDs associated with specific genes were displayed on the MGI Gene Detail pages. In the current phase of gene trap data integration, we are including detailed information about gene traps including cell lines, vectors, and sequence tag methods as well as graphical representations of the gene trap sequences in the context of gene structure. Details for over half a million sequence tags are included in this release, including 250,931 tags associated with 12,433 trapped genes. Automated integration of gene traps from dbGSS, including regular updates of gene trap-to-gene associations, coupled with literature-based phenotype annotations of mice generated from gene trapped cell lines will provide a comprehensive resource of mouse gene trap information.

MGI is a comprehensive resource of data and information about the genetics, genomics and biology of the laboratory mouse. Information in MGI is obtained from diverse sources, including the scientific literature and external databases such as EntrezGene, UniProt, and GenBank. The MGI database can be accessed by a variety of methods including web-based search forms, a genome sequence browser, and downloadable database reports. In addition to its extensive collection of phenotypic allele information for mouse genes that is curated from the published biomedical literature, MGI includes a comprehensive representation of mouse genes including sequence, functional (GO), and expression information.

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P30

GENOME BUILD 37: CURRENT PRIORITIES AND ISSUES IN MOUSE GENE NOMENCLATURE

Lois J Maltais, Judith A Blake, Carol J Bult, Janan T Eppig, MGI Staff
The Jackson Laboratory, Bar Harbor, ME, United States

NCBI Build 37 (B37) of the mouse genome sequence assembly represents the essentially complete genome sequence for the C57BL/6J strain of the laboratory mouse. The Mouse Genome Informatics (MGI) resource (www.informatics.jax.org) has available the most current gene predictions for Build 37 from three annotation providers: NCBI, Ensembl, and HAVANA (VEGA). The gene predictions were compared to one another to generate a comprehensive, unified mouse gene catalog with associations to gene records in MGI. The MGI database allows researchers to obtain a comprehensive list of mouse genes from a single source and serves as the basis for functional annotation of genes by MGI curators.

Complementing the effort to produce a comprehensive gene catalog, the MGI nomenclature group has resolved and is continuing to resolve nomenclature standardization. Some of these examples include, 1) checking markers that do not have sequence data and discontinuing database representation if warranted, such as the related sequences of the ribosomal L and S families (*Rpl#-rs#* and *Rps#-rs#*); 2) data analysis supporting the merging of two genes into one using appropriate nomenclature; 3) overlapping genes with different biotypes; 4) non-valid genes with associated data (sequences, GO, other gene models). The coordination of creating a unified gene index and standardization gene nomenclature facilitates all research endeavors.

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P31

GENE ONTOLOGY RESOURCES FOR COMPARATIVE GENOMICS: MOUSE AND THE GO REFERENCE GENOME PROJECT

Judith A. Blake, David P. Hill, Mary E. Dolan, Alexander D. Diehl, Li Ni, Harold J. Drabkin, Dmitry M. Sitnikov
The Jackson Laboratory, Bar Harbor, ME, United States

The GO Reference Genome Project is a shared curation effort among the GO Consortium members who provide molecular annotations for twelve model organisms [*Arabidopsis thaliana*, *Caenorhabditis elegans*, *Danio rerio*, *Dictyostelium discoideum*, *Drosophila melanogaster*, *Escherichia coli*, *Gallus gallus*, *Homo sapiens*, *Mus musculus*, *Rattus norvegicus*, *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*]. GO curators, mostly associated with Model Organism Databases, are coordinating their efforts to provide comprehensive annotations for sets of chosen target genes. Starting with the set of genes implicated in human disease processes, and now including genes of high research interest or highly conserved, the curators incorporate annotations for their taxa from relevant biomedical literature. As the curators are simultaneously working on the same set of genes, they are also updating the ontologies as needed in a coordinated way. This work requires close attention to the assignment of orthology/homology among these 12 groups and the result of the work is the emergence of orthology/homology sets of genes for this broad set of taxa. The comprehensive annotations of the well-studied model organisms provide broad and deep annotation of the reference genomes and serve as a basis for the annotation of emerging genomes via sequence similarity matrices.

P32

THE NEW MGI WEB SITE AND SEARCH TOOL

Lois J Maltais, James A Kadin, Joel E Richardson, Kim Forthofer, Jill Lewis, Pete Frost, Matt Hall, Jon Beal, Martin Ringwald, Judith A Blake, Carol J Bult, Janan T Eppig
The Jackson Laboratory, Bar Harbor, ME, United States

The Mouse Genome Informatics (www.informatics.jax.org) web site has changed significantly this year, with a new overall design and new search tool.

New Web Design. Exploring MGI is now assisted with a navigation bar that appears on each web page. The navigation bar features cascading menus that lead users quickly to specific search forms and information pages. The homepage boasts new major content area images, leading to specific content pages that, in turn, provide relevant data access points and FAQs. This new navigation paradigm improves intuitive navigation of MGI, providing more visual clues for users and allowing quick access to the desired MGI pages.

New Search Tool. Recently, major infrastructure enhancements have made the MGI Quick Search Tool a verbose and comprehensive search entrée into MGI data. The Quick Search now combines nomenclature and ID searches with searches of MGI annotations and ontologies. The combination of an enhanced nomenclature search (symbols, names, orthologs), and complete indexing of MGI data, and weighted word searches provides an instantaneous return of information, as well as data for the user on the nature of the returned object. The Quick Search has become a robust way for those unfamiliar with MGI to focus their interests and a simplified search for users who seek quick entry into specific information (e.g., give me detail for gene X?; what information does MGI have about retinal degeneration?). Advanced search forms in MGI continue to support complex queries such as “What genes on Chromosome 11 function as transcription factors and have mutations associated with abnormalities of the inner ear?”

Our presentation will focus on these primary changes in the MGI interface and illustrate how the new navigation paradigm and search tool improve usability and enhance the power of MGI for mouse research and translational studies.

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TRANS-REGULATION OF MEIOTIC RECOMBINATION HOTSPOTS BY RCR1

Emil Parvanov, Siemon Ng, Petko Petkov, Kenneth Paigen
The Jackson Laboratory, Bar Harbor, United States

Meiotic recombination provides genetic diversity among offspring and insures proper chromosome segregation. Among mammals, as well as yeast and higher plants, recombination preferentially occurs at highly delimited chromosomal sites 1-2 kb long known as hotspots. Although much is known about the role of various proteins participating in the molecular events of the recombination process, relatively little is understood about the factors controlling the location and relative activity of mammalian recombination hotspots. To search for trans-acting factors controlling the positioning of recombination events, we compared the locations of crossovers arising in an 8 Mb segment of a 100 Mb region of mouse Chr1 when the longer region was heterozygous C57BL/6J (B6) x CAST/EiJ (CAST) and the remainder of the genome was either similarly heterozygous or entirely homozygous B6. The lack of CAST alleles led to loss of some hotspots, others appeared and a third group remained unchanged, indicating the presence of distant trans-acting gene(s) whose CAST allele(s) activate or suppress the activity of specific hotspots. Testing the activity of three activated hotspots in sperm samples from individual male progeny of two genetic crosses, we identified a single trans-acting regulator of hotspot activity, designated *Rcr1*, that is located in a 5.30 Mb interval (11.74-17.04 Mb) on Chr 17. Using an *E. coli* cloning assay to characterize the molecular products of recombination at two of these hotspots, we found that *Rcr1* controls the appearance of both crossover and noncrossovers, indicating that it likely acts at the step of DSB site determination.

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THE GENOME REFERENCE CONSORTIUM

Valerie Schneider, on behalf of the GRC
National Center for Biotechnology Information, NIH, Bethesda, MD, United States

The production of a high quality reference sequence of the mouse genome provided a major tool for biomedical research. The reference serves as a foundation for comparative analyses to the human and other genomes, plays an important role in studies of evolutionary biology and facilitates murine biological research. Such studies have revealed, however, that there are regions of the reference mouse genome sequence that are not optimally represented by the existing assembly. The current mouse assembly has regions lacking good BAC clone representation. This is due in part to a limited number of BAC resources and to regions that are recalcitrant to propagation in BAC vectors. At other regions, highly repetitive structures have hindered clone assembly. Furthermore, inter-strain variation renders certain loci sufficiently complex as to require representation by alternate sequences. To improve the representation of the reference mouse genome, we have formed the Genome Reference Consortium. The GRC's goals are to correct the small number of regions in the reference that are currently misrepresented, to close as many remaining gaps as possible and to produce alternative assemblies of structurally variant loci when necessary. We also provide mechanisms by which the scientific community can report loci in need of further review. Information about loci currently under review and genome assembly production cycles is publicly available. The reference assembly is the cornerstone upon which modern murine genetic research is based. It is therefore essential we have the best possible view of this genome as we further our understanding of mouse biology.

P35**DEVELOPMENT OF A SEMANTIC FRAMEWORK FOR THE INTEGRATION OF MOUSE PHENOME INFORMATION**

Hiroshi Masuya¹, Nobuhiko Tanaka¹, Kazunori Waki¹, Norio Kobayashi², Tetsuro Toyoda², Toshihiko Shiroishi³, Shigeharu Wakana¹, Riichiro Mizoguchi⁴

¹RIKEN BRC, Tsukuba, Ibaraki, Japan, ²RIKEN, Yokohama, Kanagawa, Japan, ³Nat. Inst. Genet., Mishima, Shizuoka, Japan, ⁴Osaka Univ., Ibaraki, Osaka, Japan

The advent of genome science promotes world-wide large-scale mouse mutagenesis projects. In parallel, development of comprehensive phenotyping platforms for evaluations of various biological traits such as morphology, sensory, behavior, pathology and so on, are underway as well. These projects will provide advanced mutant resources associated with broad kinds of genetic and functional information. The Mouse Phenotype Database Integration Consortium initiated a process to develop standardized descriptions of phenotypes and file formats for the phenotyping protocols and phenotype data sets with an aim to make mouse phenotype data available in an integrated manner to the international mouse community (Mamm Genome. 2007 18:157-163). In addition, CASIMIR (Coordination and Sustainability of International Mouse Informatics Resources) consortium co-ordinates interoperability of further wide-range of data including sequences, and material resources relevant to the use of the mouse as a model organism for human disease. These processes need the general data model or semantic framework that integrates such a broad range of concepts across the experimental genetics studies. Using semantic web technologies, we are developing advanced information model that integrates genetic concepts that include phenotype, genotype, allele and locus, and contents of various public databases, ontologies and various data provided from mouse phenotyping analyses. We show our recent progress in these studies.

P36**STATISTICAL INFERENCE FOR MAMMALIAN OMIC DATA INTEGRATION ON THE SEMANTIC WEB**

N Kobayashi¹, Y Yoshida¹, Y Mochizuki¹, M Ishii¹, A Matsushima¹, Y Makita¹, N Heida¹, S Asano¹, H Masuya², S Wakana², T Toyoda¹

¹Bioinformatics And Systems Engineering division (BASE), RIKEN, Yokohama, Kanagawa, Japan, ²BioResource Center, RIKEN, Tsukuba, Ibaraki, Japan

The Semantic Web is a framework for knowledge description and discovery by inferences, which uses relationships given as semantic links between two entities. We apply the Semantic Web approach to realise an integrated database over the various omic entities including the complete genome sequences along with gene structures, gene products, metabolites, phenotypes, publications and any information useful to the bio-medical research communities. For the practical use of published biomedical data on the Semantic Web, it is beneficial to reinforce the acquisition of valuable data that is difficult to utilise, because of the lack of semantic links by supplying a hybrid methodology combining not only inferences over the knowledge but also those supported by statistical significance over multiple raw documents. We have established semantic links among omic entities including the genome, genes and literature, and have developed a system to generate inferences based on the data. The system termed Positional Medline (PosMed), which instantaneously ranks entities of significantly related mouse, rat, and human genes with functions mentioned in literature. This accomplishes not only a entity search directly related in literature but also an indirect search via semantic links over the entities not directly related in literature [Kobayashi, N. and Toyoda, T. Bioinformatics, 24, 1002-1010, 2008]. Furthermore, PosMed is used worldwide on the Web to select candidate genes for positional cloning, as it is possible to add a chromosomal interval to the search limiting the ranking to only those genes within the interval. PosMed is available at <http://omicspace.riken.jp>

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DEVELOPMENT OF INTERIGENT INFRASTRUCTURE FOR DESCRIPTION OF EXPERIMENTAL PROTOCOLS WITH SEMANTIC WEB TECHNOLOGY

Nobuhiko Tanaka¹, Kazunori Wali¹, Riichiro Mizoguchi³, Norio Kobayashi², Tetsuro Toyoda², Yoko Shibukawa¹, Tomoko Kushida¹, Ikuko Yamada¹, Tamio Furuse¹, Shigeharu Wakana¹, Hiroshi Masuya¹

¹*RIKEN BioResource Center, Tsukuba, Ibaraki, Japan*, ²*RIKEN Bioinformatics and Systems Engineering, Yokohama, Kanagawa, Japan*, ³*University of Osaka, Suita, Osaka, Japan*

With the progress of functional genomics study, it becomes a global major challenge to develop infrastructure for systematic evaluation of an enormous volume of mouse phenotype information. On this situation, it is very important to integrate the phenotype information with high reliability on the basis of the explicit evidence of assay results from different phenotyping procedures among institutes. In 2007, to promote efficient sharing of the information for various experimental protocols, the Mouse Phenotype Database Integration Consortium proposed a standardized data format of procedures, Phenotyping Procedure Markup Language (PPML: http://www.interphenome.org/ppxml/ppml_v1_3.html). On this background, to provide methodology for more detailed comparison of a kind of assay (e.g. protocols of open-field assay in different institutes) on PPML, we are developing a semantic framework representing experimental procedure contents using semantic web and ontological technology. In this process, we constructed a new data framework to describe procedures, SDOPs (Standardized Description of Operation Procedures), which enable direct comparison of detailed parameters of the experimental protocols among multiple laboratories, and further help to store the protocol information in the developing semantic database. We aim to develop an integrated semantic database applicable to all of general experimental protocols in the mouse behavior analysis, further, to all mouse phenotyping analyses. In this presentation, we will show examples of which we store information about experimental protocols in the mouse phenotyping analysis, especially about behavior analysis protocols, in the developing database.

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SNP DATABASE AMONG C57BL-RELATED STRAINS AND THEIR CONGENIC STRAINS

Kazuyuki Mekada, Kuniya Abe, Ayumi Murakami, Kazuo Moriwaki, Yuichi Obata, Atsushi Yoshiki
RIKEN BioResource Center, Tsukuba, Japan

The C57BL/6 (B6) is commonly used to create congenic strains as the genetic background of spontaneous and induced mutations. The B6 is also widely distributed to different facilities to establish several substrains worldwide. The C57BL/10 (B10) is well known as the genetic background of several H-2 congenic strains. We have surveyed SNPs among these C57BL-related strains by the Golden Gate assay of Illumina's Mouse MD Linkage Panel. We found 67 SNPs between B6 and B10, while 861 SNPs between B6 and BALB/c strains. These analyses identified 12 novel SNP markers, which could distinguish B6J and B6N on Chr 3, 6, 7, 9, 10, 11, 13, 14, 16 and 17. These detected SNPs were not overlapped with the SNPs previously reported by Petkov and Wiles (2005). We also found that the C57BL/6Boy background of Ly antigens congenic strains was distinct from those of B6J and B6N. Our data clearly demonstrated congenic status of B10.A, B10.D2, B10.MBR, B10.QBR and B10.BR H-2 congenic strains. These SNP database must be useful for accurate genetic monitoring of the congenic strain background.

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SOLUTIONS FOR DATABASE INTEROPERABILITY: A REPORT FROM THE CASIMIR CONSORTIUM

Damian Smedley¹, Morris Swertz², Katy Wolstencroft³, Glenn Proctor¹, Michael Zouberakis⁴, Jonathan Bard⁵, John Hancock⁶, Paul Schofield⁷

¹EBI, Cambridge, United Kingdom, ²University of Groningen, Groningen, Netherlands, ³University of Manchester, Manchester, United Kingdom, ⁴BSRC Alexander Fleming, Athens, Greece, ⁵John Radcliffe Hospital, Oxford, United Kingdom, ⁶MRC Harwell, Harwell, United Kingdom, ⁷University of Cambridge, Cambridge, United Kingdom

CASIMIR (Coordination and Sustainability of International Mouse Informatics Resources: <http://www.casimir.org.uk>) is a European Commission funded coordination action focused on the integration of the informatics infrastructure that underpins our current efforts in functional genomics, and our understanding of the biology of human disease using the mouse. This infrastructure consists of scattered databases and material repositories as well as local resources that researchers want to integrate. Interoperability of disseminated databases potentially provides enormous synergy in the provision, integration and analysis of a wide range of data with concomitant added value for research projects. One of the main goals of CASIMIR is to assess how to overcome the technical issues with database interoperability through the use of distributed architectures.

A typical “use case” for mouse biologists is the search for information on their genes and phenotypes of interest using (i) MGD/MPD¹ databases to find allelic phenotype information on their mouse strains, (ii) Ensembl² databases to find genome context information and (iii) KEGG³ databases to find pathways the gene is involved in. To achieve this, biologists need to learn to use the different database user interfaces, copy-paste data between web pages, with format conversion where necessary, and merge all these fragments into an Excel spreadsheet, typically by hand. This has to be repeated for each gene, and again when data sources are updated and becomes impracticable for genome scale analysis e.g. performing the above for all the genes upregulated in a microarray experiment. Envisioned is a situation where bioinformaticians can easily automate these steps to provide their biologists with a tailored “experiment compendium”. Here we demonstrate such a solution using technologies developed within our consortium such as BioMart⁴ (www.biomart.org), MOLGENIS⁵ (www.molgenis.org) and Taverna⁶ (<http://taverna.sourceforge.net>) as well as external Web Services.

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MOUSE GENOME RESOURCES AT NCBI

Deanna Church, on behalf of NCBI genomes group
DHHS/NIH/NLM/NIH, Bethesda, MD, United States

The mouse is a vital tool for biomedical research. Build 37.1 is the current public release of mouse genome sequence data. This includes the reference genome assembly, a clone based assembly derived from C57BL/6J that covers approximately 95% of the mouse genome. Build 37.1 also includes a mixed strain whole genome assembly produced by Celera, and eighteen strain-specific partial genome assemblies where finished, clone based sequence is available. As our understanding of mammalian genome architecture grows it is clear that the availability of sequence from many strains is critical for developing a complete understanding of the mouse genome. All of these assemblies are annotated using our annotation pipeline, the products of which include STS placements, gene annotation, gene trap sequence location, micr sequence location, genomic sequence alignments, calculation of consistent CDS annotation (CCDS) and the placements of clone end sequences. Comparative genomics information is available from our Map Viewer resource, which allows users to view multiple assemblies simultaneously. In addition, comparisons to the human and rat genome can also be viewed. New resources include a sequence viewer, which provides more of a typical browser view and Clone Finder, a tool specifically developed to identify the location of clones as they relate to a given assembly. Currently, clones from a number of strains, including NOD/LTJ, 129S7/AB2.2, C3HEB/FEJ, and MSM/MS have been processed, allowing users to place these clones in the reference coordinates system. We will discuss implementation and provide usage information for these NCBI tools..

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SIMULATION OF HAPLOTYPE LENGTH OVER MULTIPLE GENERATIONS SUGGESTS A SIMPLE LINEAR RELATIONSHIP BETWEEN NUMBERS OF HAPLOTYPES, NUMBER OF GENERATIONS AND MEAN HAPLOTYPE LENGTH

Harry Noyes, Steve Kemp

¹University of Liverpool, Liverpool, United Kingdom, ²International Livestock Research Institute (IRLI), Nairobi, Kenya

Traditionally genetic analysis has developed using the centiMorgan (cM), a measure of recombinant frequency, to describe distances between markers on a chromosome. The use of recombinant frequency has some excellent properties for genetic analysis since it requires no prior knowledge of chromosome number, size or recombination. However the cM is not a fixed unit of physical distance and the cM distance between any two markers is highly dependent on the properties of the chromosomes that are being genotyped. The availability of physical chromosome sizes and recombination rates now makes it possible to model physical chromosome structure over multiple generations and discover the distribution of haplotype sizes in megabases. A Perl script was written to simulate recombination over multiple generations between an arbitrary number of founder haplotypes. It was found that the mean number of recombinations in any 1Mb interval was a simple function of the chromosome size, the recombination rate, the number of generations and the number of founder haplotypes. The algorithm was also used to model the development of congenic lines to discover the size of donor haplotypes after any number of generations of backcrossing. Finally the algorithm was adapted to model the structured breeding programme of the Collaborative Cross using the published haplotype structure of the founder mice as an input. This simulation suggested that the mean time to fixation of mice in the collaborative cross might be only 33 generations; 5 generations less than a previous estimate.

P42**ORTHOLOGS OF HUMAN DISEASE-RELATED GENES ARE FOUND IN CONSERVED REGIONS OF THE MOUSE GENOME**

Xiting Li, Simon Lovell, [Kathryn Hentges](#)
University of Manchester, Manchester, United Kingdom

With the completion of whole genome sequences from many organisms it is now clear that genome architecture and gene organization within the genome is not random. A better understanding of the factors constraining genome organization will allow the identification of functional genomic regions. Evolutionarily conserved genome regions are of particular interest, because they are presumed to have functional features such as genes and regulatory regions. We have explored the relationship between conserved mammalian genomic regions and gene function, with emphasis on disease-related genes, in this work.

By comparing the mouse genome to the human, rat, and dog genomes, we determined the percentage of genes with conserved microsynteny for the mouse genome. This allowed us to separate the mouse genome into sliding windows of high (Z score >1), average ($1 > Z > -1$), or low ($Z < -1$) microsynteny conservation. A significant difference in the proportion of mouse orthologs of human disease genes as compared to the total number of genes per window was observed among windows of high, average, or low conservation. We find a striking correlation between conserved microsynteny and the density of mouse orthologs of human disease genes, suggesting that disease genes are clustered in regions of high microsynteny conservation.

This study not only demonstrates that gene function constrains genome organization, but also identifies regions of the mouse genome that can be experimentally examined to produce mouse models of human disease.

P43**CONSISTENCY OF LINKAGE DISEQUILIBRIUM ACROSS MOUSE POPULATIONS**

Yun Zhan¹, Vivek M. Philip², Cymbeline T. Culiati², Gary A. Churchill⁴, Michael A. Langston¹, [Elissa J. Chesler](#)²
¹*Electrical Engineering and Computer Science, Knoxville TN, United States*, ²*Genome Science and Technology Program University of Tennessee and Oak Ridge National Laboratory, Knoxville / Oak Ridge TN, United States*, ³*System Genetics Group, Biosciences Division, Oak Ridge National Laboratory, Oak Ridge TN, United States*, ⁴*The Jackson Laboratory, Bar Harbor ME, United States*

Linkage disequilibrium in mouse genetic reference populations reveals both the consequences of breeding history and the biological effects of multi-locus selection. In our ongoing studies of linkage disequilibrium in mouse genetic reference populations we have been able to compare and quantify differences among population linkage disequilibrium blocks and networks using combinatorial algorithms. The study populations now include common and wild-derived inbred strains, several recombinant inbred strain panels, and many lines from a single generation (G2:F7) of the collaborative cross. Linkage disequilibrium is assessed using the mutual information for all pairs of loci. To compare populations of different sizes, we use the mean mutual information of 1000 bootstrap samples of equal size. The linkage matrix is re-represented as an edge-weighted graph. Vertices represent genetic loci, and edges represent linkages. The extent of LD is evaluated and at varying edge-weight thresholds, which produces unweighted simple graphs. These graphs are decomposed into dense subgraphs that represent LD networks. These studies have revealed variation in the nature and extent of syntenic and non-syntenic linkage across populations. The present study emphasizes biological drivers of linkage disequilibrium through the examination of the consistency of regions of linkage disequilibrium across populations. These regions most likely reflect the biological effects of co-adaptive allele selection. Conservation of gene order across species is further indicative of functional relevance of linkage disequilibrium, and has been observed for some of the regions.

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MOUSE PHENOME DATABASE (MPD)

Molly Bogue, Stephen Grubb, Carol Bult, Terry Maddatu
The Jackson Laboratory, Bar Harbor ME, United States

The Mouse Phenome Project was launched to complement the mouse genome sequencing effort and facilitate functional annotation of the genome. The phenome approach captures complexities of biological pathways that are not accessible through conventional approaches. This powerful research approach requires that strains be systematically characterized using well-defined protocols and under controlled conditions to maximize data reproducibility and value.

We collect and annotate phenotypic data contributed by members of the research community and make it available through the Mouse Phenome Database (MPD) along with detailed protocols and environmental parameters. In addition to serving as a public data repository, MPD is also a facility for query, data retrieval, and analysis. The MPD Toolbox includes tools for comparing strains, correlating phenotypes, and linking phenotype and genotype. MPD currently contains >1500 phenotypic measurements contributed by research teams worldwide. Genotypic datasets are also collected from community sources and consolidated for access through the MPD SNP interface. The MPD SNP collection includes the imputed genotype resource contributed by the Center for Genome Dynamics at JAX. Large-scale phenotyping projects and research resources such as MPD have greatly increased the power of the laboratory mouse for the study of human health and disease. The utility and potential of MPD increases with each new dataset. Let us know if you are interested in contributing your phenotypic (quantitative or categorical) or genotypic data for community-wide access (phenome@jax.org). In addition to inbred strains, we post strain survey data for RI panels, consomics, F1 hybrids, and any other reproducible and widely available strain.

Mouse Phenome Database (MPD; www.jax.org/phenome)

New MPD tools and features will be showcased.