EPIGENETIC INHERITANCE SYMPOSIUM 2023

Impact for Biology and Society

23-25 August 2023
ETH Zurich, Switzerland

Universität Zürich[UZH] | ETH zürich

JOHN TEMPLETON FOUNDATION

FNSNF
Fonds national suisse
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Important information

WIFI: public / public-5

Emergency: 144
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Taxi: +41 44 777 77 77

Venue

Paul Scherrer Auditorium (ETA F 5)
ETH Zurich ETA Building
Gloriastrasse 39
8092 Zurich
www.ethz.ch

Summary of previous editions

Epigenetic inheritance: impact for biology and society

25-27 August 2021, Zurich, Switzerland
Rodrigo G Arzate-Mejía, Isabelle M Mansuy

Environmental Epigenetics
Volume 8, Issue 1, Nov 2022
DOI: 10.1093/eep/dvac021

26-28 August 2019, Zurich, Switzerland
Irina Lazar-Contes, Martin Roszkowski, Deepak K Tanwar, Isabelle M Mansuy

Environmental Epigenetics
Volume 6, Issue 1, May 2020
DOI: 10.1093/eep/dvaa004

Transgenerational epigenetic inheritance: from biology to society

28-30 August 2017, Zurich, Switzerland
Johannes Bohaceck, Olivia Engmann, Pierre-Luc Germain, Silvia Schelbert, Isabelle M Mansuy

Environmental Epigenetics
Volume 4, Issue 2, April 2018
DOI: 10.1093/eep/dvy012

WELCOME

Dear colleague, student and friend,

It is a great pleasure to welcome you to the 2023 Epigenetic Inheritance symposium in Zurich, as a follow-up of the previous editions in 2017, 2019 and 2021.

The symposium features important aspects of epigenetic inheritance across different disciplines, from epidemiology to behavior, metabolism, mechanisms and methodologies in humans and animal models. Discussion topics include new findings and discoveries, challenges of the discipline and perspectives for biology, medical research and the society.

The symposium offers keynote lectures from leaders in the field, short and flash talks, poster sessions with an award for the best poster, and a workshop "Questions and Challenges of Epigenetic Inheritance".

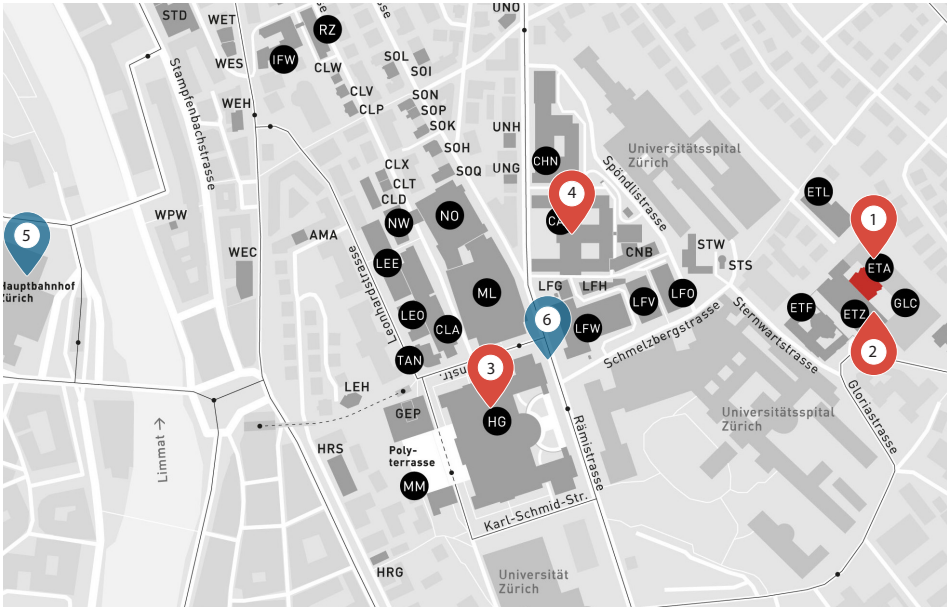
This year, the symposium is held in person and also offers an online streaming so anyone can attend all presentations, whether onsite or away.

To continue the symposium's tradition to combine science and art, we organize an art competition. Art pieces created by attendees on the theme of epigenetic inheritance are exhibited in the foyer of the ETA building, over the course of the symposium. The best piece will be rewarded with a prize.

I hope that you'll enjoy the symposium, and find it inspiring for your research and your thinking about the biology of heredity. I wish you a great and productive time in Zurich and warmly thank you for participating.

Isabelle Mansuy

VENUE



1. Epigenetic Inheritance Symposium, ETH Zurich, ETA F 5, Gloriastrasse 39, 8092 Zurich
2. Coffee and Lunch Breaks, Poster Sessions, ETH Zurich, ETZ Foyer, Gloriastrasse 35, 8092 Zurich
3. Terrace Dinner, ETH Zurich, HG K 30.5, Rämistrasse 101, 8092 Zurich (upon registration only)
4. Workshop, ETH Zurich, Food & Lab, CAB H 41, Universitätsstr. 6, 8092 Zurich (upon registration only)
5. Zürich HB / Zurich Main Station
6. PubliBike Station

Direction for Public Transportation

Tram Nr. 10	From Zurich Main Station to ETH/Universitätsspital	Ticket: Zone 110
Tram Nr. 6	From Zurich Main Station to Voltastrasse	Ticket: Zone 110

PROGRAM

Wednesday 23.08.2023

07:45 – 08:45	Registration

Introduction

08:45 – 09:00	Isabelle Mansuy, Professor in Neuroepigenetics, University and ETH Zurich

Session 1 — Epidemiological evidence and animal models I
Chair: Isabelle Mansuy

09:00 – 09:40	Impact of in utero exposures on long-term cardio-metabolic health Susan Ozanne, University of Cambridge, United Kingdom
09:40 – 10:20	Approaches to transmissible genotype, epigenotype, phenotype relationships in humans and mice Andrew Feinberg, Johns Hopkins University, USA
10:20 – 11:00	*Coffee Break - ETZ Foyer, Floor E*
11:00 – 11:20	Amelioration of transgenerational liver disease by an epigenetic modifier treatment Ramji Bhandari, University of North Carolina at Greensboro, USA
11:20 – 11:40	MicroRNAs and associated factors as mediators of trauma transmission: Comparative evidence from multiple human cohorts Ali Jawaid, Nencki Institute of Experimental Biology, Poland
11:40 – 12:00	DNA methylation constrains nucleosome retention in sperm and H3K4 methylation deposition in early mouse embryos Grigorios Fanourgakis, Friedrich Miescher Institute, Switzerland
12:00 – 13:30	*Lunch Break - ETZ Foyer, Floor E*

Session 2	Epidemiological evidence and animal models II Chair: Katharina Gapp
13:30 – 14:10	Epigenetics and transmission of psychiatric risk from parents to offspring: Lessons learned from large population-based birth studies Charlotte Cecil, Erasmus Medical Center, The Netherlands
14:10 – 14:50	How does prenatal obesogen exposure lead to a transgenerational predisposition to obesity Bruce Blumberg, University of California Irvine, USA
14:50 – 16:15	*Coffee Break and Poster Session I - ETZ Foyer, Floor E*
16:15 – 16:30	Investigating epigenetics and chromatin organization: Recent advances in transposase-based technologies Chamseddine Kifagi, Active Motif, Belgium
16:30 – 17:20	Intergenerational impact of paternal stress on hematopoeisis in mice. Lola Kourouma, University and ETH Zurich, Switzerland High nucleotide diversity accompanies differential DNA methylation in naturally diverging populations. Irene Adrian-Kalchhauser, University of Bern, Switzerland Intracrine action of conjugated estrogens contributes to a non-monotonous dose-response in porcine preimplantation embryos after maternal oral low dose exposure to estradiol-17β. Susanne E Ulbrich, ETH Zurich, Switzerland The epididymis: a window for relaying stress signals to the male germline and potential offspring. David Skerrett-Byrne, University of Newcastle & Hunter Medical Research Institute, Australia The evolution of epigenetics across multiple generations. Sonia Eynard, INRAE, France Paternal phthalate exposure alters sperm small RNAs and induces metabolic disorders in offspring. Changcheng Zhou, University of California, Riverside, USA Environmentally induced sperm RNAs transmit susceptibility to cancer growth to offspring in a mouse model. Sonia de Assis, Georgetown University Medical Center, USA Multigenerational transmission of obesity in mammals. Flavio Palmieri, Sant Joan de Déu Research Institute, Spain Epigenetic programming of the human sperm for embryonic development. Maissa Goumeidane, University of Nantes, France Running in the FAMILY – Understanding and predicting the intergenerational transmission of mental illness. Isabelle Mansuy, University and ETH Zurich, Switzerland
18:30 – 22:00	Terrace Dinner at ETH Dozentenfoyer (upon registration only)

Thursday 24.08.2023

08:30 – 09:00	Registration

Session 3 — Transmission mechanisms I
Chair: Anar Alshanbayeva, Rodrigo Gacel Arzate Mejía

09:00 – 09:40	3D chromatin remodelling in the germ line Aurora Ruiz-Herrera, Autonomous University of Barcelona, Spain
09:40 – 10:20	Molecular mechanisms of epigenetic transgenerational inheritance: Epigenetic, developmental, and disease components Michael K. Skinner, Washington State University, USA
10:20 – 10:50	*Coffee Break - ETZ Foyer, Floor E*
10:50 – 11:30	Environment-epigenome interactions in inheritance and disease Sarah Kimmins, McGill University, Canada
11:30 – 12:10	Stress hormone signalling: Across tissues and across generations Katharina Gapp, ETH Zurich, Switzerland
12:10 – 13:30	*Lunch Break - ETZ Foyer, Floor E*

Session 4 — Transmission mechanisms II
Chair: Lola Kourouma, Leonard Steg

13:30 – 14:10	Perturbing folate and folate metabolism in male germ cells: Insights into mechanisms of epigenetic inheritance Jacquetta Trasler, McGill University, Canada
14:10 – 14:50	Intergenerational hormesis regulation by heritable 18S rRNA methylation Eric Greer, Washington University, USA
14:50 – 15:50	*Coffee Break and Poster Session II - ETZ Foyer, Floor E*

Session 4	Transmission mechanisms II Chair: Lola Kourouma, Leonard Steg
15:50 – 16:30	Offspring fitness: Why your father's microbes matter Jamie Hackett, European Molecular Biology Laboratory, Italy
16:30 – 16:50	Paternal dietary challenge influences offspring metabolism via sperm-born mitochondrial signals Raffaele Teperino, Helmholtz Diabetes Center, Germany
16:50 – 17:10	Transgenerational inheritance of epigenetic signatures at CpG islands in mammals Yuta Takahashi, Altos Labs Institute of Science, USA
17:10 – 17:25	Award for best piece of art

Friday 25.08.2023

Session 5	Methodologies Chair: Maria Dimitriu
09:00 – 09:40	Modeling spermatogenesis in testicular organoids: Potential for studying epigenetic inheritance Ina Dobrinski, University of Calgary, Canada
09:40 – 10:20	Recent advances in single-cell epigenomics Bing Ren, University of California San Diego, USA
10:20 – 10:50	*Coffee Break - ETZ Foyer, Floor E*

Session 6	Impact on society and evolution Chair: Kerem Uzel
10:50 – 11:30	The role of small RNAs in response to changing environmental conditions across generations Simone Immler, University of East Anglia, United Kingdom
11:30 – 12:10	Non-genetic effects in evolution Martin Lind, Uppsala University, Sweden
12:10 – 12:30	Poster prize / Closing

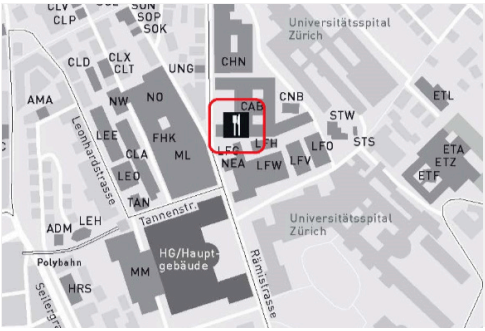
WORKSHOP

Workshop «Questions and Challenges of Epigenetic Inheritance»

13:00 – 14:00	*Lunch - food&lab (CAB)*
14:00 – 15:30	Part I
15:30 – 16:00	*Coffee Break - food&lab (CAB)*
16:00 – 17:00	Part II

Moderated by Isabelle Mansuy, University Zurich and ETH Zurich, Switzerland
Katharina Gapp, ETH Zurich, Switzerland
Jamie Hackett, European Molecular Biology Laboratory, Italy

Co-organized with Kevin Arnold under the auspices of Sir John Templeton Foundation



Workshop

ETH Zurich
Food & Lab
Building CAB H 41
Universitätsstrasse 6
8092 Zurich

ABSTRACTS

Impact of in utero exposures on long-term cardio-metabolic health

Susan Ozanne - Professor of Developmental Endocrinology, University of Cambridge, United Kingdom

It is now over 30 years since epidemiological studies revealed that there was an association between birthweight and long-term risk of traditionally adult on-set diseases such as type 2 diabetes and cardiovascular disease. This led to the concept of the Developmental Origins of Health and Disease (DOHaD)– the idea that the environment to which we are exposed during critical periods of development, such as the in utdiagnosis,d, has a permanent impact on our long-term health. One important early environmental factor known to have such programming effects is nutrition. Initial focus was directed towards the detrimental effects of low birth weight and early under-nutrition. However, in light of the growing epidemic of obesity, including in women of child-bearing age, more and more focus is now being directed towards the detrimental effects of maternal obesity during pregnancy and early over-nutrition. Both fetal under-nutrition and fetal over-nutrition appear to have the same phenotypic consequences in terms of cardio-metabolic disease risk. However, it is yet to be established if they mediate their effects through the same mechanistic pathways. Animal models have been invaluable in identifying the mechanisms underlying developmental programming. In particular, many rodent models have been established to mimic the human situation and allowing studies across the life course. From such studies three key programming mechanisms have emerged: (i) permanent structural changes- the idea that if during a critical period of development an organ is exposed to a suboptimal level of a key hormone or nutrient required for its development this will permanent impact on organ structure and consequently function, (ii) accelerated cellular ageing of key metabolic and reproductive tissues as a consequence of increased oxidative stress leading to telomere shortening and (iii) epigenetic programming of gene expression through changes in DNA methylation and/or histone modifications as well as changes in miRNA expression. Further understanding these mechanisms may give us the potential to ultimately develop markers of disease risk and help in the design of rational intervention strategies to improve the health of women and their children.

Approaches to transmissable genotype, epigenotype, phenotype relationships in humans and mice

Andrew P. Feinberg - Bloomberg Distinguished Professor, John Hopkins University, USA

My laboratory has pursued mouse and human epigenomic studies in parallel since our pre-genome project maps of comparative imprinting domains. More recently, my laboratory and collaborators have focused on the interaction of genetics and environment in defining the epigenome, and its relationship to heritability. I will discuss several of these project: precision pharmacology guided by epigenomic analysis of strain differences in response to metabolic challenge, with strain-specific pharmacological reversal (with the Threadgill lab at TAMU); comparative mouse and human analysis of the DNA sequence drivers of epigenetic entropy in development (with the Ji lab at JHU); genetic dependent- and independent transmission of epigenetic marks to offspring using long-read phased sequencing (with the Threadgill lab); and sperm DNA methylation-linked social responsivity scores in fathers and new offspring in a sibship with autism (with the Volk lab at JHU). I believe that significant new understanding of common human diseases involving the environment, i.e. all of them, will require concurrent mouse and human studies with robust cross-talk and hypothesis evolution between them.

Amelioration of transgenerational liver disease by an epigenetic modifier treatment

Ramji Bhandari - University of North Carolina at Greensboro and University of Missouri, Columbia, USA

Epigenetic inheritance of environmentally and lifestyle-induced phenotypes has been demonstrated in many model organisms, suggesting that current generations could be harboring ancestral exposure-induced molecular memories or future generations will be carrying such memories due to exposure at the current generations. Using medaka fish as a model organism, we investigated whether the transgenerational non-alcoholic fatty liver disease can be reversed by epigenetic modifiers at the time of sensitive life history stages. Ancestral bisphenol A (BPA) exposure from the day of fertilization through 15 days after fertilization led to non-alcoholic fatty liver disease (NAFLD), which persisted for five generations. The inheritance was mediated by both male and female germlines. Females showed increased severity of the disease than males. In the F2 generation, the BPA-exposure-initiated NAFLD started after puberty, developed in adulthood, and progressed toward Nonalcoholic Steatohepatitis (NASH) as the fish aged. We performed transcriptomic, metabolomic, and methylome analyses to understand the mechanism involved. A larger percentage of transgenerational differentially methylated regions (DMRs) present in the NAFLD liver at the F2 generation were removed in the F4 generation, but the phenotype persisted with comparatively reduced severity. Treating the fish with vitamin C, which seemed to correct stressor-induced DNA methylation alterations in vitro, blocked the development and progression of NAFLD in adulthood, which involved corrections of the majority of BPA-induced DMRs, irrespective of their methylation status. The present results suggest that low-concentration vitamin C may serve as a nutritional agent to correct BPA-induced liver injury. The potential of vitamin C in reversing BPA-induced intra-, inter-, and transgenerational DMRs and correcting liver injury in other species is currently under investigation.

MicroRNAs and associated factors as mediators of trauma transmission: Comparative evidence from multiple human cohorts

Ali Jawaid - Nencki Institute of Experimental Biology, Poland

Childhood trauma is an important risk factor for psychiatric and physical ailments during adulthood. Emerging evidence from rodent studies suggests that some behavioral and metabolic symptoms of childhood trauma are transmissible across generations. However, the translational implications of this novel concept are in the preliminary stages. This talk entails a systematic examination of small RNAs in the serum, sperm , and milk samples collected from ethnically diverse human trauma cohorts with an overarching aim to identify the molecular underpinnings of the long-term effects and transmission of trauma symptoms. Small RNA sequencing (sRNA-seq) followed by RT-qPCR assays were performed to identify and validate miRNA changes in the serum of children with recent trauma in the form of paternal loss and maternal separation (PLMS), in the sperm of adult men with a history of complex trauma before the age of 17, and in the milk of lactating mothers with history of adverse childhood experiences. Pathway analysis of the differentially expressed miRNAs in these diverse samples suggest a potential role for cholesterol signaling in the long-term propagation and transmission of trauma. Notably, miR-223-3p, which was similarly upregulated in the blood, sperm, and milk samples from these trauma cohorts targets SR-B1: the receptor for high-density lipoproteins (HDLs) and is implicated in cholesterol biosynthesis. Guided by these results, our current efforts are focused on modeling the role of lipids and lipid-associated factors in the long-term effects and transmission of childhood trauma via ethologically relevant mouse models and ex vivo approaches.

DNA methylation constrains nucleosome retention in sperm and H3K4 methylation deposition in early mouse embryos

Grigorios Fanourgakis - Friedrich Miescher Institute, Switzerland

DNA methylation (DNAme) serves a stable gene regulatory function in somatic cells. In the germ line and during early embryogenesis, however, DNAme undergoes global erasure and re-establishment to support germ cell and embryonic development. While de novo DNAme during male germ cell development is essential for setting genomic imprints, other intergenerational roles for paternal DNAme following fertilization are unknown. To address this question, we reduced the level of DNAme in developing male germ cells through conditional gene deletion of the de novo DNA methyltransferases DNMT3A and DNMT3B in undifferentiated spermatogonia. Mutant male germ cells nevertheless completed their differentiation to sperm. We observed that DNMT3A serves a DNAme maintenance function at many intragenic sites in undifferentiated spermatogonia while DNMT3B catalyzes de novo DNAme during spermatogonial differentiation. In spermatogonia, the acquisition of DNAme and deposition of H3K4me3 occur mutually exclusively. Failing de novo DNAme in spermatogonia leads to increased nucleosome occupancy in mature sperm at sites with high CpG content, supporting the model that DNAme constrains nucleosome retention in sperm. To assess the impact of altered sperm chromatin in the formation of embryonic chromatin, we measured H3K4me3 occupancy at paternal and maternal alleles in 2-cell embryos using a highly sensitive transposon-based tagging assay for modified chromatin. Our data show that reduced DNAme in sperm renders paternal alleles permissive for H3K4me3 establishment in early embryos, independently from paternal inheritance of sperm born H3K4me3. Together, this study provides first evidence that paternally inherited DNAme directs chromatin formation during early embryonic development.

Epigenetics and transmission of psychiatric risk from parents to offspring: Lessons learned from large population-based birth studies impacts of general anesthesia

Charlotte Cecil - Erasmus Medical Center, The Netherlands

A family history of mental illness is the most important known risk factor for the development of mental health problems: up to 50% of children with a mentally-ill parent will develop a mental disorder in their life course, suggesting a transfer of disease risk from affected parents to offspring. While both genetic and environmental factors contribute to this transmission, the underlying biological pathways remain poorly understood, and studies on this topic in humans face many difficulties. In this talk, Charlotte will present some of the latest insights from consortium initiatives based on population birth cohorts examining epigenetic markers in the context of transmission of psychiatric risk from parents to offspring, including key challenges, lessons learned and promising future directions.

How does prenatal obesogen exposure lead to a transgenerational predisposition to obesity?

Bruce Blumberg - University of California Irvine, USA

Obesity is commonly ascribed to an imbalance between caloric intake and energy expenditure - the so-called thermodynamic, or „calories in - calories out" model. However, a growing body of evidence points strongly toward the contributions of other factors in the obesity epidemic. We previously showed that in utero exposure of pregnant F0 mice to the obesogen tributyltin (TBT) led to increased white adipose depot weight, increased hepatic fat storage and a bias of mesenchymal stem cells toward the adipogenic fate and away from the osteogenic fate through the F3 generation. In a replicated transgenerational study, we found that exposure of F0 animals to TBT throughout pregnancy and lactation predisposed male F4 descendants of TBT-treated animals to weight gain and obesity when challenged with a higher fat diet later in life. Moreover, the TBT group showed impaired ability to mobilize fat during fasting periods of fasting, accompanied by elevated serum levels of leptin. Limited fat mobilization and elevated leptin levels suggest that fat accumulation results, in part, from leptin resistance. These are hallmarks of the

„thrifty phenotype“ in which an individual stores more of the calories consumed and resists weight loss during times of limited food availability. Integrated methylome and transcriptome analysis from fat and liver of F4 animals revealed that ancestral TBT exposure led to changes in global DNA methylation consistent with architectural changes in chromatin structure. Our results show that ancestral, in utero exposure to TBT alters chromatin structure to modulate expression of genes important for fat storage and mobilization and suggest that the transgenerational phenotype likely results from large scale changes in chromatin structure, rather than specific epimutations in individual genes. This altered chromatin structure is either transmitted or self-reconstructs in subsequent generations. Recent efforts toward identifying which chromatin regions are responsible for the transmission of transgenerational predisposition to obesity will be discussed.

3D chromatin remodelling in the germ line

Aurora Ruiz-Herrera - Autonomous University of Barcelona, Spain

The spatial folding of chromosomes inside the nucleus has regulatory effects on gene expression, yet the intricacies of this process and the impact of genome reshuffling on the 3D genome remains unclear. This is of relevance since chromosomal fusions represent the most common chromosomal rearrangement in nature (from plants to mammals), and are linked to recurrent miscarriages, infertility, and aneuploid offspring in humans. In fact, it has long been suggested that the presence of chromosomal fusions in the germ line can alter segregation patterns. In this talk I will resume our recent results on 3D chromatin remodelling in the germ line. Moreover, I will discuss on the effect of chromosomal fusions on the higher-order chromatin organization and recombination landscapes in germ line using the house mouse as a model system. Our results indicate that chromosomal fusions can alter the nuclear architecture during meiosis, including an increased rate of heterologous interactions in primary spermatocytes, and alterations in both chromosome synapsis and axis length. These disturbances in topology were associated with changes in genomic landscapes of recombination, resulting in detectable genomic footprints. Overall, chromosomal fusions impact the dynamic genome topology of germ cells in two ways: (i) altering chromosomal nuclear occupancy and synapsis, and (ii) reshaping landscapes of recombination.

Molecular mechanisms of epigenetic transgenerational inheritance: Epigenetic, developmental and disease components

Michael K. Skinner - Washington State University, USA

Transgenerational effects of environmental factors such as toxicants significantly amplify the biological impacts and health hazards of these exposures, as well as influence future generations. One of the most sensitive periods to exposure is during fetal gonadal sex determination when the germ line is undergoing epigenetic programming and DNA re-methylation occurs. Previous studies have shown that toxicants (e.g., Glyphosate) can transgenerationally increase in adult-onset disease such as infertility, prostate, ovary and kidney disease, cancers and obesity. Interestingly, this effect is transgenerational (F1, F2, F3 and further generations) due to a permanent (imprinted-like) altered epimutation of the germline. The transgenerational epigenetic mechanism appears to involve the actions of an environmental compound at the time of sex determination to permanently alter the epigenetic (e.g., DNA methylation) programming of the germline that then alters the embryo stem cells to alter all epigenomes developing somatic cells and organs to induce disease susceptibility and development transgenerationally. In addition to DNA methylation, alterations in sperm ncRNAs and histone retention have also been observed. A variety of different environmental compounds have been shown to induce this epigenetic transgenerational inheritance of disease including: fungicide vinclozolin, plastics BPA and phthalates, pesticides, DDT, dioxin, hydrocarbons and herbicides like atrazine and glyphosate. Interestingly, exposure specific epigenetic alterations were observed between the specific toxicants. Recently we have identified in human's epigenetic

biomarkers for parental germ cell transmission of offspring disease states such as infertility, autism, and arthritis. These epigenetic biomarkers can be used in preventative medicine. The suggestion that environmental toxicants can reprogram the germline to induce epigenetic transgenerational inheritance of disease is a new paradigm in disease etiology, toxicology, and evolutionary biology that needs to be considered in the future.

Environment-epigenome interactions in inheritance and disease

Sarah Kimmins - Université de Montréal and McGill University, Montreal, Canada

Despite the father transmitting half the heritable information to the embryo the focus on preconception health has largely been on the mother. New studies highlight the role of the father in disease transmission via non-genetic inheritance, through epigenetic mechanisms. Epigenetic mechanisms include, DNA methylation, post-translational modifications of histones and noncoding RNAs. Studies in humans and animals have linked epigenetic inheritance to the transmission of environmentally induced phenotypic traits from the father to the developing embryo and these have been associated with altered gene expression and developmental abnormalities in first and second offspring generations. Our studies have demonstrated that the effects of diet, BMI and toxicants on sperm chromatin indicate that environmental challenges can alter the sperm epigenome in a cumulative manner to negatively impact embryo development. Remarkably we have found using a mouse models that some of the alterations induced by diet to sperm chromatin are reversible. In translational studies we have determined that a man's exposures can alter the sperm epigenome at regions that are implicated in fertility, disease and embryo development. These findings indicate that paternal exposures may influence fertility and child health. Additionally, they underscore the need to amplify in depth pre-conception advice for youth and men.

Stress hormone signalling: Across tissues and across generations

Katharina Gapp - ETH Zurich, Switzerland

Stress often not only affects individuals and organisms directly exposed but can also have an impact on the progeny by impacting the germline. It can thereby potentially explain in part the missing heritability of disease that evolves around the fact that many complex diseases have a strong heritable component that cannot be attributed to single genetic factors. In my talk, I will explore different mouse models of stress with intergenerational impact and relate the transmission to a range of stress induced non-genetic alterations in sperm, with a particular focus on different classes of RNA. I will further discuss the contribution of circulating blood metabolites in the induction of crucial germline alterations that seem also reflected in a cohort of children exposed to early life stress. Furthermore, I will present unpublished findings on the relationship of specific epigenetic modifications and chromatin in sperm and establish a connection to stress hormone signaling. The findings are partially also conserved in human sperm and might hence also be relevant to human sperm integrity and intergenerational transmission of effects.

Perturbing folate and folate metabolism in male germ cells: Insights into mechanisms of epigenetic inheritance

Jacquetta Trasler - McGill University, Montreal, Canada

Sperm DNA methylation (DNAme) patterns are unique and contribute to the health of the next generation. Both folate in the diet and folate metabolic pathway enzymes such as 5,10-methylenetetrahydrofolate reductase (MTHFR) impact the delivery of methyl groups for DNAme. The fetal period is a key time of DNAme reprogramming in developing male germ cells. Dietary folate deficiency (FD) and folic acid supplementation (FS) are model exposures for investigating the effects of environmental factors on epigenetic perturbations across generations. Using a mouse model, we showed that lifetime F1 FD and FS

beginning in utero and spanning the entirety of male germ cell development resulted in epigenetic and reproductive consequences. DNAme of imprinted genes was altered in F1 sperm as well as in the somatic tissues of the F2. Both FD and high dose FS resulted in lower litter sizes and increases in neonatal mortality. DNAme at a genome-wide level was examined in the spermatogonia and sperm of the F1, and the sperm of the F2 and F3 males. In FD and FS exposed F1 germ cells, more differentially methylated cytosines (DMCs) were found in spermatogonia as compared to sperm. Numbers of DMCs decreased in F2 versus F1 sperm, while an unexpected increase was found in F3 sperm. DNA hypomethylation predominated, with genes in neurodevelopmental pathways commonly affected in F1, F2 and F3 germ cells. DMCs were not inherited across generations. Notably, we observed over-representation of repetitive elements, particularly young LINEs in F1-F3 sperm. We also examined sperm DNAme across generations in an alternate model of perturbation of folate metabolism resulting in lower levels of folate in fetal male germ cells at the time of de novo DNAme. In this model, MTHFR-deficiency, there was striking DNA hypomethylation of sperm, with hypomethylated regions enriched for young LINE-1 elements as noted in the FD and FS exposed mice. MTHFR deficiency resulted in a worsening of reproductive effects across generations. Based on the dietary folate and MTHFR-deficiency models, we hypothesize that retrotransposons, and in particular young, potentially active retrotransposons, that enter embryogenesis in a hypomethylated state, may play a role in epigenetic inheritance and be implicated in abnormal development.

Intergenerational hormesis regulation by heritable 18S rRNA methylation

Eric Greer - Washington University, USA

Heritable non-genetic information can regulate a variety of complex phenotypes. However, what specific non-genetic cues are transmitted from parents to their descendants are poorly understood. Here, we perform metabolic methyl-labelling experiments to track the heritable transmission of methylation from ancestors to their descendants in the nematode Caenorhabditis elegans. We find that methylation is transmitted to descendants in DNA, RNA, proteins, and lipids. We further find that in response to parental starvation, fed naïve progeny display reduced fertility, increased heat stress resistance, and extended longevity. This intergenerational hormesis is accompanied by an heritable increase in N6'-dimethyl adenosine (m6,2A) on the 18S ribosomal RNA at adenosines 1735 and 1736. We identified the conserved DIMT-1 as the m6,2A methyltransferase in C. elegans and find that dimt-1 is required for the intergenerational hormesis phenotypes. This study provides a labeling and tracking of heritable non-genetic material across generations and demonstrates the importance of rRNA methylation for regulating the heritable response to starvation.

Offspring fitness: Why your father's microbes matter

Jamie Hacket - European Molecular Biology Laboratory, Italy

The gut microbiota operates at the interface of host-environment interactions to influence human homeostasis and metabolic networks. Environmental factors that unbalance the gut microbiome can therefore elicit molecular and physiological responses across somatic tissues. However, the systemic impact of the gut microbiome on the germline - and consequently on the F1 offspring it gives rise to - is not explored. Our work reveals that the gut microbiota act as a key interface between paternal preconception environment and intergenerational health. Specifically, re-modelling the gut microbiota of prospective fathers drives an increased probability of F1 offspring presenting with low birthweight, severe growth retardation, and premature mortality. Here, I will discuss the mechanisms that underlie paternal reproductive responses to gut microbiome perturbations, and how this in turn probabilistically impacts offspring fitness.

Paternal dietary challenge influences offspring metabolism via sperm-born mitochondrial signals

Raffaele Teperino - Helmholtz Diabetes Center, Munich, Germany

Spermatozoa harbour a complex and environment sensitive pool of small non-coding RNAs (sncRNA), which influences offspring development and adult phenotypic trajectories. Whether mature spermatozoa in the epididymis can directly sense the environment is still not fully understood. Here, we used two distinct paradigms of preconception acute High Fat Diet challenge to dissect epididymal vs spermatogenic contributions to the sperm sncRNA pool and offspring health. We show that epididymal spermatozoa, but not developing germ cells, are sensitive to the environment and identify mitochondrial tRNA fragments (mt-tsRNA) as sperm-born sensors. In human spermatozoa, we found mt-tsRNAs in linear association with BMI and showed that paternal overweight at conception is sufficient to double offspring obesity risk and compromise metabolic health. Using mouse genetics and metabolic phenotypic data, we show that alterations of mt-tsRNAs are downstream of mitochondrial dysfunction in mice. Most importantly, single embryo transcriptomics of genetically hybrid two-cell embryos demonstrated sperm-to-oocyte transfer of mt-tsRNAs at fertilisation and implied them in the control of early embryo metabolism. Our study supports the importance of paternal health at conception for offspring metabolism, propose mt-tsRNAs as sperm-borne environmental effectors of paternal inheritance and demonstrate, for the first time in a physiological and unperturbed setting, father-to-offspring transfer of sperm mt-tsRNAs at fertilisation.

Transgenerational inheritance of epigenetic signatures at CpG islands in mammals

Yuta Takahashi - Altos Labs Institute of Science, USA

Transgenerational epigenetic inheritance in mammals remains a debated subject. We recently demonstrated that DNA methylation of promoter-associated CpG islands (CGIs) can be transmitted from parents to their offspring in mice (Y. Takahashi, et al., Cell. 2023, PMID: 36754048). We generated DNA methylation-edited mouse embryonic stem cells (ESCs) in which CGIs of two metabolism related genes, the Ankyrin repeat domain 26 (Ankrd26) and the low-density lipoprotein receptor (Ldlr), were specifically methylated and silenced using our DNA methylation editing strategy (Y. Takahashi, et al., Science. 2017, PMID: 28473583). DNA methylation-edited mice generated by microinjection of the methylated ESCs exhibited abnormal metabolic phenotypes. Both the acquired methylation of the targeted CGI and the phenotypic traits were maintained and transmitted across multiple generations. The heritable CGI methylation was subjected to reprograming in parental PGCs and subsequently reestablished in the next generation at post-implantation stages. These observations provide a concrete step in support of transgenerational epigenetic inheritance in mammals, which may allow for a better understanding of biological evolution and the etiology, diagnosis and prevention of non-genetically inherited human diseases. In this meeting, I would like to discuss the mechanism underlying transgenerational epigenetic inheritance in mammals.

Modeling spermatogenesis in testicular organoids: Potential for studying epigenetic inheritance

Ina Dobrinski - University of Calgary, Calgary, Alberta, Canada

Inherited epigenetic changes can be transmitted through the male germline. Elucidating the mechanisms by which somatic cells communicate with germ cells requires representative in vitro models. The testicular somatic microenvironment is critical to the process of spermatogenesis. In vitro spermatogenesis in species other than rodents represents a major challenge in reproductive biology. Primarily three methods have been used to model spermatogenesis in vitro: 2D cell culture, organ/tubule culture, and 3-D/organoid culture. In 2D culture of enzymatically digested testicular cells, the microenvironment is not restored. In organ culture, germ cells and somatic cells remain spatially arranged as they are in vivo, and cells are protected from enzymatic digestion, but long-term maintenance of tissue is challenging. In vitro production of functional sperm in cultured neonatal rodent testis tissue was achieved, yet successful culture in non-rodent species has remained intractable. The most recent advance is 3D/organoid culture.

In this system germ cells and somatic cells self-organise to reassemble the microarchitecture of the niche and allow tissue typical cell interactions. Testicular cells in microwells form organoids consisting of germ cells, Sertoli cells, Leydig cells, peritubular myoid cells with distinct seminiferous epithelium and interstitial compartments separated by a basal membrane. These organoids have been developed in several larger mammals including pigs, macaques, and humans which may facilitate in vitro study of testicular function and mechanisms of epigenetic transmission, and ultimately support spermatogenesis in vitro.

Recent advances in single-cell epigenomics

Bing Ren - University of California San Diego, USA

I will present two recent advances in single-cell epigenomics for the study of dynamic gene regulation in complex tissues during development and disease pathogenesis. (1) We previously reported Paired-Tag, a combinatorial-indexing-based method that can simultaneously map histone modifications and gene expression at single-cell resolution at scale. However, the lengthy procedure of Paired-Tag has hindered its general adoption in the community. To address this bottleneck, we develop a droplet-based Paired-Tag protocol that is faster and more accessible than the previous method. Using cultured mammalian cells and primary brain tissues, we demonstrate its superior performance at identifying the candidate cis-regulatory elements and associating their dynamic chromatin state to target gene expression in each constituent cell type in a complex tissue. (2) A major computational challenge in analyzing single cell epigenomics datasets is to project the large-scale and high dimensional data into low-dimensional space while retaining the relative relationships between cells in order to decompose the cellular heterogeneity and reconstruct cell-type-specific gene regulatory programs. Conventional dimensionality reduction methods suffer from computational inefficiency, difficulty to capture the full spectrum of cellular heterogeneity, or inability to apply across diverse molecular modalities. We have developed a fast and nonlinear dimensionality reduction algorithm that not only more accurately captures the heterogeneities of single-cell omics data, but also features runtime and memory usage that is computational efficient and linearly proportional to cell numbers. We implement this algorithm in a Python package named SnapATAC2, and demonstrate its superior performance, remarkable scalability and general adaptability using an array of single-cell omics data types, including single-cell ATAC-seq, single-cell RNA-seq, single-cell Hi-C, and single-cell multiomics datasets.

The role of small RNAs in response to changing environmental conditions across generations

Simone Immler, University of East Anglia, United Kingdom

The effects of environmental variation experienced by parents on the following generation(s) is a much debated topic. Several mechanisms of non-genetic inheritance have been proposed among which the possible role of small non-coding RNAs (sRNAs). These sRNAs may be transferred in sperm and eggs and a key question is whether their transfer generates an adaptive response in the offspring or whether they are a side product of defence mechanisms in the germ cells against environmental stressors to protect the genome. I will present mechanisms by which an adaptive response may evolve based on theoretical models and discuss these in the light of empirical evidence mainly looking at the effects of environmental stressors on RNA profiles in the germ cells of adult males and females, in the sperm of males and in the resulting offspring using the zebrafish Danio rerio. We specifically aim to understand how the response of sRNAs to environmental changes in the germ cells may be linked to their role in defence mechanisms against the activity of transposable elements (TE). Our data suggest that the genome is showing a dynamic response to environmental changes and that the primary role of sRNAs may be the defence of the genome against stressors including TE activity.

Non-genetic effects in evolution

Martin Lind, Uppsala University, Sweden

Evolutionary biology has traditionally focused on genetic effects. However, non-genetic effects such as epigenetic inheritance, maternal effects and phenotypic plasticity are common in nature, and can potentially influence genetic evolution. Non-genetic effects are often induced by the environment, but does not necessarily have to be adaptive for the organism. Moreover, not all individuals and populations express non-genetic effects to the same degree, suggesting that it may be under selection. This raises two questions: (1) are non-genetic effects likely to evolve in certain environments, and (2) how do they influence genetic evolution? Theory maintains that environmental variation is important for the evolution of non-genetic effects, with fast fluctuations favouring plasticity, while maternal effects and epigenetic inheritance may instead be favoured by slow environmental fluctuations. Moreover, non-genetic effects may help or hinder genetic evolution, depending upon whether these effects are generally adaptive or not. Using experimental evolution in the nematode Caenorhabditis remanei, we have investigated these questions. We found that environmental variation is indeed an important driver for the evolution of non-genetic effects. Moreover, non-genetic effects do influence genetic evolution, and the responsiveness of the genes to non-genetic effects influence how likely they are to evolve.

POSTERS

Posters marked with * have been selected for short and flash talks

P1 Miriam Kretschmer et al. Paternal transmission of glucocorticoid receptors to the early embryo

*P2 Irene Adrian-Kalchhauser et al. High nucleotide diversity accompanies differential DNA methylation in naturally diverging populations

P3 Alexander Murashov et al. The paternal Western diet results in alterations in brain proteome and microRNAs linked to transgenerational increases in offspring feeding behavior

*P4 Susanne E Ulbrich et al. Intracrine action of conjugated estrogens contributes to a non-monotonous dose-response in porcine preimplantation embryos after maternal oral low dose exposure to estradiol-17β

P5 Mariano Stornaiuolo et al. Paternal influence on offspring Aromatase and IGFII methylation status predisposes male progeny to intergenerational inheritance of dysmetabolism

P6 Sarah Stucchi et al. From pluripotency to germ cells and back: modeling intergenerational inheritance and human neurodevelopment in a dish

*P7 Grigorios Fanourgakis et al. DNA methylation constrains nucleosome retention in sperm and H3K4 methylation deposition in early mouse embryos

P8 Zora Lazarov et al. What should every business executive know about epigenetics?

P9 Alexandra Weyrich et al. Epigenetic signatures of social status across age classes in a wildlife population

P10 Flavio Santilli et al. Intergenerational effects of paternal low protein diet on mouse embryonic development and metabolic homeostasis

P11 Benedetta Coppe et al. The intergenerational investigation of paternal cardiac injury

P12 Gemma Comas-Armangué et al. Intergenerational sexual dimorphism and neurobehavioral effects of paternal circadian disruption

P13 Benjamin Walters et al. Epigenetic Inheritance of Cancer Risk via the Kdm6a-null Male Germline

P14 Shruta Pai et al. Paternal programming of offspring immune development

P15 Victoria George et al. The impact of diet on the sperm epigenome: A twin study

P16 Tohru Shibuya et al. Kanemi Yuso and transgenerational epigenetic inheritance

P17 Ramya Potabattula et al. Male aging effects on BEGAIN methylation and its possible role in autism

P18 Rashmi Ramesh et al. Dietary sugar shifts mitochondrial metabolism and small RNA biogenesis in sperm

P19 Signe Skog et al. Seqpac – a biologist's guide to sRNA-seq analysis

P20 Unn Kugelberg et al. The miRNA-309-cluster is important for male fertility

P21 Vincent Coustham et al. Increasing egg incubation temperature in birds to improve thermotolerance is associated with transgenerational effects and epigenetic signatures

P22 Shefa' Aljabali et al. Tracking male-tract small RNAs to understand their role in paternal epigenetic inheritance

P23 Maria A. Dimitriu et al. NanoTag – A novel IgG-free method for targeted epigenomic profiling

P24 Cyrielle Holuka et al. Maternal DNA methylation mediates inter-generational transmission of the effects of early-life adversity

P25 Candela González et al. Transcriptome profiling of histone writers/erasers enzymes across spermatogenesis, mature sperm and pre-cleavage embryo: implications in paternal epigenome transitions and inheritance mechanisms

P26 Frederique Pitel et al. Transgenerational epigenetics in quail: whole genome DNA methylation analysis

*P27 David Skerrett-Byrne et al. The epididymis: a window for relaying stress signals to the male germline and potential offspring

P28 Keyvan Karami et al. Investigating the molecular responses of chicken embryos to their mothers heat stress using DNA methylation analysis

P29 Anna Asratian et al. The impact of a paternal sugar diet intervention on the small RNA profiles in pig sperm and embryo

P30 Uyen Tran, Gail Cornwall et al. Sperm amyloids: Epigenetic carriers of inheritance?

P31 Archana Tomar et al. Parental genetics and epigenetic programming of offspring phenotype

*P32 Lola Kourouma et al. Environmental enrichment mitigates the intergenerational impact of paternal stress on hematopoeisis in mice

P33 Katalin Fejes Toth et al. The Role of SUMOylation in piRNA-directed chromatin silencing

*P34 Flavio Palmieri et al. Multigenerational transmission of obesity in mammals

P35 Anar Alshanbayeva et al. Blood extracellular-enriched fractions can vesicle signals of early life stress from the periphery to the germ cells in males

*P36 Sonia Eynard et al. The evolution of epigenetics across multiple generations

P37 Vincent Fischer et al. Potential biases in analyzing the effects of stress on sperm chromatins

P38 Weronika Tomaszewska et al. Immunometabolic and circulating microRNA signatures of childhood trauma in humans: Implications for long-term sequelae and propagation

P39 Carlos Guerrero-Bosagna et al. Genetic and germ line methylomic dynamics following a multigenerational exposure related to metabolic diseases in mouse

*P40 Maissa Goumeidane et al. Epigenetic programming of the human sperm for embryonic development

P41 Violeta de Anca Prado et al. Genetic and germ line methylomic dynamics following a multigenerational exposure related to metabolic diseases in mouse

P42 Michela Di Criscio and Adeolu Ogunleye Direct RNA sequencing using Oxford Nanopore - A pipeline for investigating mechanisms involved in transgenerational epigenetic inheritance

P43 Sieglinde Hastreiter et al. Variability of metabolic phenotype in male TALLYHO/JngJ mice is determined by body weight at weaning

P44 Xinyang Yu and Sylvane Desrivières Epigenome-wide association studies as a tool to identify biological mechanisms and genes conferring vulnerability to mental health symptoms

*P45 Changcheng Zhou et al. Paternal phthalate exposure alters sperm small RNAs and induces metabolic disorders in offspring

*P46 Sonia de Assis et al. Environmentally induced sperm RNAs transmit susceptibility to cancer growth to offspring in a mouse model

P47 Chamseddine Kifagi et al. Investigating epigenetics and chromatin organization: Recent advances in transposase-based technologies

SPEAKERS

Ramji Bhandari, University of North Carolina at Greensboro and University of Missouri Columbia, USA

Dr. Bhandari is an Associate Professor in the Division of Biological Sciences at the University of Missouri Columbia. He is a reproductive biologist by education and environmental health scientist and epigeneticist by training. His research group investigates how gene-environment interactions lead to reproductive and metabolic diseases within the gut-liver-gonad axis, aiming to develop diagnostic and predictive biomarkers for environmental health and disease. Dr. Bhandari has been supported by funding from the National Institutes of Health, the U.S. Geological Survey, the University of Missouri, and the University of North Carolina as a PI.

Bruce Blumberg, University of California Irvine, USA

The Blumberg laboratory studies the biology of nuclear hormone receptors in development, physiology and disease. . They aim to understand how physiological, pharmaceutical and environmental nuclear receptor ligands pattern the vertebrate embryo and how exposure to such chemicals leads to the development of obesity, diabetes and cancer. His laboratory showed that (1) exposure to obesogenic chemicals led to increased adiposity, in vivo, and that many candidate obesogens can predispose mesenchymal stem cells to differentiate into fat cells; (2) maternal obesogen exposure led to epigenomic changes in chromatin structure that can be transgenerationally inherited through at least 4 subsequent generations.

Charlotte Cecil, Erasmus Medical Center, The Netherlands

Charlotte Cecil is an Associate Professor in Biological Psychopathology at the Department of Child and Adolescent Psychiatry and PI of the inDEPTH Lab based at the Erasmus Medical Centre, the Netherlands. Her work aims to better understand how mental health problems develop in childhood and adolescence, in order to improve strategies for early risk detection and the prevention of chronic mental illnesses later in life. She is involved as PI or Work Package Leader in multiple EU projects and consortia investigating epigenetics in the context of mental health, including TEMPO, MIND, FAMILY, EarlyCause and HappyMums.

Ina Dobrinski, University of Calgary, Calgary, Alberta, Canada

Ina Dobrinski, Dr.med.vet., MVSc, PhD, Dip. ACT, is Professor of Reproductive Biology in the Cumming School of Medicine and Faculty of Veterinary Medicine at the University of Calgary. Her research is focused on mammalian germline stem cell biology. The Dobrinski lab was the first to establish germ cell transplantation in non-rodent models to transmit a genetic change introduced into germline stem cells to the next generation. They also developed xenografting of testis tissue and cells, and they established organotypic testicular organoids to investigate cell-cell interactions in the testis.

Andrew Paul Feinberg, School of Medicine, Johns Hopkins University, USA

Andrew P. Feinberg, M.D., M.P.H., is the Bloomberg Distinguished Professor at Johns Hopkins University. Known for establishing the fields of cancer epigenetics and epigenomics, he is also the founding director of the first NIH-supported Center of Excellence for epigenomics research, the Center for Epigenetics at the Johns Hopkins School of Medicine. Dr. Feinberg discovered epigenetic alterations in human cancer (1983) and is also credited with the discovery of gene imprinting in humans. More recently, he pioneered the first comprehensive genome-scale methylation analyses of normal tissues and cancer, and has helped to create the field of epigenetic epidemiology.

Katharina Gapp, ETH Zurich, Switzerland

Katharina Gapp is an assistant professor at the Institute for Neuroscience at ETH Zürich, Switzerland and head of the Epigenetics and Neuroendocrinology lab. She spent the last 12 years studying the impact of paternal stress on offspring phenotype and the mechanisms that mediate non-genetic information transfer vironmentally triggered traits in mammals. Her team's current SBFI-ERC funded work focuses on nuclear receptors in the germline and brain, the detrimental long-term consequences of chronic stress and the development of novel translational tools to interfere with their function.

Eric Greer, Washington University, USA

Dr. Eric Greer is an Assistant Professor at Harvard Medical School and Boston Children's Hospital. His work demonstrated that longevity can be inherited epigenetically in a transgenerational manner, and he identified a novel form of DNA modification, methylation on adenines, in metazoan that might be responsible for stable transgenerational epigenetic inheritance. The Greer lab focuses on 1) heritable non-genetic cues that are inherited across generations, 2) the role of chromatin and epitranscriptomic modifications in regulating cellular processes, 3) new epigenetic modifications and the enzymes that add, remove, and recognize these modifications and their role in regulating various biological processes, and 4) the role of epigenetics in the evolution of multicellularity.

Jamie Hackett, European Molecular Biology Laboratory, Italy

Jamie Hackett is a group leader at the European Molecular Biology Laboratory (EMBL), within the Epigenetics and Neurobiology unit in Rome, Italy. He obtained his PhD at the University of Edinburgh, and completed postdoctoral training at the University of Cambridge, UK, under Prof. Azim Surani. Jamie's research group has two overarching scientific themes. (i) To dissect the regulatory impact and logic of chromatin changes in health and disease, by engineering precision epigenome manipulations. (ii) To investigate the potential for (altered) epigenetic states to be transmitted through mitosis or meiosis and influence phenotype.

Simone Immler, University of East Anglia, United Kingdom

Simone Immler is Professor of Genetics and Reproduction at the University of East Anglia, UK. Her research focuses on the genetics and genomics of male reproduction and fertility and her lab works on zebrafish and humans. The main focus of her research lies on the mechanisms and processes occurring in germ cells particularly at all stages from the germ line into the mature gametes, fertilisation and the next generation. She uses a wide range of tools including mathematical modelling, experimental manipulations and genomics to study the importance of selection on male gametes in zebrafish and humans.

Ali Jawaid, Nencki Institute of Experimental Biology, Poland

Dr. Ali Jawaid, M.D., Ph.D., currently heads the Laboratory for Translational Research in Neuropsychiatric Disorders (TREND lab) at the BRAINCITY: Center of Excellence for Neural Plasticity and Brain Disorders, Nencki Institute of Experimental Biology (Warsaw, Poland). TREND lab is focused on dissecting the liaison between non-coding RNAs and metabolic factors in the long-term sequelae of childhood trauma; and investigates how the metabolism can be manipulated to counter its neuropsychiatric manifestations.

Sarah Kimmins, University of Montreal and McGill University, Montreal, Canada

Dr. Kimmins is a Full Professor in the Department of Pathology and Cell Biology at the University of Montreal and senior group leader at the Hospital Research Center (University of Montreal). She was awarded a Junior then Senior Canada Research Chair as a professor at McGill University (2005-2022). She is founder and CEO of HisTurn, a company providing a personalized epigenomics based approach for the diagnosis and treatment of male fertility. Her research is focused on understanding the molecular mechanisms underpinning epigenetic inheritance, specifically paternal health and how environmental exposures alter fertility, clinical outcomes, the sperm epigenome, embryo development and health of offspring.

Martin Lind, Uppsula University, Sweden

Martin Lind is an Associate professor in Conservation Biology at Halmstad University, Sweden and a Researcher at Uppsala University, Sweden. His research focus on the evolution of non-genetic effects as well as their influence on genetic evolution. He mainly investigates their role for life-history traits such as lifespan, reproduction, and development, using nematode model systems such as Caenorhabditis remanei and C. elegans.

Susan Ozanne, University of Cambridge, United Kingdom

Susan Ozanne, FMedSci, is Professor of Developmental Endocrinology and an MRC Investigator in the University of Cambridge Institute of Metabolic Science-Metabolic Research Laboratories and the MRC Metabolic Diseases Unit. She is also a Fellow of Churchill College, Cambridge. Her research interests are focused on understanding the mechanistic basis of the relationship between suboptimal early nutrition and risk of diseases such as type 2 diabetes, obesity and cardiovascular disease in later life. Professor Ozanne is the author of over 200 peer-reviewed full papers on the early origins of health and disease and is an elected member of council of the Society for the Developmental Origins of Health and Disease.

Bing Ren, University of California San Diego, USA

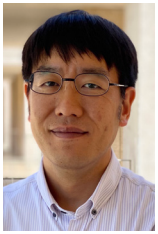
Dr. Ren is Director of the Center for Epigenomics and Professor of Cellular and Molecular Medicine at the University of California, San Diego. His research focuses on the discovery and characterization of transcriptional regulatory sequences in the human genome, to understand how these DNA elements direct spatiotemporal patterns of gene expression, and how DNA variants in these sequences contribute to human diseases. He has contributed to annotation of the transcriptional regulatory elements in the human and mouse genomes, characterization of their activities at single cell resolution in diverse tissues and developmental stages, and elucidation of the general principles of genome architecture and regulation.

Aurora Ruiz-Herrera, Autonomous University of Barcelona, Spain

Dr. Ruiz-Herrera is an associate professor at the Faculty of Biosciences of Autonomous University of Barcelona (UAB), Spain. She leads the Genome Architecture and Evolution Group at UAB and has more than 20 years of experience on the study of the structural, functional, and evolutionary aspects of genome organisation, paying special attention to the germ line. Her current research is focused on the study of the dynamics and function of the three-dimensional chromatin structure of germ cells by combining computational and experimental methods, and by studying the genomes of vertebrate species.

Michael K. Skinner, Washington State University, USA

Dr. Michael Skinner is a professor in the School of Biological Sciences at Washington State University, Pullman Washington, USA. He is the Founding Director of the Center for Reproductive Biology at WSU and University of Idaho, which is the largest reproduction biology center in the world, with nearly 100 faculty. Dr. Skinner's current research has demonstrated the ability of environmental exposures (e.g., toxicants) to promote the epigenetic transgenerational inheritance (non-genetic form of inheritance) of disease phenotypes due to abnormal germline epigenetic programming in gonadal development. He is the Editor-in-Chief of the Encyclopedia of Reproduction and the Oxford Publishing journal Environmental Epigenetics.



Yuta Takahashi, Altos Labs Institute of Science, USA

Dr. Yuta Takahashi is a senior scientist at Altos Labs Inc., San Diego Institute of Science, under the leadership of Director Dr. Juan Carlos Izpisua Belmonte. Yuta's research focuses on the role of epigenetic regulation in various aspects of animal development, tissue physiology, aging, disease progression, and transgenerational transmission. Their groundbreaking research showed that the introduction of CpG-free DNA into targeted CpG islands triggers de novo methylation methylation of all CpG islands in human PSCs (Science, 2017) and the occurrence of transgenerational epigenetic inheritance in mammals using the mouse models with epigenetically modified DNA methylation patterns and associated phenotypes (Takahashi et al., Cell, 2023).

Raffaele Teperino, Helmholtz Diabetes Center, Munich, Germany

Dr. Raffaele Teperino is a mouse geneticist and metabolic physiologist by training. Since 2015, he leads the group of Environmental Epigenetics at the Institute of Experimental Genetics of the Helmholtz Diabetes Center in Munich. Their overarching goal is to understand the epigenetic control of metabolism between and across generations by using mouse genetics and several environmental exposures coupled to in-depth phenotyping and bulk and single-cell omics.

Jacquetta Trasler, McGill University, Canada

Jacquetta Trasler, MD, PhD is a Distinguished James McGill Professor in Pediatrics, Human Genetics and Pharmacology & Therapeutics at McGill University and Senior Scientist at the Research Institute of the McGill University Health Centre (RI-MUHC). She directs the Developmental Genetics Laboratory at the RI-MUHC. Her translational research profile focuses on the epigenetic, molecular, and developmental regulation of gene expression in the germline and early embryo. Ongoing studies include effects of drugs, diet (folate) and assisted reproductive technologies on the epigenome of germ cells and embryos and the implications for transgenerational passage of epigenetic defects.

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