# EPIGENETIC MECHANISMS IN HEALTH AND DISEASE

BARCELONA CONFERENCE ON EPIGENETICS AND CANCER

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Dear Invited Speakers and Participants,

We are pleased to welcome you to Barcelona and to the fifth edition of the Barcelona Conference on Epigenetics and Cancer (BCEC) on "Epigenetic mechanisms in health and disease". The 2017 edition is co-organized by B-Debate, an initiative of Biocat and "la Caixa" Foundation, and the Molecular Biology Institute of Barcelona (IBMB-CSIC), together with the Josep Carreras Leukaemia Research Institute (JIC).

The BCEC series is a joint effort of six Barcelona research institutes with the aim of providing an annual forum to discuss the progress made in the field of chromatin regulation and epigenetics and by bringing together young and established scientists in an interdisciplinary forum.

Among the most important challenges in biomedicine is to understand the role of chromatin and epigenetics in human health and disease. During the last 15 years, epigenetics has consolidated as a new multi-disciplinary field on its own with an enormous scientific and therapeutic potential for cancer and many other relevant human pathologies such as cardiovascular diseases, aging, neurodegenerative diseases and diabetes.

On behalf of IBMB-CSIC, IJC, PMPPC-IGTP, CRG, PEBC-IDIBELL, IRB, and B-Debate, we thank you for joining us in this exciting debate. Although this is the last planned of a series of five annual BCECs, we hope to be able to put together a similar initiative to be able to host you in the future.

Yours sincerely,

Albert Jordan, Marcus Buschbeck, Ferran Azorin, Marian Martínez-Balbas, Jordi Bernués and B-Debate
PROGRAM

Wednesday, October 25th, 2017

8:45  Registration

9:00  Welcome
    Jordi Portabella, La Caixa Foundation
    Jordi Fabrega, Biocat
    Albert Jordan, Molecular Biology Institute of Barcelona (IBMB-CSIC)
    Marcus Buschbeck, Josep Carreras Leukaemia Research Institute

9:30  SESSION 1:
    Chair: Albert Jordan, Molecular Biology Institute of Barcelona (IBMB-CSIC), Barcelona, Spain
    Cooperation of heterochromatin and BRCA1 stabilizes repeats
    Susan Gasser, Friedrich Miescher Institute, Basel, Switzerland
    Analysis of linker histones H1 functions in Drosophila
    Ferran Azorin, Molecular Biology Institute of Barcelona (IBMB-CSIC), Barcelona, Spain
    Short talk from selected abstracts:
    Assembly of CENP-A chromatin at Fission Yeast Centromeres
    Alison Pidoux, University of Edinburgh, Edinburgh, UK
    Short talk from selected abstracts:
    Chromatin-encoded memory of transcriptional programs inferred from cell clones: novel views from single cell omics
    Olivier Cuvier, French National Center for Scientific Research (CNRS), Tolouse, France

11:00  Coffee break

11:40  SESSION 2
    Chair: Jordi Bernues, Molecular Biology Institute of Barcelona (IBMB-CSIC), Barcelona, Spain
    The EMBO keynote lecture:
    Chromatin architecture and histone dynamics at eukaryotic gene promoters
    Carl Wu, Johns Hopkins Hospital, Baltimore, USA
    In vivo analysis of centromeric proteins reveals a stem cell-specific asymmetry and an essential role in differentiated, non-proliferating cells
    Sylvia Erhardt, University of Heidelberg, Heidelberg, Germany
    Short talk from selected abstracts:
    Nucleosomes stabilize RNA-DNA triple helix interactions
    Rodrigo Maldonado, University of Regensburg, Regensburg, Germany
    Single slide speed presentations from selected posters

13:30  Lunch and poster session
15:00  **SESSION 3**  
Chair: Guillaume Filion, Centre for Genomic Regulation (CRG), Barcelona, Spain

*Polycomb — master weaver of the 3D genome*  
**Wendy Bickmore**, University of Edinburg, Edinburgh, UK

*Chromatin plasticity in stem cells and cancer: A tale of 2 histone variants*  
**Eran Meshorer**, The Hebrew University of Jerusalem, Jerusalem, Israel

*Short talk from selected abstracts:*  
**Role of HDAC8 and higher-order chromatin structure in melanoma metastasis**  
**Kunal Rai**, University of Texas MD Anderson Cancer Center, Houston, USA

*Short talk from selected abstracts:*  
**Using alterations in nascent chromatin to affect differentiation-related diseases and progression of cancer**  
**Alexander Mazo**, Thomas Jefferson University, Philadelphia, USA

16:30  **Coffee break**

17:10  **SESSION 4**  
Chair: Travis Stracker, Institute for Research in Biomedicine (IRB Barcelona), Barcelona, Spain

*Epigenetic basis of germinal center derived B-cell lymphomas*  
**Wendy Béguélin**, Weill Cornell Medical College, New York, USA

*Plcg1 expression affects differentiation and self-renewal of hematopoiesis and leukemia*  
**Florian Heidel**, Jena University Hospital, Jena, Germany

*Short talk from selected abstracts:*  
**Isoform-specific localisation of DNMT3A regulates DNA methylation turnover at bivalent CpG islands**  
**Tuncay Baubec**, University Of Zurich, Zurich, Switzerland

18:40  **Poster session, Cocktail and Networking**

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**Thursday, October 26th, 2017**

9:00  **SESSION 5**  
Chair: Sandra Peiró, Vall d’Hebron Institute of Oncology (VHIO), Barcelona, Spain

*The power of epigenomics to uncover (dys)regulated pathways*  
**Henk Stunnenberg**, The Radboud University Medical Center, Radboud, Netherlands

*Single cell epigenomics and epigenetic memory in development and cancer*  
**Amos Tanay**, The Weizmann Institute, Rehovot, Israel

*Enhancers integrate TGFβ signaling, transcription factors and epigenetic regulators to induce neuronal cell fate*  
**Marian Martínez-Balbás**, Molecular Biology Institute of Barcelona (IBMB-CSIC), Barcelona, Spain

*Short talk from selected abstracts:*  
**Dynamic epigenetic regulation: Single cells can make the difference**  
**Permette Verschure**, University of Amsterdam, Amsterdam, Netherlands

10:40  **Coffee break**
11:20  **SESSION 6**  
Chair: Sonia Forcades, Institute of Health Research Germans Trias i Pujol (IGTP), Barcelona, Spain

**Bromodomain proteins: Epigenetic readers in the DNA damage response and cancer**  
Kyle Miller, University of Texas at Austin, Austin, USA

*Short talk from selected abstracts*

**Tousled like kinase activity is required for histone deposition, DNA replication, heterochromatin maintenance and (epi)genome stability**  
Travis Stracker, Institute for Research in Biomedicine (IRB Barcelona), Barcelona, Spain

*Short talk from selected abstracts:*

**Functional analysis in vivo of the mouse tyrosinase expression domain using CRISPR tools**  
Lluís Montoliu, National Centre for Biotechnology (CNB), Madrid, Spain

**Cancer Epigenetics: From Knowledge to Applications**  
Manel Esteller, Bellvitge Institute for Biomedical Research (IDIBELL), Bellvitge, Spain

12:50  **Closing remarks and farewell**

15:00  **PMPPC symposium** (see p. 35 for more info)
Albert Jordan, Group Leader at Molecular Biology Institute of Barcelona (IBMB-CSIC), Barcelona, Spain
Organizer BCEC 2017

Since 2008 Albert Jordan is a CSIC (the Spanish Research Council) Scientist at the Molecular Biology Institute of Barcelona (IBMB-CSIC), and Group Leader of the Chromatin Regulation of Human and Viral Gene Expression Laboratory. He graduated in Biology (1991) and did his PhD studies in Molecular Microbiology (1996) at the Autonomous University of Barcelona, and stayed there afterwards for three years as a Lecturer. There he identified and characterized a new class of ribonucleotide reductases. In the meantime he spent five consecutive summer periods in the laboratory of Peter Reichard at the Karolinska Institute, Stockholm. He then moved to San Francisco to undertake his postdoctoral work in the laboratory of Eric Verdin at the Gladstone Institutes (1999-2001), where he became interested in the role of chromatin in HIV gene expression control and latency. In 2002 he got a Ramon y Cajal appointment to join the laboratory of Miguel Beato at the Centre for Genomic Regulation (CRG) in Barcelona where he became Staff Scientist afterwards. There he studied mechanisms of gene expression regulation by steroid hormone receptors. Finally, in 2008 he got a permanent CSIC position to start a new group at IBMB where he studies the functional specificity of human histone H1 variants applying genomics and proteomics techniques, as well as HIV latency mechanisms and reactivation. He is Director of the IBMB Molecular Genomics department, and member of the Directive Committee of the Catalan Society of Biology where he was funder the Chromatin and Epigenetics section.

Marcus Buschbeck, Group Leader at Josep Carreras Leukaemia Research Institute, Barcelona, Spain
BCECcoordinator, co-organizer 2017

I have been trained in molecular cancer research and chromatin biology at several institutions that include the Max-Planck-Institute of Biochemistry, the University of Oxford and the Center of Genomic Regulation. In 2009 I have combined the two fields to start my own lab at the IMPPC, a small institute embedded in the biomedical research Campus Can Ruti located in the outskirts of Barcelona, Spain. By joining the Josep Carreras Leukaemia Research Institute on the same campus at the beginning of 2015, I have also started new lines of research focusing on the hematopoietic stem cell defects known as myelodysplastic syndromes and the blood cancer myeloid leukemia.

Ferran Azorín, Research Professor at IBMB, CSIC and IRB Barcelona, Barcelona, Spain
Co-organizer 2017

Research Professor at the Spanish Research Council (CSIC). Director of the Institute of Molecular Biology of Barcelona (IBMB). Group leader at the Institute for Research in Biomedicine, IRB Barcelona. EMBO member. Author of more than 100 publications in the field of "Chromatin and Epigenetics".
Marian Martínez-Balbás, Research Scientist at Barcelona Molecular Biology Institute (IBMB-CSIC), Barcelona, Spain
Co-organizer 2017

Marian Martínez-Balbás. Research Scientist and Group Leader of Molecular Signaling and Chromatin group at the Barcelona Molecular Biology Institute (IBMB)-CSIC, Barcelona, Spain.

Graduated in pharmacology from the Santiago de Compostela University, Marian Martínez-Balbás obtained her PhD at the Polytechnic University of Barcelona studying DNA and chromatin structure. She was a postdoctoral Fellow at the NIH (USA) where she focused on chromatin remodeling and dynamics at Dr C Wu's laboratory. Subsequently, she moved to the J Gurdon Institute (group of Dr T Kouzarides) in Cambridge (UK), to study the contribution of histone modifications to cell cycle progression and cell proliferation. In year 2000 she got a permanent CSIC position at the IBMB, where she created the “Molecular signaling and chromatin” laboratory. Presently, her research is focused on understanding the role of several chromatin regulators controlling the transcriptional program during development. Her group analyzes different aspects of chromatin dynamics during neurogenesis, using in vitro and in vivo models.

Jordi Bernués, Permanent Research Scientist at Barcelona Molecular Biology Institute (IBMB-CSIC), Barcelona, Spain
Co-organizer 2017

Graduated in Biological Sciences from the Autonomous University of Barcelona, obtained his Ph.D. at the Autonomous University of Barcelona (1987) studying the interactions of non-histone HMGB1 and 2 proteins with histones and chromatin. After a short postdoctoral stay at the CSIC working on triplex DNA (H- and +H-DNA) he moved to EMBL(Heidelberg) in 1990 with an EEC fellowship where he studied the transcription factor requirements and the pol II/polIII determinants of U1 and U6 snRNAs at professor Iain W. Mattaj's laboratory. In 1993 he got a permanent position at IBMB-CSIC where he has been working on several topics about chromatin and epigenetics in Drosophila.
Eduard Batlle, ICREA Research Professor and Head of the Oncology Program, Institute for Research in Biomedicine in Barcelona (IRB Barcelona), Barcelona, Spain

Collaborator (BCEC 2016)

Eduard Batlle (Barcelona, 1970) obtained a BSc degree in Biology and a PhD in Molecular Biology by the University of Barcelona. After his postdoctoral training in Hans Clevers lab (Utrecht, the Netherlands), he joined the Institute for Research in Biomedicine (IRB Barcelona) as ICREA Research Professor and Head of the Oncology Program. His research activity has focused on the mechanisms that drive colorectal cancer initiation and progression. Amongst other findings, his research originally identified the transcription factor Snail as a repressor of E-Cadherin gene expression during the Epithelial-to-Mesenchymal Transition (2000); the first connection between intestinal stem cells and colorectal cancer (2002-2011); and more recently a key role for TGF-beta signaling in stromal cells during metastatic colonization (2012-2015). His track record has been recognised through several awards/honours such as the Debiopharm Life Science Award (2006), an ERC starting Grant (2007), Banc de Sabadell Award for Biomedical Research (2010), Josep Steiner Cancer Research Award (2013), Drs. Diz-Pintado award (2013), ERC Advanced Grant (2013) and the Pezcoller foundation-EACR award (2014).

Manel Esteller, Director of Cancer Epigenetics and Biology Program (PEBC) at Bellvitge Biomedical Research Institute (IDIBELL), Barcelona, Spain

Collaborator (BCEC 2014)

Dr Esteller graduated in Medicine (1992) and obtained his Ph.D. in molecular genetics of endometrial carcinoma (1996). He was Invited Researcher at the School of Biological and Medical Sciences at the U. of St. Andrews, during which time his research interests focused on the molecular genetics of inherited breast cancer. From 1997 to 2001, he was Postdoctoral Fellow and Research Associate at the Johns Hopkins University and School of Medicine, where he studied DNA methylation and human cancer. His work was decisive in establishing promoter hypermethylation of tumour suppressor genes as a common hallmark of all human tumours. From 2001 to 2008 he was the Cancer Epigenetics Laboratory’s of the CNIO, in Madrid, where he studied the alterations in DNA methylation, histone modifications and chromatin in human cancer. Since 2008, Dr Esteller is the Director of the Cancer Epigenetics and Biology Program of the Bellvitge Biomedical Research Institute, in Barcelona, Chairman of Genetics in the School of Medicine of the U. of Barcelona and ICREA Research Professor. Author of more than 500 biomedical manuscripts, many of them as Highly Cited articles, he’s also associated editor for several journals and the recipient of the Swiss Bridge Award 2006, Debiopharm-EPFL Award 2009, Dr Josef Steiner Cancer Research Award 2009, Biomedical Research Award-Lilly Foundation 2009, World Health Summit Award 2010, European Research Council Advanced Grant 2011, Severo Ochoa Prize 2013, Research Award in Life Sciences Royal Academy of Natural and Physical Sciences 2013, National Award in Oncology 2014, National Research Prize of the Catalan Government 2015, Parliament of Catalonia Gold Medal 2016 and the International Award of Catalonia 2016. His current research is devoted to the establishment of the epigenome maps of normal and transformed cells, the study of the interactions between epigenetic modifications and non-coding RNAs, and the development of new epigenetic drugs for cancer therapy.

Luciano Di Croce, Group Leader at Centre for Genomic Regulation (CRG), Barcelona, Spain

Collaborator (BCEC 2015)

Dr. Di Croce's laboratory is addressing the molecular basis of epigenetic alterations during the early phase of tumorigenesis, that is: how epigenetic modifications and chromatin changes are established and, once in place, how they affect gene expression, cell differentiation and transformation. His research focuses in particular in understanding the role of several protein complexes that are involved in chromatin dynamics and metabolism (Polycomb and others), which when altered could participate in the establishment and maintenance of the aberrant silencing of tumor suppressor genes during transformation.
Manuel Peruco, Director of the Institute of Predictive and Personalized Medicine of Cancer (IMPPC), Barcelona, Spain

Collaborator (BCEC 2013)

Manuel Peruco studied a master in Biological Sciences at University of Madrid in 1971, where he also obtained his Ph.D. degree in Biological Sciences, in 1976. From 1977 to 1978, Peruco was a Postdoctoral Fellow at the Max-Plank-Institute für Molekulare Genetik, (Berlin, Germany) where he studied isolation and characterization of mRNA for the tissue-specific histone H5 from immature chicken erythrocytes. From 1979 to 1980, he did a postdoctoral work at Cold Spring Harbor Laboratory, where he became staff investigator during 1981 and 1982. In 1982 he moved to Dept. of Biochemistry at State University of New York, where he was Assistant Professor and, in 1987 Peruco became Associate Professor at the same university until 1988. From 1995 to 2007 he had been linked with California Institute of Biological Research (La Jolla, California) as a research program director (1988-1995) and professor and program director (1995-2007). Currently, Manuel Peruco is a Visiting Professor at Universitat Autònoma de Barcelona, Associate Investigator at Fundación Investigación Sanitaria Castilla-La Mancha, Member Advisory Board at Instituto Canario Investigación, Professor and Program Co-Director at Sanford-Burnham Medical Research Institute and Director of Institute of Predictive and Personalized Medicine of Cancer (Badalona, Spain). Peruco has also organized more than twenty meetings and courses and he has about 130 scientific publications.

Albert Jordan, Group Leader at Molecular Biology Institute of Barcelona (IBMB-CSIC), Barcelona, Spain

BCEC 2017

(Read bio in page 7)

Marcus Buschbeck, Group Leader at Josep Carreras Leukaemia Research Institute, Barcelona, Spain

Coordinator of BCEC, Collaborator BCEC 2013, 2015, 2017

(Read bio in page 7)
DETAILED PROGRAM AND INVITED SPEAKERS

Wednesday, October 25th, 2017

Session 1

**Albert Jordan**, Group Leader at Molecular Biology Institute of Barcelona (MBMB-CSIC), Barcelona, Spain

(Read bio in page 7)

Chair of the SESSION 1

**Susan Gasser**, Director at Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland

Prof. Susan M. Gasser is a Swiss molecular biologist and is currently the Director of the Friedrich Miescher Institute for Biomedical Research. She studied biology and biophysics at the Uni. of Chicago, did her PhD at the Uni. of Basel in Biochemistry, and a postdoc at the Uni. of Geneva. She began her own research on chromatin at the Swiss Institute for Experimental Cancer Research in Lausanne from 1986-2001, and then returned to the Uni. of Geneva as Professor of Molecular Biology. In 2004, she was recruited as Director of the FMI, and nominated as Professor of Molecular Biology at the Uni. of Basel.

Starting with the discovery that the enzyme topoisomerase II plays a structural role in the organization of metaphase chromosomes, Susan Gasser has explored how nuclear and chromosomal context establishes and maintains heritable patterns of gene expression. From the telomere position effect in yeast, to the inheritance of repressed tissue-specific genes in C. elegans, her studies have examined how the clustering and spatial organization of heterochromatin contributes to heritable gene silencing. In worms, she showed that histone modifications directly determine the spatial organization of chromatin, and that the positioning of heterochromatin, which contributes to the stable inheritance of gene expression states. Its loss generates degenerative disease in man.

In parallel to these studies, Susan Gasser optimized live imaging techniques to pioneer the analysis of chromatin dynamics with time-lapse fluorescence imaging. By analyzing chromatin movement in living yeast cells, she found that chromatin has constant subdiffusive motion in the nucleus. In yeast, as in other organisms, DNA damage and double-strand breaks increase chromatin movement in a checkpoint kinase-and chromatin remodeler-dependent manner, due to histone degradation.

Professor Gasser has authored more than 250 primary articles and reviews, and has received a number of award in 2013.

**Cooperation of heterochromatin and BRCA1 stabilizes repeats**

Histone H3K9 methylation is a conserved modification that correlates broadly with gene repression in organisms ranging from fission yeast to man. In C. elegans, di- and tri-K9 methylation is abundant on repetitive elements (RE), including both transposons and simple repeats, and coats both pseudogenes and silent tissue-specific genes. Using a double mutant that eliminates the two C. elegans H3K9 histone methyltransferases, SET-25 and MET-2, we find that H3K9me is dispensable for development, although worms become sterile. This correlates with extensive DNA damage-driven apoptosis in the germline, without elevated mitotic or meiotic chromosome missegregation. Instead, we find that the loss of H3K9 methylation leads to the promiscuous and widespread expression of all classes of repetitive elements (DNA and RNA transposons, and simple repeats) in both germline and somatic tissues. The loss of transcriptional silencing correlates with an accumulation of insertions and deletions at repetitive sequences, and renders worms sensitive to replication fork stalling, but not ionizing radiation. RNA-DNA hybrids accumulate in the absence of H3K9me even without exogenous stress, which
is exacerbated by the loss of the C. elegans BRCA1 complex, specifically at tandem repeats and not at RNA or DNA transposons. We conclude that a key function of H3K9me is to ensure the stability of a repeat-rich genome, most specifically by suppressing the transcription of simple repeats.


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**Ferran Azorín**, Research Professor at IBMB, CSIC and IRB Barcelona, Barcelona, Spain

(Read bio in page 7)

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**Analysis of linker histones H1 functions in Drosophila**

Linker histone H1 is an important structural component of chromatin that stabilizes the nucleosome and compacts the nucleofilament into higher-order structures. The biology of histone H1 remains, however, poorly understood. Histones H1 are less well conserved than core histones and, in metazoa, they generally exist in multiple variants that play partially redundant functions. In contrast, H1 diversity in Drosophila melanogaster is low since it contains only one somatic (dH1) and a second germine specific (dBigH1) variant. Here we will summarize our studies addressing functional characterization of linker histones H1 in Drosophila. Our results show that somatic dH1 plays an essential role in preventing genome instability in heterochromatin. On the other hand, dBigH1 is required for stem cell lineage differentiation and prevents premature activation of the zygotic genome during early embryogenesis.

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**Short talk from selected abstracts: Alison Pidoux**, Postdoc at **University of Edinburgh**, Edinburgh, UK

**Authors:** Alison Pidoux, Pin Tong, Ryan Ard, Jesus Torres-Garcia, Manu Shukla, Nick Toda, Harald Berger and Robin Allshire

**Assembly of CENP-A chromatin at Fission Yeast Centromeres**

Despite the conserved essential function of centromeres, centromeric DNA is not conserved between species and centromeres are epigenetically regulated. Although centromeres normally assemble on preferred sequences, these sequences are neither necessary nor sufficient for centromere assembly. Presence of the histone H3 variant, CENP-A, is the epigenetic mark that specifies centromere identity. We aim to understand how CENP-A assembly is influenced by sequence and by chromatin context. Schizosaccharomyces pombe centromeres are composed of a central domain that is assembled in CENP-A chromatin and forms the kinetochore, flanked by the heterochromatic (H3K9me2) outer-repeat regions.

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**Short talk from selected abstracts: Olivier Cuvier**, Group Leader at **French National Center for Scientific Research (CNRS)**, Tolouse, France

**Authors:** Depierre, D., Heurteau, A., Martin, P., Liang, J., Lhoumaud, P., Schaack, S., Perrois, C., Mourad, R., Cuvier, O.

**Chromatin-encoded memory of transcriptional programs inferred from cell clones: novel views from single cell omics**

We will present our genome-wide analyses illustrating how long-range contacts in chromosomes, as detected from hidden information in ChIP-Seq, support the role of functional long-range contacts in regulating gene expression including of oncogenes, as confirmed through analysis of looping by Hi-C data along with further development of computational methods to probe long-range contact maps at a high resolution (< 500 bp). Furthermore, we will present recently published data together with unpublished stuffs highlighting a role of histone lysine-methyl transferases (KMTs) together with additional chromatin factors in regulating the inherited transmission of gene expression states, as inferred from single cell omics. We shall show the mechanisms of protection of active genes including oncogenes that are protected from heterochromatin-mediated gene silencing, at genome-wide levels. In particular, our data support the view that KMTs contribute to cell identity by protecting genes from stochastic changes in expression, thereby maintaining transcriptional programs through cell divisions.
Session 2

Jordi Bernués, Permanent Research Scientist at Barcelona Molecular Biology Institute (IBMB-CSIC), Barcelona, Spain

(Read bio in page 8)

Chair of the SESSION 2

The EMBO keynote lecture:

Carl Wu, Bloomberg Distinguished Professor at Johns Hopkins University, Baltimore, USA

Carl Wu joined Johns Hopkins University in 2016 as Bloomberg Distinguished Professor with appointments in the Department of Biology, and the Department of Molecular Biology and Genetics. He received his Ph.D. in Biology at Harvard University and did post-doctoral work as a Harvard Junior Fellow. He was a Principal Investigator at the National Cancer Institute for 30 years, and a member of the Transcription Imaging Consortium at HHMI-Janelia (2012 - 2016). He is a member of the US National Academy of Sciences, National Academy of Medicine, American Academy of Arts and Sciences, Academia Sinica, and European Molecular Biology Organization.

Chromatin architecture and histone dynamics at eukaryotic gene promoters

Our lab is interested in understanding the structure and function of chromatin, which has a key role in regulating essentially all chromosome activities. We are studying the biochemistry of the conserved histone variant, H2A.Z, which is uniquely incorporated at all eukaryotic promoters and enhancers genome-wide, and has an important role in the proper control of transcription. By elucidating the mechanisms underlying site-specific incorporation of H2A.Z into nucleosomes and the functions of nucleosomal H2A.Z in the transcription pathway, we hope to acquire general insights on nucleosome dynamics and transcription at eukaryotic promoters and enhancers, with implications for gene regulation in growth, development and disease. We use the budding yeast model organism for the relative ease of performing molecular genetics and biochemistry in the same system.

We discovered the pathway by which histone H2A.Z is incorporated into nucleosomes by SWR1, a 14-component, 1-megadalton chromatin remodeler conserved from yeast to humans. SWR1 has two distinct substrates—the canonical nucleosome and the variant H2A.Z-H2B dimer. In the histone exchange reaction, SWR1 mediates ATP-dependent eviction of one nucleosomal histone H2A-H2B dimer coupled with deposition of H2A.Z-H2B, followed by a second histone dimer exchange. Biochemical studies have elucidated how SWR1 captures the H2A.Z-H2B dimer and targets nucleosomes flanking free promoter DNA — both actions primarily through the Swc2/YL1 subunit—but little is known about the specific roles of eleven SWR1 components in the multi-step pathway. We are currently investigating how SWR1 engages and is activated by its second substrate—the canonical nucleosome, and how histone modifications affect this process. In collaboration with T.J. Ha's lab, we are developing a single-molecule, real-time fluorescence colocalization and fluorescence resonance energy transfer approach to detect sequential reaction intermediates and measure their lifetimes during histone exchange. We are also using live-cell, single-molecule fluorescence microscopy approaches aimed at dissecting the interaction between native chromatin and transcription-related factors and enzymes such as SWR1. The live-cell approach avoids fixation artifacts, measures the dynamics of single molecules at high spatiotemporal resolution, and will help us understand how different factors gain access to chromatin in vivo. By comparing the diffusive parameters in wild-type and mutant cells exhibiting chromatin defects, we aim to gain new insights on the functions of chromatin organization and dynamics on transcription factor binding and activity.
Sylvia Erhardt, Professor at Center for Molecular Biology of Heidelberg University (ZMBH), Heidelberg, Germany

SCIENTIFIC VITAE
1998 Diploma thesis at the University of Heidelberg with Prof. Renato Paro
1999-2003 PhD at the University of Cambridge (UK) with Prof. Azim Surani
2003-2007 Postdoc, University of Berkeley, CA (USA) with Prof. Gary Karpen
2008-2016 Independent junior group leader of the Excellence cluster CellNetworks at the ZMBH, University of Heidelberg and DKFZ-ZMBH Alliance.
Since 2017 W2 Professorship (6 year term) at the University of Heidelberg.

FIELDS OF INTEREST
Centromeric chromatin and chromosome segregation in normal cells and tumors, Epigenetics, DNA damage repair, and Non-coding RNAs, RNA and protein modifications

AWARDS AND FELLOWSHIPS
2016 Performance award from the University of Heidelberg
2015 ERC Consolidator grant (activation date: July 2016)
2015 Hella Bühler Prize for Cancer research from the University of Heidelberg
2007 Pathway of Independence grant from the NIH, USA (not activated)
2003-2006 Wellcome Trust International Post-doc Research Fellowship, UK
2002 Darwin Travel Award, Cambridge, UK
1999-2002 Ph.D.-fellowship of the Boehringer Ingelheim Fonds, Germany
1998 Diploma with distinction, University of Heidelberg, Germany

In vivo analysis of centromeric proteins reveals a stem cell-specific asymmetry and an essential role in differentiated, non-proliferating cells

Stem cells of the Drosophila midgut (ISCs) are the only mitotically dividing cells of the epithelium and therefore, presumably the only cells that require functional kinetochores for microtubule spindle attachment during mitosis. The histone variant CENP-A epigenetically marks centromeric chromatin as the site of kinetochore formation and spindle attachment during chromosome segregation. We show here that centromeric proteins distribute asymmetrically during ISC division. Whereas newly synthesized CENP-A is enriched in differentiating progeny, CENP-C is undetectable in these cells. Remarkably, CENP-A persists in ISC for long time periods without being replaced, in accordance with an epigenetic mark responsible for maintaining stem cell properties. Furthermore, our work shows that CENP-A and its loading machinery are essential for post-mitotic differentiating cells. Removal of any of these factors interferes with endoreplication. Taken all together, we propose two novel roles of CENP-A in maintaining stem cell unique properties and as essential regulator of post-mitotic cells.

Short talk from selected abstracts: Rodrigo Maldonado, Postdoctoral Investigator at University of Regensburg, Regensburg, Germany

Authors: Rodrigo Maldonado, Uwe Schwartz, Elisabeth Silberhorn, and Gernot Längst

Nucleosomes stabilize RNA-DNA triple helix interactions

The epigenetic landscape of chromatin and its associated gene expression program is modulated through the interaction with long noncoding RNAs (lncRNAs). Cancer-associated lncRNAs have been shown to form triple helix structures and the interaction with chromatin mediates a mechanism to modulate gene expression. However, the molecular details of this mechanism and the targeting of lncRNAs through triplexes are still unclear to date. A triplex helix is formed by a ssRNA that binds to the major groove of the dsDNA, being stabilized by specific Hoogsteen bonds between the bases. Triplexes are rather unstable structures due to charge repulsion and it is believed that chromatin presents a major obstacle for its formation. In the present study we analyzed the effect of nucleosomes on the stability and sequence specific binding of ssRNA to dsDNA. Importantly, we discovered a stabilizing role for the nucleosomes in triplex formation. We show that the histone tails, especially the histone H3 tail, does specifically contribute to the stable binding of third strand to chromatin. Triplexes are preferentially formed in the linker regions adjacent to the nucleosome. Surprisingly, stable triple helix formation could also be detected within the first two helical turns of DNA within the nucleosome. Genome wide analyses revealed a structure function relationship between nucleosome positioning and putative triplex targeting sites, correlating accessible triplex targeting sites with active chromatin structures and gene activity.
Session 3

Guillaume Fillion, Team Leader at Centre for Genomic Regulation (CRG), Barcelona, Spain

My current focus is to understand how genomes are organized. To this aim, we are developing technologies to study position effects and chromosome organization. This requires new statistical and computational methods that are also developed within the team.

Chair of the SESSION 3

Wendy Bickmore, Professor at MRC Human Genetics Unit, Edinburgh, UK

Wendy Bickmore is Director of the MRC Human Genetics Unit, Institute of Genetics and Molecular Medicine at the University of Edinburgh. Her undergraduate degree is in Biochemistry from the University of Oxford and her PhD was on the evolution of the X and Y chromosomes in primates. She is fascinated by the structure and organization of chromosomes in the nucleus. She showed that different human chromosomes have preferred positions in the nucleus, related to their gene content, and addressed how genes are organized and packaged in the nucleus and how they move in the cell cycle and during development. Current research in Wendy Bickmore’s laboratory focuses on how the spatial organization of the nucleus influences genome function in development and disease. Wendy is an EMBO member, a fellow of the Royal Society and of the Academy of Medical Sciences and is the president of the Genetics Society of Great Britain. She is an editor on many journals including PLoS Genetics and Cell.

Polycomb – master weaver of the 3D genome

Whilst it is widely appreciated that histone modifications correlate to gene expression states and can directly impact on gene expression and repression, our understanding of chromatin states beyond the level of the nucleosome, and how higher-order chromatin structures contribute to the regulation of gene expression, is more rudimentary.

The polycomb repressive complexes are important mediators of epigenetic regulation during mammalian development. Both the PRC2 and the PRC1 complexes contain enzymes capable of catalyzing histone modifications. However, we have shown that the E3 ligase activity (H2AK119 ubiquitination) of the PRC1 complex is not required for the major functions of PRC1 during early embryonic development. Catalytically inactive PRC1 is still able to form compact chromatin domains at Pcg target loci and to mediate longer-range cis-interactions between distant Pcg target loci. Thus we suggest that PRC1 acts to repress gene expression through higher-order chromatin structure rather than by histone modification and that polycomb is a major player in structuring the three-dimensional genome.

We show that polycomb target loci become decompact in embryonic stem cells grown under 2i conditions and that this is attributable to DNA hypomethylation titrating polycomb away from its target loci, and not the ‘naïve pluripotency’ developmental status of 2i cells. Therefore, DNA methylation also has a major impact on 3D genome organisation, but we suggest that is principally played out through its effect on focussing polycomb targeting.

Eran Meshorer, PI at The Hebrew University of Jerusalem, Jerusalem, Israel

Prof. Meshorer completed his PhD at the Hebrew University and performed his post-doctoral studies at the National Cancer Institute, NIH. In 2007 he returned to the Hebrew University as an Alon Fellow and is currently heading the Stem Cell Chromatin laboratory in the Department of Genetics and the Edmond and Lily Center for Brain Sciences (ELSC). Meshorer's research focuses on single cell and genome-wide approaches to understand chromatin plasticity and epigenetic regulation in embryonic and neuronal stem cells, during reprogramming, and in pluripotent models of neurodegenerative diseases. Prof. Meshorer is a recipient of the Elkes award of the Israel Society for Psychobiology (2010), an ERC award from the European Union (2011), the Hestrin prize of the Israeli Society of Biochemistry and Molecular Biology (2012), the Sir Zelman Cowen Award (2013), the Vigeans Research Prize (2015), and a Gold Medal from Charles University, Prague (2016). Prof. Meshorer holds the Arthur Gutterman Family Chair for Stem Cell research.

Chromatin plasticity in stem cells and cancer: A tale of 2 histone variants

Histone variants and their chaperones are key regulators of eukaryotic transcription, and are critical for normal development. In recent years, several such replacement histones, including both core histone variants and linker histone variants, were directly implicated in different types of cancer. We identified the linker histone variant H1.0 as a critical regulator of cancer cells’ long-term proliferative potential. Numerous cancer types exhibit high inter- and intra-tumor heterogeneity in H1.0 levels, correlating with tumor differentiation status, patient survival and, at the single cell level,
with cancer stem cell markers. Loss of H1.0 promotes self-renewal by destabilizing chromatin structure at regulatory DNA regions and inducing genome-wide de-repression of megabase-sized gene domains harbouring downstream effectors of oncogenic pathways. An additional variant, found to be mutated in several malignancies is the core histone variant H3.3. To begin unravelling its genome-wide dynamic behaviour and the potential role that its specific mutations might play in this process, we generated mouse ESC lines carrying a single copy of a doxycycline (Dox)-inducible HA-tagged version of H3.3, and monitored the rate of H3.3 incorporation by ChIP-seq at varying time points following Dox induction, before and after RA-induced differentiation. Comparing H3.3 turnover profiles in ESCs and RA-treated cells, we identified a hyperdynamic H3.3-containing nucleosome at the -1 position in promoters of genes expressed in ESCs. This dynamic nucleosome is restricted and shifted downstream into the +1 position following differentiation. Cancer-causing mutations in H3.3 affected its genome-wide incorporation as well as its dynamic behavior. Taken together, our results highlight the importance of histone variants in cellular homeostasis, and delineate some of the mechanisms by which loss of function and gain of function mutations lead to cellular malfunction.

Short talk from selected abstracts: Kunal Rai, Assistant Professor at UT MD Anderson Cancer Center, Houston, USA

Authors: Christopher Terranova, Elias Orouji, Kadir C Akdemir, Dong Yang, Mayura Dhamdhere, Neha S Samant, Aniksha Shah, Sneha Sharma, Danielle A Johnson, Lynda Chin and Kunal Rai

Role of HDAC8 and higher-order chromatin structure in melanoma metastasis

Melanoma is a major world health problem with most deaths occurring due to metastatic spread of the disease. Although genetic basis of melanoma formation has been well established, epigenetic events driving melanoma metastasis remain unclear. With a hypothesis that epigenetic events may be a key driving force for metastatic progression, we performed an in vivo gain-of-function screen that identified 10 epigenetic regulators as potent drivers of melanoma metastasis. Series of loss-of-function and gain-of-function experiments established pro-metastatic roles for screen hits including HDAC8, the top hit from the screen. HDAC8 deacetylated a subset of nucleosomes as well as Smc3, a cohesin subunit. While we noted histone deacetylation events at limited number of loci, drastic alterations in Smc3 binding were observed in HDAC8 overexpressing cells suggesting important role of aberrant higher-order chromatin structure during metastatic transition. Independent Hi-C based profiling of genome-wide contacts in matched primary and metastatic melanoma cells revealed alterations in TAD domains during evolution of metastatic clones. Alterations in Smc3 bindings occurred on WWC1, DKK1 and DLK1 that are negative regulators of important pro-metastatic cell signaling pathways, such as YAP1/hippo, wnt and notch pathways respectively. Further, we observed TAD domain alterations on other hitherto unknown regulators of melanoma cell invasion such as LARGE, which were further studied in depth. Overall, our findings suggest critical roles of higher-order chromatin structure and its regulators, such as HDAC8, in driving melanoma metastasis.

Short talk from selected abstracts: Alexander Mazo, Professor at Thomas Jefferson University, Philadelphia, USA

Authors: A. Mazo, S. Petruk, P. Porazzi, M. De Dominici, D. Deming, D.C. Hooper and B. Calabretta

Using alterations in nascent chromatin to affect differentiation-related diseases and progression of cancer

Objectives: These studies were aimed at understanding whether the structure of nascent post-replicative chromatin may be targeted in differentiation-related diseases and in acute myeloid leukemia (AML). Methods: PLA-based single cell assay to study the structure of nascent chromatin assays (Petruk et al. Cell, 2012); conventional molecular and immunocytochemical techniques. Results: Our recent studies suggest that differentiation of multiple stem/progenitor cells requires transient de-condensation of post-replicative chromatin at repressed genes (Petruk et al. Molecular Cell, 2017; Petruk et al. Cell Reports, 2017; Huang and Wang, Molecular Cell, 2017). The follow-up studies suggest that these findings have a number of important disease-related implications. We found that manipulating the structure of nascent chromatin may be an essential tool in preventing major differentiation-related diseases like fibrosis. We will describe our recent results suggesting that this allows to prevent development of the fibrotic scarring following the eye cataract surgery. On the other hand, it is possible that the inability of cancer cells to differentiate may be caused by alterations in this nascent chromatin related mechanism. Our data provides evidence of the altered structure of nascent chromatin in cancer cells of multiple origins. We will present two related approaches aimed at affecting proliferation and survival of the acute myeloid leukemia (AML) cells. Conclusions: Manipulating structure of nascent chromatin may have multiple applications in preventing differentiation-related diseases and may provide new tools in cancer treatment.
Session 4

**Travis Stracker**, Principal Investigator at **Institute for Research in Biomedicine (IRB Barcelona)**, Barcelona, Spain

Dr. Stracker received his BS in Genetics from the University of Georgia and moved to the University of California, San Diego to perform his PhD in Biology in the laboratory of Matthew Weitzman at the Salk Institute. There he identified a role for Adenovirus oncoproteins in the inactivation of the cellular DNA damage response. He then moved to the lab of John Petreni in Sloan-Kettering Institute to pursue the analysis of the DNA damage response using mouse models of human genetic instability disorder. This work uncovered key roles for the MRE11 complex, a key sensor of DNA breaks, in regulating apoptosis and defined its role in tumor suppression. In 2009, Dr. Stracker moved to the IRB Barcelona to form his own group. There he group has pursued the role of genomic instability in the pathology of rare diseases and undertaken the characterization of numerous DNA damage response factors and their roles in cancer or as potential targets for cancer therapy.

Chair of the SESSION 4

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**Wendy Béguelin**, Instructor at **Weill Cornell Medicine**, New York, USA

Dr. Wendy Béguelin is a basic and translational research scientist working in the field of lymphoma epigenetics. She obtained her degree of Biology at the University of Buenos Aires, Argentina. As a postdoctoral scientist and Instructor in Medicine at Weill Cornell Medical College in New York, under the supervision and mentorship of Prof. Ari Melnick she has identified novel epigenetic and transcriptional mechanisms that contribute to B-cell differentiation and lymphomagenesis. She has studied the biological and transcriptional mechanisms of action of Polycomb proteins in germinal center B-cells and human lymphomas. Dr. Béguelin is committed to a career in basic/translational cancer research, bringing new ideas into the field of epigenetic control of lymphomagenesis and making discoveries that can be translated from the diagnostic and therapeutic standpoints.

### Epigenetic basis of germinal center derived B-cell lymphomas

During the T-cell dependent humoral immune response, subsets of activated B-cells can migrate within lymphoid follicles to form germinal centers (GCs). GC B-cells undergo massive proliferation and clonal expansion along with simultaneous somatic hypermutation of their immunoglobulin loci, within the GC dark zone. The proliferative and mutagenic nature of the GC B-cells make them prone to malignant transformation and hence a majority of B-cell neoplasms including follicular lymphoma (FL) and diffuse large B-cell lymphoma (DLBCL) originate from the GC reaction. Mature B-cells are epigenetically programmed to undergo plasma differentiation upon T-cell induced activation. However for the subset of B-cells destined to form GCs, the B-cell differentiation program must be silenced, as are key proliferation and DNA damage checkpoint genes. The histone methyltransferase EZH2 is required for B-cells to form GCs. During the GC reaction EZH2 specifically mediates H3K27me3 at the promoters of genes related to B-cell differentiation and cell cycle checkpoint. Approximately 30% of patients with FL and GCB-DLBCL manifest gain of function mutations of EZH2, that drive aberrantly efficient H3K27me3. The increased efficiency of mutant EZH2 causes GC B-cells to accumulate in the GC light zone and eventual undergo malignant transformation. EZH2 mediated H3K27me3 is not sufficient to repress its key genes alone. Instead it requires the binding of the BCL6 transcriptional repressor to enable stable tethering of a non-canonical Polycomb complex for repression to occur. EZH2 mutant DLBCL and FL cells are strongly suppressed by specific EZH2 inhibitors, which are proving effective in clinical trials for patients with FL and DLBCL. Approximately 40% of FL and DLBCL carry loss of function mutations in CREBBP or EP300, which function as tumor suppressors in murine lymphoma models. Profiling gene expression and histone marks in primary murine or human CREBBP mutant patients reveals repression and loss of H3K27 acetylation in enhancers of genes involved in antigen presentation and B-cell receptor signaling. This repression is caused by HDAC3, which can now deacetylase enhancers. Hence HDAC3 inhibitors may be suitable to restore immune-surveillance in CREBBP mutant lymphomas. KMT2D is affected by loss of function mutations in ~40-50% of DLBCL and FL. KMT2D mediates H3K4me1, predominantly at enhancers that enable the activation of nearby genes. During the normal GC reaction, KMT2D mediates H3K4me1 at enhancers responsive to CD40 signaling, which is critical for B-cells to undergo class switch recombination and terminal differentiation. Loss of KMT2D causes prolongation of the GC response, as B-cells fail to respond to GC exit signals, which culminates in malignant transformation. Collectively the data implicate dynamic promoter and enhancer epigenetic switches as controlling the humoral immune response and driving lymphomagenesis when perturbed by somatic mutations.
Florian Heidel, Associate Professor at Leibniz Institute on Aging and University Hospital Jena, Jena, Germany

Florian Heidel attended Medical School at the Friedrich-Alexander University in Erlangen, Germany and completed his residency (Internal Medicine) and fellowship (Hematology and Medical Oncology) at the Johannes-Gutenberg University Medical Center in Mainz, Germany. From 2009 until 2012, he was a postdoctoral research fellow at the Laboratory of Professor Scott A. Armstrong, Dana-Farber Cancer Institute (DFCI), Harvard University, Boston, MA, USA. During that time he focused on functional studies of hematopoietic and leukaemia stem cells. After his post-doctoral training he started his own laboratory and junior research group at the Otto-von-Guericke University Medical Center in Magdeburg, Germany and was also the responsible attending physician for the leukemia program. In 2015, Florian Heidel and his group re-located to the Friedrich-Schiller-University Medical Center in Jena, where he is currently holding a professorship for stem cell biology and is heading the collaborative research group for stem cell biology at the Leibniz Institute on Aging. Focus of his group is the functional characterisation of signaling pathways in the aging hematopoietic system and in myeloid neoplasia.

**Plcg1 expression affects differentiation and self-renewal of hematopoiesis and leukemia**

Phospholipase C family members are key mediators of cellular signal transduction. The PLC gamma (Plcg) family consists of two different isoforms, Plcg1 and Plcg2. Within the hematopoietic system, Plcg1 is highly expressed in hematopoietic stem- and progenitor cells and also in primary samples of myeloid leukemia. In previous studies, we identified Plcg1 as a regulator of erythroid differentiation by altering expression histone variants. Moreover, Plcg1 is functionally relevant in genetically defined subtypes of acute myeloid leukemia. Inactivation of Plcg1 impairs self-renewal capacity and affects differentiation of leukemia stem cells in vitro and in vivo.

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Short talk from selected abstracts: **Tuncay Baubec**, Professor at **University of Zurich**, Zurich, Switzerland

**Authors:** Tuncay Baubec

**Isoform-specific localisation of DNMT3A regulates DNA methylation turnover at bivalent CpG islands**

DNA methylation is a prevalent epigenetic modification involved in transcriptional repression and essential for mammalian development. Although the genomic distribution of this mark has been profiled at unprecedented detail, the mechanisms responsible for its correct deposition, as well as the cause for its aberrant localisation in cancers, have not been fully elucidated.

The de novo DNA methyltransferases DNMT3A and DNMT3B are essential for deposition of DNA methylation. We have previously identified that specific targeting of DNMT3B activity to transcribed genes is regulated by readout of H3K36me3 (Baubec et al., Nature 2015). In recent, unpublished work we report a division of labor between two tissue-specific DNMT3A isoforms. We show that the longer isoform DNMT3A1 preferentially localises to the methylated shores of CpG islands marked by H3K27me3, whereas the shorter isoform DNMT3A2 is globally distributed throughout the genome. DNMT3A1 localisation further coincides with elevated hydroxymethylcytosine (5-hmC) deposition, suggesting an involvement of this isoform in mediating turnover of DNA methylation at these sites. We demonstrate that DNMT3A1 recruitment is required to protect CpG island shores from hypomethylation by counteracting TET-mediated oxidation of methylated cytosines.

We propose that this mechanism is required to define cell type-specific transitions between methylated and unmethylated domains - with further implications on H3K27me3 deposition and related gene regulation in healthy and diseased cells. The isoform-specific activity of DNMT3A extends our current understanding on how the writers of DNA methylation target specific genomic regions and cooperate to shape the epigenetic landscape of mammalian cells.
Thursday, October 26th, 2017

Session 5

**Sandra Peiró**, Principal Investigator at **Vall d’Hebron Institute of Oncology** (VHIO), Barcelona, Spain

Sandra Peiró Sales, Head of the Chromatin Dynamics in Cancer Group, Vall d’Hebron Institute of Oncology (VHIO)

Background in Biochemistry (Bsc in Biochemistry, PhD in Biochemistry in 2001, Universitat de Barcelona). She did her PhD in cell signalling and later switched to gene regulation and epigenetics in epithelial to mesenchymal transition (EMT) and cancer progression. She is currently leading a group that focuses on the cutting-edge topic of elucidating epigenetic mechanisms in normal and miss-regulated cell behaviour and on discovering drugs that target these mechanisms.

Chair of the SESSION 5

**Hendrik Stunnenberg**, Head of Department at **Radboud University**, Radboud, Netherlands

Henk Stunnenberg is full professor at the Science and Medical faculty and head of the Department of Molecular Biology and Director of the Radboud Institute for Molecular Life Sciences of the Science faculty at Radboud University, Nijmegen. He is member of EMBO, was the chair of Scientific Steering Committee of the International Human Epigenome Consortium (IHEC), he is a member of the Council of Scientists of Human Frontier Science Program Organization (HFSP0), Program Committee member for the International Cancer Genome Consortium (ICGC) and member of the Organising Committee of the Human Cell Atlas.

He is taking epigenome and single-cell approaches to advance and exploit our knowledge of the underlying biological processes and mechanisms in health and disease with the focus on innate immune memory. He applies a systems biology approach to the transition of mouse embryonic stem cells from serum-to-2i to uncover gene regulatory networks.

**The power of epigenomics to uncover (dys)regulated pathways**

*Abstract not available*

**Amos Tanay**, Department of Computer Science and Applied Mathematics at the **Weizmann Institute**, Rehovot, Israel

The Tanay lab is developing probabilistic algorithms for modeling epigenetic and chromosomal organization and for the inference of such models from experimental data. The group is combining the derived models with genomic sequences, constructing sequence-based predictions for epigenomic features while taking into account the multiple correlations among different genomic activity patterns. In particular, the group is collaborating with network members to study chromosomal organization in flies and DNA methylation in normal cells and cancer. As an interdisciplinary team that combines within the same group theoretical and computational work with the development of new experimental approaches to epigenetics, the Tanay lab also coordinates the construction of a computational toolbox that aims to promote the integration of the computational biology and epigenetics communities.

**Single cell epigenomics and epigenetic memory in development and cancer**

We will discuss tools for analysing the epigenomic landscapes of heterogeneous cell populations at single cell resolution. Using single cell Hi-C we study the variation in chromosomal conformation as nuclei proceed through the cell cycle while establishing flexible regulatory programs. Using targeted single cell bisulfite sequencing we study dynamics in DNA methylation during early development in tumorigenesis. We combine these data with extensive characterization of transcriptional landscapes to evaluate the links between epigenomic build up and cellular differentiation, with a particular emphasis on process that involve simultaneous change in DNA methylation and transcriptional reprogramming.
Marian Martínez-Balbás, Research Scientist at Barcelona Molecular Biology Institute (IBMB-CSIC), Barcelona, Spain

(Read bio in page 8)

Marian Martínez-Balbás. Research Scientist and Group Leader of Molecular Signaling and Chromatin group at the Barcelona Molecular Biology Institute (IBMB)-CSIC, Barcelona, Spain. Graduated in pharmacology from the Santiago de Compostela University, Marian Martínez-Balbás obtained her PhD at the Polytechnic University of Barcelona studying DNA and chromatin structure. She was a postdoctoral Fellow at the NIH (USA) where she focused on chromatin remodeling and dynamics at Dr C Wu's laboratory. Subsequently, she moved to the J Gurdon Institute (group of Dr T Kouzarides) in Cambridge (UK), to study the contribution of histone modifications to cell cycle progression and cell proliferation. In year 2000 she got a permanent CSIC position at the IBMB, where she created the “Molecular signaling and chromatin” laboratory. Presently, her research is focused on understanding the role of several chromatin regulators controlling the transcriptional program during development. Her group analyzes different aspects of chromatin dynamics during neurogenesis, using in vitro and in vivo models.

Enhancers integrate TGFβ signaling, transcription factors and epigenetic regulators to induce neuronal cell fate

During development, dynamic cues, transcription factors and histone modifying enzymes regulate the gene expression programs by modulating the activity of neural-specific enhancers. How transient developmental signals coordinate transcription factor recruitment to enhancers and to which extent chromatin modifiers contribute to enhancer activity impacting the tridimensional chromatin structure is not totally understood. We take advantage of neural stem cells as a model to unravel the mechanisms underlying neural enhancer activation in response to the TGFβ signaling. Our genome-wide experiments show that the proneural factor ASCL1 assists SMAD3 in the binding to a subset of enhancers.

Once located at the enhancers, SMAD3 recruits the histone demethylase JMJD3 and the remodeling factor CHD8, creating the appropriate chromatin landscape to allow enhancer transcription and posterior gene activation. To analyze the phenotypical traits owed to enhancer regions, we use CRISPR-Cas9 technology to demonstrate that the TGFβ-induced Neurog2 gene poised enhancer is essential for proper neuronal polarization. Our results establish an essential hierarchical order of factor recruitment at enhancers within the three-dimensional chromatin structure in response to TGFβ developmental signal.

Short talk from selected abstracts: Pernette Verschure, Associate Professor at University of Amsterdam, Amsterdam, Netherlands

Authors: William Beckman, Ilona M. Vuist, Mannus Kempe, Lisette C. M. Anink-Groenen, Diewertje G. E. Piebes and Pernette J. Verschure

Dynamic epigenetic regulation: Single cells can make the difference

Dynamic epigenetic changes can create tumour heterogeneity and are expected to influence tumour evolution and response to treatment. We study how dynamic epigenetic interactions emerge in single cells and how they contribute to biological functionality. We focus on the role of epigenetic cell state switching in estrogen receptor positive (ER+) breast cancer progression. Methods: We developed tools to obtain mechanistic insight in dynamic aspects of epigenetic regulation in single cells. Using computational stochastic simulations we studied the generation of posttranslational histone modification patterns upon varying epigenetic regulatory conditions. We developed engineered mammalian cells and tools to modulate the epigenetic state of (trans)genes to measure cause-effect relationships between the presence of epigenetic regulatory proteins, chromatin folding and transcriptional activity. We used MS2 transcript tagging and single molecule RNA FISH as systematic, quantitative measurements of transcription dynamics as function of the epigenetic chromatin state in single cells. Results: We show that chromatin connectivity introduces epigenetic state switching in single genes1,2. We identified that the precise relationship between transcript number and cell volume sets transcriptional stochasticity and that mRNA statistics is gene location dependent3. ER+ breast cancer cells are strikingly heterogeneous and upon endocrine treatment defined cancer subpopulations drive resistance development. We noted that amplification of the Aromatase gene CYP19A1 is a specific early mechanism of resistance development upon aromatase inhibitor treatment4. Conclusions: Our data illustrate that the use of epigenetically engineered mammalian cells and dedicated experimental and computational tools to modulate the epigenetic composition, are extremely powerful to interpret epigenetics-related dynamics and heterogeneity1,2,3. We put forward that cell-to-cell variability in epigenetic regulation allows particular cell types to escape from treatment taking transcriptional bursting into account4. Our single cell approach, pinpointing the role of epigenetic plasticity in pathological conditions, opens an unexplored exciting field of research with great potential for individualized medicine.
Session 6

Sonia Forcales, Research Associate at Program of Predictive and Personalized Medicine of Cancer (PMPPPC), Institute of Health Research Germans Trias i Pujol (IGTP), Barcelona, Spain

Sonia Forcales obtained her PhD at the University of Barcelona studying a mechanism of IFNγ-induced expression in macrophages. She obtained a Marie Curie fellowship to pursue a post-doctoral study on p38 kinase-dependent transcriptional control of myogenic differentiation at Fondazione Andrea Cesalpino, Rome. Her work showed the recruitment of p38 kinase to gene promoters and that p38 activity is required to remodel chromatin by SWI/SNF complex at myogenic regulatory regions (Simone C at al., Nat Genet. 2004 Jul;36(7):738-43). During her second postdoctoral time in the laboratory of Dr. Pier Lorenzo Puri at the Sanford Burnham Institute (2006-2010) in La Jolla, she continued to work on the mechanisms targeting SWI/SNF complex to myogenic loci (Forcales et al., EMBO J. 2012 Jan 18;31(2):301-16) and on embryonic stem cells a source for myogenic progenitors. In 2010 she joined the Institute of Predictive and Personalized Medicine of Cancer in Badalona, as a research associate in the group of Manuel Peruchó, and studies the contribution of chromatin, with special focus in SWI/SNF alterations, in colorectal cancer disease and chemoresistance. From March 2017 she is also associate professor at the Pathology and Experimental Therapeutics department from the Faculty of Medicine at the University of Barcelona.

Chair of the SESSION 6

Kyle Miller, Associate Professor at Department of Molecular Biosciences, University of Texas at Austin, Austin, USA

9/2017 - 2014 - Associate Professor, Dept of Molecular Biosciences, U. of Texas at Austin. Austin, Texas, US

Member, Livestrong Cancer Institute, Dell Medical School, U. of Texas at Austin.

Member, Dan L Duncan Cancer Center, Baylor College of Medicine

2004 – 2011 Postdoc, UCSF (David Toczyski) and Cambridge University (Steve Jackson)

2000 – 2004 PhD, UCL (Julia Cooper)

PUBLICATIONS (out of 40)


Bromodomain proteins: Epigenetic readers in the DNA damage response and cancer

Chromatin plays a substantial role in the regulation of DNA damage response (DDR) pathways, which represent specialized genome surveillance mechanisms that detect, signal and repair DNA lesions. Loss of functional DNA damage responses can greatly impair genome and epigenome integrity, which contribute to diseases including cancer. Histone acetylation represents an important epigenetic mark involved in the DDR and cancer. This histone modification regulates chromatin structure and function, including by serving as a molecular signal for reader proteins containing acetyl-lysine binding domains, including the bromodomain (BD). Our group has shown that around one-third of the 42 human BD proteins are localized to DNA damage sites, which highlights the involvement of this class of chromatin proteins in the DDR. We have recently identified a DDR pathway consisting of KDM5A-ZMYND8-NuRD chromatin remodeling complex that coordinates transcription and DNA repair activities, including homologous recombination, within chromatin. Members of this pathway have been shown to be highly dysregulated in cancer and inhibitors targeting this pathway have been identified. We will discuss our ongoing studies that are aimed at deciphering the molecular mechanisms that regulate this pathway, as well as our attempts to understand how mutations and inhibition of these pathways contribute to cancer and its treatments.
**Tousled like kinase activity is required for histone deposition, DNA replication, heterochromatin maintenance and (epi)genome stability**

The Tousled like kinases 1 and 2 (TLK1 and TLK2) have been implicated in DNA repair and chromsome stability but their cellular functions remain poorly defined. The histone chaperone ASF1 and DNA damage signaling protein RAD9 are proposed targets of TLK activity but the extent to which they rely on TLK1/2 or TLK2 has not been clearly established. Our objective was to characterize the relative functions of TLK1 and TLK2, identify their cellular targets, mode of regulation and consequences of their deficiency during development and in cancer.

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**Functional analysis in vivo of the mouse tyrosinase expression domain using CRISPR tools**

Tyrosinase encodes the key enzyme in melanin synthesis. In its absence, or when the tyrosinase gene is mutated, a genetic condition is established known as oclocutaneous albinism type 1 (OCA1), associated to severe visual deficits and general hypopigmentation. The tyrosinase gene expression domain has been classically investigated using genetically modified mice, easily rescuing the albino phenotype of recipient mouse embryos. Those approaches involved the use of standard and artificial chromosome-type transgenes. Through the generation and analysis of numerous YAC tyrosinase transgenic mice, several key regulatory elements had been identified and their role investigated in ectopic genomic environments, as a second-best solution to address these questions. For many years, the real experiment, namely, exploring these regulatory elements at the endogenous mouse tyrosinase locus, was prevented by the existence of many LINE1-related repeated sequences in the area, thus interfering with any attempt using standard homologous recombination techniques. The situation entirely changed with the discovery of the gene-editing nucleases, particularly the CRISPR-Cas9 tools. These nucleases only require a guide RNA with 20 bp homology to target sequences and, through bioinformatics analyses, two of these unique short sequences could always we found surrounding the element of interest to be deleted. Using the CRISPR system we have been able to tackle in vivo, in gene-edited mice, each and every relevant DNA regulatory element previously identified within the mouse tyrosinase locus. The results obtained will be presented in this short talk.

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**Cancer Epigenetics: From Knowledge to Applications**

For the last twenty-five years an increasing amount of evidence has shown the relevance of epigenetics in cell biology and tissue physiology, being DNA methylation aberrations in cancer the flagship for the recognition of its disturbance in human diseases. From the candidate gene approaches, new powerful technologies such as comprehensive DNA methylation microarrays and whole genome bisulfite sequencing has recently emerged that have reinforced the notion of epigenetic disruption in the crossroad of many sickness. From the post-bone cases of MGMT and GSTP1 hypermethylation in the prediction of alkylating drug response and prostate cancer detection, respectively, to the personalized treatment of leukemia with small molecules targeted to fusion proteins involving histone modifiers, the field has walked a long path. The current talk will focus in the epigenetic profiling, basically at the level of DNA methylation and histone modifications, that is starting to provide clinical value in the diagnosis, prognosis and prediction of response to drug therapies. For cancer, we have already a wide view of the undergoing DNA methylation events that expand beyond classical promoter CpG islands of tumor suppressor genes and we have a growing list of mutated chromatin remodeler genes that contributes to the tumorigenesis process. It is time to apply this knowledge in practical clinical situations like the diagnosis of cancers of unknown primary, the screening of malignancies in high-risk populations or a biomarker selection of the patients that should receive treatment with anticancer drugs. Beyond our comfort zone, we should be aware that chemical modifications not only affect the DNA molecule, but also RNA. The epigenetics of RNA or the analysis of the epitranscriptome represents another relevant step to understand the complex relationship between genotypes and phenotypes in human tumors.
1. *Giacomo Grillo, Laure Ferry, Ivana Ivkovic, Guillaume Velasco and Claire Francastel.* When studying the etiology of a rare disease sheds new light in the field of DNA methylation.

2. *Ilias Tzelepis, Marco Martino, Noriyuki Sumida, Anna L. Ronnegren, Honglei Zhao, Marta Imreh and Anita Göndör.* TGFbeta resets the phase of circadian transcription by rewiring 3D genome organization.

3. *Jose A. Guerrero-Martínez, María E. Soler-Oliva and Jose C. Reyes.* Analysis of the relationship between coexpression domains and chromatin 3D organization.


7. *S. Petruk, J. Cai, S.A. Mariani, Marco De Dominici, L. Iacovitti, B. Calabretta and A. Mazo.* The roles of nascent chromatin in differentiation and proliferation of normal stem/progenitor cells and cancer cells.


10. Alba Maques-Diaz, Gary J Spencer, James T Lynch, Sudhakar Sahoo and Tim CP Somervaille. Pharmacologic displacement of LSD1 from GFI1 activates primed enhancers to induce differentiation in acute myeloid leukemia.


* indicates the poster has been selected for a speed presentation
stromal protection and inhibits expansion of residual leukemia-initiating cells in FLT3-ITD+ AML with concurrent epigenetic mutations.


18. Chang Ho Lee, Seung Ryul Han, Joo Han Lee, Ji Hyun Kim, Tae Hyung Kim, Yun-Hee Kim, Jin Sook Jeong, and In-Hoo Kim and Seong-Wook Lee. Gene replacement based on RNA reprogramming as an effective approach to cancer theranostics.


23. Elisabet Figuerola, Guillem Pascual-Pasto, Mónica Vila, Ángel M Carcaboso, Sara Sánchez-Molina and Jaume Mora. Usage of MLN4924 as an approach to target RING1B in Ewing sarcoma tumorigenesis.


27. John-Mario Roussis, Grigoris Tsakankis, Elena Karkoulia and John Strouboulis. Functional characterization of the GATA/FOG-1 regulatory axis in erythroid/megakaryopoiesis and in hematological disease.


33. Laura Marruecos, Sara Arce, Anna Bigas and Lluís Espinosa. Histone PTMs are restricted to Intestinal Stem Cells and regulate iKBα chromatin association.

35. Michaël Broux, Charles de Bock, Sofie Demeyer, Marlies Van den Bempt, Roel Van de Wype, Nicole Mentens, Carmen Vicente and Jan Cools. **PRC2 inactivation cooperates with activating JAK3 mutations in T-ALL development.**

36. Nefeli Dellepiane, Shipra Bhatia, Veronique Vitarti and Wendy Bickmore. **Identifying functional non-coding variation and its role in gene regulation in a region associated with Central Corneal Thickness.**

37. Nikolaos Trasandis, Valentina Caputo, Katerina Goudevenou, Kyriaki Petevi, Xiaolin Xiao, Kanagaraju Ponnusamy, Deena Iskander, David Pitcher, Antonia Rotolo, Holger Auner, Aristeidis Chaidos and Anastasios Kardamakis. **Myeloma cell addition to the transcription factor TCF11.**

38. Oriol Llorà-Batlle and Alfred Cortés. **Determinants of heterochromatin nucleation in Plasmodium falciparum using the pfap2-g locus as a model.**

39. Ourania Chatzidoukaki, Kalliopi Stratigi, Georgia Chatzinikolaou, and George A. Garinis. **Dissecting the functional link between DNA damage signaling and innate immune responses in macrophages.**

40. Raquel Casquero, Jeanine Diesch, Michael Maher, Sonia V. Forcales, Eva Martinez-Balbrea, Lorenzo Pasquali, Katharina Gótz, Johannes Zuber, Blanca Xicoy on behalf of CETLAM, Lurdes Zamora, and Marcus Buschbeck. **RESPONSE project: predicting biomarkers in myelodysplastic syndrome patients treated with azacitidine.**

41. Raquel Fuego, Simona Iacobucci, Sergio Lois, Conchi Estarás, Sara de la Cruz-Molina, Álvaro Rada-Iglesias, Xavier de la Cruz and Marian Martínez-Balbás. **TGFbeta pathway triggers neuronal differentiation transcriptional program by coordinating local events in the context of enhancer-promoter interaction.**

42. Raquel Ordoñez, Marta Kulis, Nuria Russiñol, Renée Beekman, Cem Meydan, Núria Verdaguer-Dot, Arantxa Carrasco, Teresa Ezponda, Joost H.A. Martens, Hendrik G. Stunnenberg, Bruno Paiva, Jesús San Miguel, Ari Melnick, Elias Campo, Xavier Agirre, Felipe Prosper and José I. Martín-Subero. **Widespread activation of the regulatory chromatin landscape of multiple myeloma.**

43. Roni H. G. Wright, Antonios Lioutas, François Le Dily, Jofre Font-Mateu, Baldo Oliva and Miguel Beat. **Investigating the role of NUDIXS in Cancer Progression.**

44. Roser Zaurín, A. Silvina Nacht, Valentina Scabia, Roberto Ferrari, Javier Quilez, Cathrin Brisken, Miguel Beato and Guillermo P. Vicen. **C/EBPα crosstalks with progesterone receptor to control hormone-dependent cell growth in breast cancer cells.**

45. Melanija Posavec Marjanovic, Sarah Hurtado-Bages, Oscar Yanes, Raffaele Teperino, Andrew Pospisilik and Marcus Buschbeck. **MafH2A1.1 regulates mitochondrial respiration by limiting nuclear NAD + consumption.**

46. Teresa Morales-Ruiz, María Victoria García-Ortiz, Iván Devesa-Guerra, Laura Rayas-Ruiz, Juan R. Tejedor, Gustavo F. Bayón, Marta I. Sierra, Mario F. Fraga, Rafael Ariza and Teresa Roldán-Arjona. **DNA methylation reprogramming of human cancer cells by expression of a 5-methylcytosine DNA glycosylase.**

47. T. Savvidis, T. Zelenka, P. Tzepos, G. Panagopoulos and C. Spilianakis. **SATB1 forms a base for gene expression regulation of CD4+ T cells.**

48. François Le Dily, Enrique Vidal, Yasmina Cuartero, Javier Quilez, Silvina Nacht, Guillermo Vicent, Gaetano Verde, Marc A. Marti-Renom and Miguel Beato. **Hormone Controlled Regions mediate steroid receptor dependent intra-TAD folding and global genome organization in breast cancer cells.**

49. Anna Labejso, Lidia Gackowska, Justyna Kalisz, Martyna Sysakiewicz, Jarosław Czyz, Andrzej Koltan, Jan Styczynski and Daniel Gackowski. **Comparison of expression of enzymatic proteins involved in active demethylation of DNA in patients with acute myeloid and lymphoblastic leukemia.**

50. Priyanka Shama, Antonios Lioutas, Javier Quilez, Narcís Fernandez Fuentes, Roni H.G Wright and Miguel Beato. **Citrullination of RNA polymerase II CTD regulates transcriptional pause release.**

51. Iwona Belczacka, Agnieszka Latosinska, Justyna Siwy, Jochen Metzger, Axel S. Merseburger, Harald Mischak, Antonia Vlahou, Maria Frantzi and Vera Jankowski. **Urinary CE-MS peptide marker pattern for detection of solid tumors.**
PRACTICAL INFORMATION

Venue: CosmoCaixa Barcelona

CosmoCaixa Barcelona
C/ Isaac Newton, 26
08022 Barcelona, Spain

Conferences Meeting
Auditori (-2 floor)

Free wifi
1. Select wifi_cosmocaixa_bcn
2. Open an Internet Browser
3. The page of cosmocaixa will appear. Follow the instructions

Contact persons during the event

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www.bdebate.org | www.biocat.cat
SUGGESTED READING

- The Hierarchy of Transcriptional Activation: From Enhancer to Promoter
  Vernimmen D, Bickmore WA.
  Trends Genet. 2015

- The interplay of epigenetic marks during stem cell differentiation and development
  Atlasi Y, Stunnenberg HG.
  PMID: 28804139

- Variations on a nucleosome theme: The structural basis of centromere function
  Moreno-Moreno O, Torras-Llort M, Azorín F.
  PMID: 28220502

- Chromatin organization and dynamics in double-strand break repair
  Seeger A, Gasser SM.
  PMID: 27810555

- Precision medicine based on epigenomics: the paradigm of carcinoma of unknown primary
  Moran S, Martínez-Cardús A, Boussios S, Esteller M.
  PMID: 28675165

- Variants of core histones and their roles in cell fate decisions, development and cancer
  Buschbeck M, Hake SB.
  PMID: 28144029
OUTCOMES

B-Debateca

On the website of B-Debate, you will find all the information related to the celebration of the meeting that includes reports, conclusions, scientific documents, interviews with the experts, speaker’s CVs, videos, images, press documentation and other related materials. We invite you to visit the section B-Debateca on www.bdebate.org

Contents of the meeting: “Epigenetic Mechanisms in Health and Disease. Barcelona Conference on Epigenetics and Cancer”

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**B-Debate** International Center for Scientific Debate Barcelona is a joint initiative of **Biocat** and "la Caixa" Foundation. It drives first-rate international scientific debates, to foster dialogue, collaboration and open exchange of knowledge with prestigious national and international experts, to approach complex challenges of high social interest in life sciences. B-Debate sees debate as a powerful, effective way to generate knowledge and strives to help position Barcelona as a benchmark in generating knowledge and Catalonia as a country of scientific excellence.

The debates are top-notch international scientific meetings featuring a selection of experts of renowned international prestige and scientists that work in Barcelona and Catalonia, moderated by scientific leaders. Since 2009 B-Debate has invited about 1750 recognized speakers and over 13,000 attendees. B-Debate seeks out answers to the challenges and needs of society in the field of life sciences, taking into account the complex, ever-changing conditions of this global world. The debates foster the integration of different disciplines of science and deal with such diverse topics as ageing, new therapeutic approaches to various diseases, innovative technology to improve knowledge of the human genome, food resources, new tools to integrate knowledge management, clinical genomics, neurosciences, climate change, and new energy sources, among others. The knowledge and results obtained through these events is spread throughout both the scientific community and general society through the various **B-Debate** channels and instruments.

More info: [www.bdebate.org](http://www.bdebate.org)

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**Ibmb**

The **Molecular Biology Institute of Barcelona** (IBMB) is one of the leading centers of the Spanish Research Council (CSIC) in the areas of Biology and Biomedicine and located within the highly active Barcelona Science Park (PCB). Distinguishing us from other institutes is the priority we give to interdisciplinary research, and our 28 groups are organized into four different research programs covering structural biology, genomic regulation, cell biology and development. Researchers of all four departments address questions of chromatin function in gene regulation, development and disease.

More info: [www.ibmb.csic.es](http://www.ibmb.csic.es)

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**Josep Carreras**

The mission of the **Josep Carreras Leukaemia Research Institute (JIC)** is to carry out research into the basic, epidemiological, preventive, clinical and translational aspects of leukemia and other hematologic malignancies.

The institute is based on three campuses in the Barcelona area, in each case next to a teaching hospital in the public health system. It is a member of the CERCA group, supported and supervised by the Autonomous Catalan Government.

More info: [www.carrerasresearch.org](http://www.carrerasresearch.org)
CO-ORGANIZERS

The Centre for Genomic Regulation (CRG) is an international biomedical research institute of excellence, founded in December 2000 whose mission is to discover and advance knowledge for the benefit of society, public health and economic prosperity. The CRG believes that the medicine of the future depends on the groundbreaking science of today. This requires an interdisciplinary scientific team focused on understanding the complexity of life from the genome to the cell to a whole organism and its interaction with the environment, offering an integrated view of genetic diseases. Research at the CRG falls into four main areas: gene regulation, stem cells and cancer; cell and developmental biology; bioinformatics and genomics; and systems biology.

More info: www.crg.eu

Researchers at the Institute for Research in Biomedicine (IRB Barcelona) work at the interface between molecular and cell biology, computational and structural biology, and chemistry to tackle questions related to human health and disease, including cancer and epigenetics. IRB Barcelona is one of 13 Spanish institutes to be recognized as a Severo Ochoa Center of Excellence; five of its researchers are recipients of distinguished ERC advanced and starting grants.

More info: www.irbbarcelona.org

The Cancer Epigenetics and Biology Programme (PEBC) is the latest research programme incorporated at the Bellvitge Biomedical Research Institute (IDIBELL) and represents the largest epigenetics department in southern Europe, with over 120 scientists, and the latest investment of the national government for cutting edge biomedical research.

More info: www.pebc.cat

The Institute for Health Science Research Germans Trias i Pujol (IGTP) is a public research centre in the Autonomous region of Catalonia in Northern Spain dedicated to increasing scientific knowledge and transferring it to improve the care and lives of patients.

The institute is attached to one of the large teaching hospitals in the Barcelona area; the Germans Trias University Hospital (HUGTP), and is located on the biomedical campus that surrounds it, Campus Can Ruti. It is a CERCA centre; a member of the biocluster supported and supervised by the Autonomous Catalanian Government. It is also accredited as a Centre of Excellence by the Instituto Carlos III (Spanish Government) and in this capacity acts as an umbrella organization for scientific research on the campus, where it works closely with the other centres located there.
The **Program for Predictive and Personalized Medicine of Cancer** is a transversal program of the IGTP directed by Manuel Peruchó. The program includes groups working on research all along the spectrum from basic to translational to improve the methods of diagnosis, prognosis, treatment and prevention of cancer and to improve the lives of patients.

More info: [www.germanstias.org](http://www.germanstias.org)

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**COLLABORATORS**

**Societat Catalana de BIOLOGIA**

The **Catalan Society of Biology**, funded in 1912, is one of the most active scientific societies in our country. Currently is composed by 1500 members, of which 80% are doing active research in our universities or research centers. The scientific sessions of the SCB have a long tradition and are meeting points that allow researchers to make networks and collaborations that are very effective. The SCB organizes activities around its 21 thematic sections in the most current aspects of basic or applied Biology, and 4 territorial sections. It also brings together a large number of high school teachers and other people close to the BIO area. The SCB is the point of reference for those interested in Biology in Catalonia.

More info: [http://scb.iec.cat/](http://scb.iec.cat/)

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**The Company of Biologists** is a not-for-profit publishing organisation dedicated to supporting and inspiring the biological community. We are run by distinguished practicing scientists. We exist to profit science, not shareholders. We inspire new thinking and support the worldwide community of biologists. We do this by publishing leading peer-reviewed journals, facilitating scientific meetings and communities, providing travel grants for young researchers and by supporting societies and gatherings.

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More info: www.mdpi.com/journal/epigenomes

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EMBO is an organization of more than 1700 leading researchers that promotes excellence in the life sciences. The major goals of the organization are to support talented researchers at all stages of their careers, stimulate the exchange of scientific information, and help build a European research environment where scientists can achieve their best work.

EMBO helps young scientists to advance their research, promote their international reputations and ensure their mobility. Courses, workshops, conferences and EMBO Press publications disseminate the latest research and offer training in techniques to maintain high standards of excellence in research practice. EMBO helps to shape science policy by seeking input and feedback from our community and by following closely the trends in science in Europe.

More info: http://www.embo.org/

CliniSciences commercialises reagents (antibodies, recombinants, ELISA kits, RNAi, cDNA clones, probes, PCR/qPCR reagents...) to diagnostic and research labs. As very dynamic company, we do our best to be close to our customers’ needs in terms of high quality reagents that we propose and in terms of service that we provide (search for a particular antibody, technical support, delivery time, etc.).

More info: www.clinisciences.com

BioNova is a well-positioned and expanding Spanish company representing leading companies, producers of reagents, kits and instruments for research in life sciences and diagnostics. The company provides Spanish researchers and clinicians with
high quality products that allow them to perform their work more easily and quickly. With this aim, bioNova distributes not only well-known and well-positioned companies in the biotechnology market, but also innovative and newly created companies.

As an epigenetics company, **Epigentek Group Inc.** is the leading developer and provider of innovative technologies and products for epigenetic-related research. Founded in 2005, the company has since developed a comprehensive portfolio of proprietary products to provide complete and systematic solutions for epigenetics-related research and drug discovery. Epigentek products are used all around the world by esteemed academia, leading pharmaceuticals, and cutting-edge biotechnology companies. These unique products are specifically designed to make assays much simpler, faster, more convenient, and highly more efficient than currently used methods.

More info: [www.bionova.es](http://www.bionova.es), [www.epigentek.com](http://www.epigentek.com)

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**Diagenode** is a leading global provider of complete solutions for epigenetics research, biological sample preparation, and diagnostics assays based in Liege, Belgium and NJ, USA. The company has developed a comprehensive approach to gain new insights into epigenetics studies. The company offers innovative Bioruptor® shearing and IP-Star® automation instruments, reagent kits, and high quality antibodies to streamline DNA methylation, ChIP, and ChIP-seq workflows. The company's latest innovations include a unique, full automation system, the industry's most validated antibodies, the Megaruptor shearing system for long fragment generation in sequencing, and epigenetics assay services. At Diagenode, our goal is to build products with pride and the highest level of performance. Our team of epigenetics experts develop products by getting feedback from our customers as well as the scientific and medical communities around us. We strive to develop superior and easy-to-use products to bring epigenetics research and diagnostics to new frontiers.


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**Promega** is a global leader in providing innovative solutions and technical support to life scientists in academic, industrial and government settings. Promega products are used by life scientists who are asking fundamental questions about biological processes as well as by scientists who are applying scientific knowledge to diagnose and treat diseases, discover new therapeutics, and use genetics and DNA testing for human identification. Originally, founded in 1978 in Madison, Wisconsin, USA, Promega has branches in 16 countries and more than 50 global distributors serving 100 countries.

More info: [www.promega.es](http://www.promega.es)

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**Roche** is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives. The combined strengths of pharmaceuticals and diagnostics under one roof have made Roche the leader in personalised healthcare – a strategy that aims to fit the right treatment to each patient in the best way possible. Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Twenty-nine medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and cancer medicines. The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2016 employed more than 94,000 people worldwide.

More info: [www.roche.com](http://www.roche.com)
Active Motif is the industry leader in developing and delivering innovative tools to enable epigenetics and gene regulation research. We are committed to providing the highest quality products along with superior service & support to the life science, clinical and pharmaceutical/drug discovery communities.

Active Motif has developed a variety of tools and services to overcome many of current challenges in the field of Epigenetics and Transcription Regulation. Apart of our rigorously validated kits, antibodies and recombinant proteins, we are offering a series of Epigenetic Research Services to better study Chromatin based interactions, Histone Modifications and DNA methylation. A list of high impact factor papers from our customers supports our capabilities in every research area.

At Celgene, we seek to deliver truly innovative and life-changing drugs for our patients. Our vision as a company is to build a major global biopharmaceutical corporation while focusing on the discovery, the development, and the commercialization of products for the treatment of cancer and other severe, immune, inflammatory conditions.

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There are more than 300 clinical trials at major medical centers using compounds from Celgene. Investigational compounds are being studied for patients with incurable hematological and solid tumor cancers, including multiple myeloma, myelodysplastic syndromes, chronic lymphocytic leukemia (CLL), non-Hodgkin's lymphoma (NHL), triple-negative breast cancer and pancreatic cancer. We also focus our investigation in immune and inflammatory disease as psoriasis and psoriatic arthritis. As committed as we are to clinical accomplishment, we are equally committed to patient support, which is a guiding principle at Celgene. We believe all who can benefit from our discoveries should have the opportunity to do so. Celgene puts patients first with industry-leading programs that provide information, support and access to our innovative therapies.

More info: [www.celgene.es/](http://www.celgene.es/)
PROGRAM OF THE 2ND PMPPC CONFERENCE

All the participants to the B-Debate are granted access to the second PMPPC Conference, which will be held in CosmoCaixa on Thursday 26th after the closing of the BCEC.

Epigenetic Architecture in Health and Disease

15:00  **SESSION 1:**
Welcome: Miguel A. Peinado, PMPPC-I-GTP, Barcelona
Victor Corces, Emory University, Atlanta
David Corujo*, PMPPC-IJC, Barcelona
Gabrijela Dumbovic*, PMPPC-I-GTP, Barcelona
Jose-Luis Gomez-Skarmeta, Andalusian Centre for Developmental Biology (CABD), Seville

16:35  Coffee break

17:00  **SESSION 2:**
Allan Balmain, University of California, San Francisco
Izaskun Mallona*, PMPPC-I-GTP, Barcelona
Carlo M. Croce, Ohio State University, Columbus
Closing remarks and adjourn: Manuel Peruchó, PMPPC-I-GTP, Barcelona

* indicates it is a short talk