EMBL Australia

European Molecular Biology Laboratory Australia

EMBL Australia Showcase

Tuesday 5th July 2016

EMBL Australia acknowledges the support of The John Curtin School of Medical Research and Australian National University in sponsoring the 2016 EMBL Australia Showcase.

Australian National University

THE JOHN CURTIN SCHOOL OF MEDICAL RESEARCH

EMBL Australia

European Molecular Biology Laboratory Australia

What is EMBL Australia?

Building international links

Empowering young researchers

Embedding bioinformatics in Australian life science

Promoting systems biology

EMBL Australia is a life science network that supports research projects and provides infrastructure and training.

It was created in 2008 to maximise the benefits of Australia's associate membership of the European Molecular Biology Laboratory (EMBL).

EMBL Australia is jointly run by Universities Australia, the Association of Australian Medical Research Institutes, CSIRO and Bioplatforms Australia.

"EMBL Australia has created a unique advantage for emerging Australian scientific talent with an enriched and sustainable international collaborative framework which positions Australian discoveries in the spotlight and offers our scientists access to an extraordinarily valuable professional knowledge network."

Professor Brandon Wainwright,
Chair, EMBL Australia Council

About EMBL—Europe's life science flagship

The European Molecular Biology Laboratory was founded in 1974, when the field was strongly dominated by the United States.

Its 20 member states realised that together they could compete and achieve more than each could by themselves.

With nodes in the UK (Hinxton, near Cambridge), France (Grenoble), Germany (Heidelberg and Hamburg) and Italy (Monterotondo, near Rome), EMBL now comprises about 85 independent research groups and more than 1,400 people.

Among its many features are:

- nine years of funding security for research leaders (subject to performance), after which they move on
- training for young researchers—over 3,000 per year
- highly-sought post-doctoral positions
- research networks across Europe and around the world
- a culture that focuses on young scientists and builds strong research alliances.

In 2008, Australia became EMBL's first Associate Member State.

Tuesday 5th July 2016

Program

9.10am	**Introduction, Thomas Preiss**
9.15am	**Welcome Address, Simon Foote, Director, John Curtin School of Medical Research**
9.20am	**Matthias Hentze –** *A new view on RNA-binding proteins and RNA*
9.50am	**Ville-Petteri Makinen –** *Integrative genomics and network biology of common chronic diseases*
10.20am	**Max Cryle –** *Understanding Glycopeptide Antibiotic biosynthesis as a pathway to new antimicrobial agents*
10.50am	**Break**
11.15am	**Mate Biro –** *The actin cortex at the interface of cancer and immunity: T cell migration and cytotoxic interactions*
11.45am	**Mirana Ramialison –** *From regulatory elements to cardiac enhanceropathies*
12.15pm	**Presentation by Matthias Hentze to new EMBL Australia Collaborating Group Leader, Mirana Ramialison**
12.25pm	**Lunch**
1.10pm	**Michael Parker –** *Cholesterol-dependent cytolysins: from water-soluble state to membrane pore*
1.40pm	**Edwina McGlinn –** *Regulation of Hox cluster dynamics during development*
2.10pm	**Andrew Lonie –** *Building the EMBL Australia Bioinformatics Resource*
2.40pm	**Break**
2.55pm	**David Lynn –** *The impact of the neonatal microbiome on specific and non-specific vaccine responses*
3.25pm	**Chen Davidovich –** *Mechanism of RNA binding by the Polycomb repressive complex 2 (PRC2)*
3.55pm	**Thomas Preiss –** *Dynamics of ribosome scanning and recycling revealed by translation complex profiling*
4.25pm	**Finish**

Speaker Bios

Ville-Petteri Mäkinen

EMBL Australia Group Leader, South Australia Health and Medical Research Institute

Ville-Petteri Mäkinen holds an EMBL Australia Group Leader position within the Heart Health Theme in the South Australian Health and Medical Research Institute, and affiliate professorship in the School of Molecular and Biomedical Science at the University of Adelaide. He is also a part-time Senior Research Fellow in Computational Medicine in the Institute of Health Sciences in Oulu, Finland. Mäkinen's research focuses on the molecular features of metabolic dysfunction in human populations and the genetic causes that increase the risk of diabetes, atherosclerosis and dementia in vulnerable subgroups. He has published several key findings in the field, particularly related to type 1 diabetes and metabolic phenotyping of diabetic nephropathy, and he is determined to develop network and systems biology approaches to elucidate the pathogenic processes that predispose young individuals to chronic morbidity later in life. Moreover, he is actively developing novel study designs to improve the match between the findings in animal models and the corresponding phenomena in human cohorts.

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Integrative genomics and network biology of common chronic diseases"

Aging and sedentary life style drive the current worlwide epidemics of obesity, diabetes, heart disease and dementia. The complex etiology and the tendency to co-occur in vulnerable individuals make it difficult to investigate the specific molecular pathways or environmental risk factors of these progressive chronic conditions in detail. Omics technologies and network biology have opened new ways of collecting vast amount of molecular information and there is great potential in translating the data into preventative and curative approaches in public health and clinical practice. However, the complex and overlapping nature of these data does not fit well with the traditional reductionist approaches that still dominate the generation of wet lab hypothesis and testing in animal models. In this talk, I will provide examples of our work in defining human phenotypes that convey a high risk of disease, how to integrate cross-species multi-omics datasets, and I will also discuss new ways to create coherent research projects that span the gap between epidemiology and experimental validation in vivo in the era of big data.

Edwina McGlinn

EMBL Australia Group Leader, Australian Regenerative Medicine Institute, Monash University

Edwina McGlinn is an EMBL- Australia Partner Network Lab Group Leader, based at the Australian Regenerative Medicine Institute, Monash University. Edwina's research focuses on deciphering genetic networks during early embryonic development, with particular emphasis on microRNA control of Hox gene networks. Edwina completed a PhD in developmental and molecular biology at the Institute for Molecular Bioscience UQ, identifying novel downstream effectors of Sonic hedgehog in the developing mouse limb. She then became a research fellow in the laboratory of Professor Clifford Tabin, Harvard Medical School USA, dissecting genetic networks involved in patterning the vertebrate limb and axial skeleton.

Regulation of Hox cluster dynamics during development"

Hox gene regulatory networks are critical in the development of almost every mammalian organ system, providing the positional information necessary for region appropriate identity and function. This importance extends to regulatory mechanisms that contribute to refining or stabilising Hox expression. The identification of numerous microRNAs that are not only embedded within Hox clusters, but also target numerous Hox genes, suggests an important role for these regulatory molecules in shaping Hox protein output. Here, we use an extensive allelic series of mouse knock-in/knockouts to address the function of a Hox-embedded microRNA family (miR-196) within Hox gene networks. We demonstrate that miR-196 has the ability to regulate the correct temporal progression of Hox gene activation from all four Hox clusters, with specific focus on how this impacts formation of the vertebral column and neural networks of the spinal cord.

Speaker Bios

David Lynn

EMBL Australia Group Leader, Infection & Immunity, SAHMRI

David is an EMBL Australia Group Leader in the Infection and Immunity Theme at the South Australian Health and Medical Research Institute (SAHMRI). He also holds a joint faculty appointment as Associate Professor at the School of Medicine, Flinders University. David heads a multi-disciplinary group that is equally divided between bioinformatics and experimental systems biology. On the wet-lab side, his group employs *in vitro* and *in vivo* experimental and clinical models coupled with systems biology approaches to investigate the interplay between the microbiome, vaccines and the immune system. On the bioinformatics side, his group leads the development of InnateDB.com, an internationally recognised systems biology platform for innate immunity networks and he also leads the computational biology aspects of €12 million European Commission funded project called PRIMES, which is investigating how to model and subsequently therapeutically target protein interaction networks in cancer.

His Group is currently supported by: EMBL Australia, The European Commission, NHMRC, and The Garnett Passe and Rodney Williams Memorial Foundation. He has attracted >$5 million in funding in the last 5 years. He has published 50+ papers in journals including Science, Science Translational Medicine, Molecular Systems Biology, Journal of Infectious Diseases and his publications have received more than 3,400 citations. He has given invited talks on 6 continents.

“The impact of the neonatal microbiome on specific and non-specific vaccine responses”

In their first months of life, infants worldwide receive vaccinations providing protection against many serious infectious diseases. However, vaccine efficacy varies substantially among individuals and clinical trials show consistently lower vaccine immunogenicity in developing world populations. One potential, but poorly considered, contributor to this variation is the intestinal microbiome. The gut hosts an enormous abundance and diversity of microbes, which perform a range of essential and beneficial functions. In neonates, the gut microbiome is rapidly established and, in vaginally-born infants, its composition is strongly determined by the maternal microbiome. However, up to 40% of neonates are exposed to antibiotics, either directly or maternally, during the perinatal period and this has been documented to lead to a dysregulation of the normal development of the microbiome, causing dysbiosis. It is increasingly well-established that the consequences of dysbiosis can be long-lasting and extend far beyond the gut, leading to a dysregulation of systemic metabolism and immunity. We hypothesise that antibiotic-induced intestinal dysbiosis, particularly in this critical neonatal period, could lead to impaired immune responses to routine infant immunisations, which commence in close proximity to perinatal antibiotic exposure. We have now proven this to be the case in a neonatal mouse model, where we have demonstrated significant impairment of antigen-specific responses to three different routinely-administered infant vaccines.

Maté Biro

EMBL Australia New South Wales Node

Single Molecule Science and ARC Centre of Excellence in Advanced Molecular Imaging, University of New South Wales, Sydney, Australia

Maté Biro received his PhD at the Max Planck Institute of Molecular Cell Biology and Genetics in Germany in 2011. His doctoral work focused on the biophysics of cellular actin cortex assembly. He previously studied Physics (BSc) and then Bioinformatics and Theoretical Systems Biology (MSc) at the Imperial College in London, UK, and did his Masters research at MIT, Cambridge, MA, USA. He has worked at a particle accelerator in Tsukuba, Japan and as a Research Associate at the Bioinformatics Institute of the A*STAR in Singapore. In 2012, he moved to Sydney and the Centenary Institute at the University of Sydney, where he initially worked as a postdoc and then as of 2014 as group leader of the Cellular Mechanobiology lab. Maté joined EMBL Australia as a group leader at Single Molecule Science node at UNSW in January 2016. His research, highly multidisciplinary in nature, focuses on the dynamics and regulation of the actin cytoskeleton, notably during the migration of T cells and tumour cells, and the immunological interactions between them.

The actin cortex at the interface of cancer and immunity: T cell migration and cytotoxic interactions”

The cellular actin cortex is the cytoskeletal structure primarily responsible for the control of animal cell shape and as such plays a central role in cell migration. In adaptive immune responses to solid cancers, and in burgeoning adoptive transfer immunotherapies, T cells need to navigate various barriers and organs to reach the tumour and then effectively find and engage their targets. These types of tissue-invasive cell migrations and interactions rely on polarised shape changes and forces mediated by the actomyosin cortex, which manifest in different cellular protrusions, such as lamellipodia, filopodia and blebs, whose functional significance remain incompletely understood. We develop and adapt novel tools to resolve the composition, dynamics and regulation of the cell cortex and protrusions in motility and cytotoxic interactions, based on an integrative and multidisciplinary method encompassing microscopy, innovative image analysis, biophysical manipulation and computational modelling. We aim to uncover the cytoskeletal mechanisms that underpin effective target scanning by cytotoxic T cells, as well as their tumour rejection potential.

Speaker Bios

Thomas Preiss

EMBL – Australia Collaborating Group Leader

Department of Genome Sciences, The John Curtin School of Medical Research, The Australian National University

Thomas Preiss is Professor of RNA Biology at The Australian National University (ANU). From 1986–91 he studied Chemistry in Marburg (Germany) and Bristol (UK). He joined the field of RNA research with his PhD (1992–95) in Newcastle upon Tyne (UK) and postdoctoral training (1995–2002) at the EMBL, Heidelberg (Germany). In 2002 he moved to the VCCRI in Sydney. At ANU since 2011, his lab focuses on the mechanisms of mRNA utilisation and its regulation by RNA-binding proteins, RNA modifications and non-coding RNAs. He studies these phenomena in the contexts of cardiac disease, stem cell biology and cancer.

Dynamics of ribosome scanning and recycling revealed by translation complex profiling”

Regulation of mRNA translation is central to eukaryotic gene expression control. Regulatory inputs are specified by the mRNA untranslated regions (UTRs) and often target translation initiation. Initiation involves binding of the 40S ribosomal small subunit (SSU) and associated initiation factors (eIFs) near the mRNA 5’ cap; the SSU then ‘scans’ in the 3’ direction until it detects the start codon and is joined by the 60S ribosomal large subunit (LSU) to form the 80S ribosome (RS). Scanning and other dynamic aspects of the initiation model remain conjecture as methods to trap early intermediates are lacking. Here we uncover the dynamics of the complete translation cycle in live yeast cells using translation complex profile sequencing (TCP-Seq), a method developed from the ribosome profiling6 approach. We document scanning by observing SSU footprints along 5’UTRs. Scanning SSU have 5’-extended footprints (up to ~70 nt), indicative of additional interactions with mRNA emerging from the exit channel, enforcing forward movement. We visualise changes in initiation complex conformation as SSU footprints coalesce into three major sizes at start codons (19, 29 and 37 nt). These share the same 5’ start but differ at the 3’ end, reflecting successive changes at the entry channel from an open to a closed state following start codon recognition. We also observe SSU ‘lingering’ at stop codons after LSU departure. Our results underpin mechanistic models of translation initiation and termination, built on decades of biochemical and structural investigation, with direct genome-wide in vivo evidence. Our approach captures ribosomal complexes at all phases of translation and will aid in studying translation dynamics in diverse cellular contexts. Dysregulation of translation is common in disease and, for example, SSU scanning is a target of anti cancer drug development. TCP-Seq will prove useful in discerning differences in mRNA-specific initiation in pathologies and their response to treatment.

Chen Davidovich

EMBL Australia Group Leader

Department of Biochemistry and Molecular Biology, School of Biomedical Sciences, Monash University, ARC Centre of Excellence in Advanced Molecular Imaging, Clayton Campus, Monash University

Chen Davidovich is an EMBL-Australia Group Leader in Monash University, studying the molecular events that underlie the recruitment and regulation of chromatin-modifying complexes by their co-factor proteins, RNA transcripts and DNA. During his PhD study (Ada Yonath lab, Weizmann Institute, 2004–2010) he used X-ray crystallography to determine structures of ribosomal complexes. In his postdoctoral study (Tom Cech lab, The University of Colorado at Boulder, 2010–2015), he focused on studying the epigenetic modifier polycomb repressive complex 2 (PRC2) and its recruitment and regulation by long non-coding RNAs (lncRNAs) and RNA transcripts in general; an arena he is still active in.

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Mechanism of RNA binding by the Polycomb repressive complex 2 (PRC2)”

Polycomb repressive complex-2 (PRC2) is a histone methyltransferase required for epigenetic silencing during development and in cancer. Among chromatin modifying factors that were shown to be recruited and regulated by RNA, PRC2 is one of the most studied. Mammalian PRC2 binds thousands of RNAs in vivo, including coding and long non-coding RNAs (lncRNAs), and its histone methyl transferase activity is inhibited by RNA. We previously showed that PRC2 binds RNA promiscuously in vitro and in vivo. In contrast to nonspecific protein-RNA interactions, where various target RNAs are indistinguishable, promiscuous RNA binding by PRC2 allows it to discriminate transcripts to a certain degree, though so far the mechanism was obscured and binding motifs within target RNAs remained elusive. We have now identified low complexity RNA motifs that allow for variations in affinity to PRC2. Although the PRC2-binding motif within RNAs is simple and low in complexity, multiple bases are required for high affinity interactions. Such interactions with RNA involve multiple PRC2 subunits. We will present new mechanistic information describing the interactions between PRC2 and RNA, from both protein and RNA sides, and will describe a model for how these protein-RNA interactions facilitate the maintenance of repressed chromatin.

Speaker Bios

Michael Parker

EMBL Alumni, St. Vincent's Institute of Medical Institute and University of Melbourne

Michael Parker is Deputy Director of St. Vincent's Institute of Medical Research in Melbourne where he heads its Structural Biology Laboratory and the ACRF Rational Drug Discovery Centre. He is an NHMRC Senior Principal Research Fellow and a Professor at the University of Melbourne. The work of the laboratory is internationally recognised with the determination of more than 140 crystal structures including those of membrane-associating proteins, detoxifying enzymes and protein kinases. He has published over 300 papers and his work has been recognised with numerous awards including the 1999 Gottschalk Medal of the Australian Academy of Science, a 2006 Federation Fellowship from the Australian Research Council, the 2011 Lemberg Medal of the Australian Society for Biochemistry and Molecular Biology, the 2011 Ramaciotti Medal for Excellence in Biomedical Research and the 2012 Federation of Asian and Oceanian Biochemists and Molecular Biologists Award for Research Excellence. He was elected a Fellow of the Australian Academy of Science in 2010 and a Fellow of the Australian Academy of Health and Medical Sciences in 2015. He is currently Chair of the National Committee of Crystallography under the auspices of the Australian Academy of Science.

Cholesterol-dependent cytolysins: from water-soluble state to membrane pore"

The cholesterol-dependent cytolysins (CDCs) are one of the most widely distributed toxins known, having been identified in 5 different genera of Gram-positive bacteria. The CDCs exhibit a number of unique features amongst pore-forming toxins including an absolute dependence on the presence of cholesterol-rich membranes for their activity and the formation of oligomeric transmembrane pores greater than 150 Å in diameter. There are more than 20 members of the CDC family so far identified and there exists a high degree of sequence homology (40–70%) suggesting they all have similar activities and 3D structures. The first crystal structure of a CDC was that of perfringolysin O[1] and most of our understanding of CDC function is based on studies of this toxin.[2,3] We have subsequently determined structures of other family members that have confirmed that the 3D fold first seen in PFO is shared by all family members.[5–7] Functional studies have revealed that CDCs undergo a highly regulated stepwise process in assembling as a large membrane pore consisting of more than 30 monomers. Not only is the conversion from water-soluble monomer to pore highly complex, it is essential that the pore does not form prematurely otherwise the target cell won't be successfully breached. The crystal structures of the water-soluble states of these toxins, together with cryoelectron microscopy, small angle X-ray scattering data, fluorescence spectroscopy and molecular dynamics simulations have proved very useful for modelling their membrane pores.

1. Rossjohn, J. *et al.,* (1997) Structure of a cholesterol-binding, thiol-activated cytolysin and a model of its membrane form. *Cell* 89, 685–692.
2. Shatursky, O. *et al.,* (1999) The mechanism of membrane insertion for a cholesterol-dependent cytolysin: a novel paradigm for pore-forming toxins. *Cell* 99, 293–299.
3. Gilbert, R.J. *et al.,* (1999) Two structural transitions in membrane pore formation by pneumolysin, the pore-forming toxin of *Streptococcus pneumoniae. Cell* 97, 647–655
5. Polekhina, G. *et al.,* (2005) Insights into the action of the superfamily of cholesterol-dependent cytolysins from studies of intermedilysin. *Proc. Natl. Acad. Sci. USA* 102, 600–605.
6. Feil, S.C. *et al.,* (2012) Structure of the lectin regulatory domain of the cholesterol-dependent cytolysin lectinolysin reveals the molecular basis for its Lewis antigen specificity. *Structure* 20, 248–258.
7. Feil, S.C. *et al.,* (2014) Structural studies of *Streptococcus pyogenes* streptolysin O provides insights into the early steps of membrane penetration. *J. Mol. Biol.* 426, 785–792.

Max Cryle

EMBL Australia Group Leader

Department of Biochemistry and Molecular Biology, School of Biomedical Sciences, Monash University, ARC

Max Cryle is an EMBL Australia Group leader in the Victorian Node, based in the Department of Biochemistry and Molecular Biology at Monash University. After obtaining his PhD in chemistry from the University of Queensland in 2006, he moved to the Max Planck Institute for Medical Research in Heidelberg as a Cross Disciplinary Fellow of the Human Frontiers Science Program. He was subsequently awarded funding from the German Research Foundation (Deutsche Forschungsgemeinschaft) to establish his own group to investigate glycopeptide antibiotic biosynthesis as part of the Emmy Noether program. His group works at the boundary of chemistry and biology, where they apply a multidisciplinary approach including synthetic chemistry, biochemistry, structural biology and enzyme catalysis. In 2016 he joined EMBL Australia to continue his research into understanding the biosynthesis of important natural antibiotics and developing new antimicrobial agents. His group has made a number of important breakthroughs in understanding how nature synthesises the glycopeptide antibiotics, which are clinically relevant and synthetically complex molecules. For this work he was awarded the 2016 Otto Schmeil prize by the Heidelberg Academy of Arts and Sciences. Currently, his group is investigating the biosynthesis of several important antibiotics as well as investigating novel strategies and targets for antimicrobial development.

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Understanding Glycopeptide Antibiotic biosynthesis as a pathway to new antimicrobial agents”

The glycopeptide antibiotics, which include the clinical compounds teicoplanin and vancomycin, are natural products that we use in the last line of medical defence against resistant Gram-positive bacterial infections such as MRSA. The biosynthesis of the glycopeptide antibiotics centres on the actions and interplay of the peptide-producing non-ribosomal peptide synthetase (NRPS) megaenzyme and the Oxy proteins, which are members of the Cytochrome P450 superfamily of monooxygenases. These P450s are responsible for installing the multiple oxidative phenolic and aryl crosslinks between aromatic side chains of the linear precursor peptide, finally yielding the glycopeptide antibiotic aglycones in their active 3D-conformation. As the production of all glycopeptide antibiotics currently stems from in vivo biosynthesis, understanding the molecular processes behind their formation is crucial for future efforts to reengineer the machinery and produce new glycopeptide antibiotics. Given that the oxidative crosslinking reactions performed by the Oxy proteins are not only crucial for antibiotic activity but also represent a significant challenge in the chemical synthesis of glycopeptide antibiotics, my group has concentrated on understanding this process. We have shown that the Oxy proteins access their peptide substrates whilst they remain directly bound to the NRPS machinery: this occurs through recruitment by a conserved domain of previously unknown function, known as the X-domain. My team has now determined the structure of a complex of the X-domain with the first Oxy protein from teicoplanin biosynthesis, which reveals how this essential recruitment process is mediated on a molecular level during peptide maturation. In addition, we have characterised subsequent Oxy enzymes involved in the teicoplanin oxidative crosslinking cascade, which indicates that the enzymes involved in the teicoplanin oxidative cascade rely upon different active site architectures to bind their substrates in spite of their common mechanism and highly similar substrates.

Speaker Bios

Andrew Lonie

Director, EMBL Australia Bioinformatics Resource

Andrew Lonie is Director of the Victorian Life Sciences Computation Initiative (VLSCI: http://vlsci.org.au), Director of the EMBL Australia Bioinformatics Resource (EMBL-ABR: http://embl-abr.org.au), and an associate professor at the Faculty of Medicine, Dentistry and Health Sciences at the University of Melbourne, where he coordinates the MSc (Bioinformatics). Andrew directs a group of bioinformaticians, computational biologists and HPC specialists within the VLSCI and EMBL-ABR to collaborate with and support life sciences researchers in a variety of research projects across Australia.

Building the EMBL Australia Bioinformatics Resource”

The EMBL Australia Bioinformatics Resource is a distributed national research infrastructure providing bioinformatics support to life science researchers in Australia. The Resource was set up as a collaboration with the European Bioinformatics Institute (EMBL-EBI) to maximise Australia’s bioinformatics capability. This close partnership is made possible in the context of Australia’s associate membership of EMBL. In this talk I will discuss progress in establishing the EMBL-ABR network including an overview of activities, strategic planning and funding.

Matthias W. Hentze

European Molecular Biology Laboratory (EMBL), Heidelberg, Germany

Matthias Hentze is a native German. He attended Münster University Medical School, and studied at Oxford, Cambridge, Glasgow and Southampton. Following on from his medical degree and a M.D. in Biochemistry (Münster), Matthias began his research career as a post-doctoral research fellow at the National Institutes of Health (Bethesda, Maryland, USA) before joining EMBL Heidelberg in 1989 as a Group Leader. After obtaining the Habilitation from Heidelberg University in 1990, Matthias served as the Dean of Graduate Studies from 1996 until 2005. In 2002 when he was Dean, Matthias co-founded the Molecular Medicine Partnership Unit (MMPU) between EMBL and the Medical Faculty of Heidelberg University which he still co-directs. Here the Matthias research group conducts translational research on common diseases of iron metabolism and of altered mRNA metabolism. In July of 2005, Matthias was promoted from Dean to the position as EMBL Associate Director. In that same year, he became Professor for Molecular Medicine. As EMBL Director, Matthias advises and works closely with EMBL's Director General. Matthias oversees the areas of Resource Development and Alumni Relations, and is supported by the Director's Office. Matthias has many varied functions in his role, including supporting and representing the Director General at international scientific research, training and service organisations. Matthias also generates additional opportunities for the Laboratory, by promoting aspects of EMBL via public engagement and communication strategies as well as generating visibility and positive awareness of the Laboratory.

A new view on RNA-binding proteins and RNA"

We recently discovered that hundreds of cellular proteins, previously well known for other biological functions, also unexpectedly bind RNA (termed "enigmRBPs" for enigmatic RNA-Binding Proteins. Since many enigmRBPs are conserved from yeast to humans, their existence raises pressing questions. One of the most stunning surprises was the discovery that almost all enzymes of the glycolytic pathway are conserved as enigmRBPs. Overall, more than 50 metabolic enzymes were found to bind RNA. Could the combination of enzymatic and RNA-binding functions represent a general biological principle for coordination between gene expression and metabolism? Applying a newly developed technique, RBDmap, to identify the RNA-binding domains of enigmRBPs, we uncovered new RNA-binding architectures yielding functional insights. Integrating all information, we discuss a possible new function for genomes in addition to their classical role in driving protein biosynthesis via mRNAs, rRNAs, and tRNAs and their associated modifying and regulatory RNAs.

Speaker Bios

Mirana Ramialison

Research Group Leader
Scientific Liaison Officer,
South America

Mirana is head of the Systems Developmental Biology Laboratory at the Australian Regenerative Medicine Institute in Melbourne. She is an NHMRC/NHF Career Development Fellow and leads a multi-disciplinary team of bioinformaticians and molecular biologists, to study heart development, evolution and disease. She takes a systems biology approach to uncover the gene regulatory networks that control gene expression during cardiac development combined with experimental validation in zebrafish, and identify abnormal interactions that cause congenital diseases. Prior to joining ARMI in February 2014, Mirana received her Engineering degree from the Ecole Superieure d'Ingenieurs de Luminy (France) and PhD *summa cum laude* at the European Molecular Biology Laboratory (Germany). She then joined the Victor Chang Cardiac Research Institute in Sydney as an EMBO and HFSP post-doctoral Fellow.

From regulatory elements to cardiac enhanceropathies"

Every day in Australia, 8 babies are born with heart defects. It is a heavy burden for them and the families as the only effective treatment available is invasive surgery in the first year of life. Mild forms of heart defects will allow survival until adulthood, which will put the patient at risk of heart failure. Hence, understanding the causes of congenital heart disease (CHD) is crucial for its early diagnosis and for the care of patients suffering from it. In a few cases, the causes of CHD can be attributed to gene mutations and environmental factors, but to date, the majority of these cases are of unknown origin.

Here we propose that CHD is caused by a new class of DNA-mutations that do not reside within the sequence of protein-coding genes but lie within the regulatory regions (enhancers or promoters) of our genome. The contribution of regulatory mutations in various diseases has been well established (termed enhanceropathies), nevertheless their role in CHD remains largely unexplored. This is because unlike protein-coding genes, regulatory elements are difficult to identify and characterize. I will discuss the bioinformatics pipelines that we are using in our laboratory to systematically map novel regulatory regions essential for heart development and that are relevant to cardiac enhanceropathies.