

# XIX Jornades de Biologia Evolutiva



Organized by Oscar Lao and Olga Dolgova

### "Nothing makes sense in Biology Except in the Light of Evolution" or Why *Les Jornades de Biologia Evolutiva* are so important

The sentence "Nothing in Biology Makes Sense Except in the Light of Evolution" that Theodosius Dobzhansky wrote in 1973 wildly synthesizes the thinking of each scientist that claims to work in any of the disciplines that comprises the broad field of evolution. Moreover, this sentence is a quite concise reply to the insidious question that from time to time we have to face from any member of our family (as well as friends and/or random citizens) "but this that you are working on, what is helpful for?".

Les Jornades de Biologia Evolutiva offer an unbeatable opportunity to meet once a year all the people that is working in evolution in Catalunya, to show our own work -particularly for PhD students- to inhouse colleagues, and to -hopefully- initiate fruitful collaborations with other groups. Moreover, all of this is conducted in Casa de la Convalescència, a marvelous gothic building and a part of the Santa Creu hospital.

This year we will have two invited speakers.

Our first speaker, Stefano Mona is a researcher at L'Institut de Systématique, Évolution, Biodiversité, Paris. He is an evolutionary biologist particularly interested in population genetics. He has been working on different organisms. His focus is on how genetic markers can be exploited to reconstruct demography of population and species. Most of his work has focused on developing and applying models taking into account the fact that species are dynamic entities and are, most of the time, structured into sub-populations exchanging migrants.

Our second speaker, Marc Marti-Renom is an ICREA Research Professor. He holds a degree in Biology and a PhD in Biophysics from the Autonomous University of Barcelona. He trained in the modelling of protein structure in the laboratory of Prof. Andrej Sali at Rockefeller University, in the USA. Later, he was appointed adjunct assistant professor at the University of California in San Francisco, also in the USA. Between 2006 and 2011, he was head of the Structural Genomics Laboratory in the Prince Felipe Research Centre in Valencia (CIPF). Since 2012, he is also the Group Leader of the CNAG-CRG Structural Genomics Group. Marc A. Marti-Renom is associate editor of the journal PLoS Computational Biology and has co-authored over 60 articles published in prestigious scientific journals.

We hope you will enjoy the meeting.

Oscar Lao and Olga Dolgova

### Program

8:45-9:10 Registration

9:10-9:20 Welcome

9:20-10:00 Invited speaker: Stefano Mona. Population structure: how much should we worry?

*Moderator*: Julio Rozas

10:00-10:25 Anna Barbanti (UB). The potential of founder effect evaluated in reintroduced populations of *Chelonia mydas*.

10:25-10:50 lago Maceda-Porto (CNAG-CRG). The PIRENE project: a new genetic isolate in southern Europe.

10.50-11:15 Neus Font Porterias (UPF). European Roma groups show complex West Eurasian admixture footprints and a common South Asian genetic origin.

11:15-11:40 Jesús Murga (IBB-UAB). IMKT: Comparing and applying four MKT methods to detect and quantify natural selection at the genome level.

11:40-12:05 Coffee break

Moderator: Stefano Mona

12:05-12:30 Eduard Ocaña-Pallarès (CSIC-Universitat Pompeu Fabra). Reticulate evolution in eukaryotes: Origin and evolution of the nitrate assimilation pathway.

12:30-12:55. Konstantina Mitsia (IBE). The genome of a new filasterean parasite recovered from a metagenome provides insights into the unicelular ancestry of animals.

12:55-13:20 Miquel Àngel Schikora Tamarit (BSC). Shared evolutionary footprints suggest mitochondrial oxidative damage underlies multiple Complex I losses.

13:20-14:20 Lunch break

14.20-15.00 Invited speaker: Marc Marti-Renom (CNAG-CRG). 3DGenomics

Moderator: Oscar Lao Grueso (CNAG-CRG)

15.00-15.25 Miriam Merenciano (CSIC-UPF). Molecular and phenotypic characterization of *roo* elements inserted in a unique insertional cluster under different environmental challenges.

15.25-15.50 Joel Vizueta (UB). Chance and predictability in evolution: the genomic basis of convergent dietary specializations in an adaptive radiation.

15.50-16.15 Sandra Acosta (UPF). A Human Accelerated Region regulates forebrain expansion through the control of Foxg1 expression during neurulation.

16.15 - 16:30 Coffee Break

Moderator: David Comas (UPF)

16:30-16:55 Alberto Perez-Posada (CSIC-Universitat Pompeu Fabra). Gradual evolution of cell cycle regulation during the transition to animal multicellularity.

16:55-17:20 Víctor Gámez Visairas (UAB). Estudio de los genes de la ruta PIWI y la metilación de histonas en la desregulación de elementos transponibles en hibridos de Drosophila.

17.20-17.45 Joan Pere Pascual-Díaz (*IBB-CSIC*)<sup>-</sup> **Repeat contribution to genome size ups and downs in family Asteraceae.** 

17.45-18.00 Break/Prevosti Prize Committee Meeting

18.00 Announcement of the Prevosti Prize winner. End of the meeting.

### XI Premi Antoni Prevosti de Biologia Evolutiva, any 2019

Amb l'objectiu de fomentar la participació i la discussió de la recerca dels joves investigadors, pre i postdoctoral, en tots els camps de la Biologia Evolutiva, l'any 2007 fou instaurat per primera vegada el premi Antoni Prevosti de Biologia Evolutiva per premiar la millor comunicació a la jornada presentada per un jove investigador (que faci menys de 3 anys que ha llegit la tesi). El premi consisteix aquest any en 250 € que es lliuraran al finalitzar la darrera sessió de la Jornada. El receptor del premi haurà de ser present a la sala per rebre'l. Si no és així, el premi passarà a la comunicació que hagi quedat en segon lloc, si n'hi hagués, o podria ser declarat desert. La comissió que decidirà el premi de l'edició de l'any 2018 estarà formada per.

President: Jaume Bertranpetit

Secretari: Mauro Santos

Vocal 1: Ignasi Roig Navarro

Vocal 2: Miguel Perez

Vocal 3: Marta Riutort

La comissió atorgarà el premi en base a la qualitat científica i presentació del treball, així com a les respostes a les intervencions dels assistents. Els membres de la comissió no podran votar a les persones del seu grup.

### ABSTRACTS

### IMKT: Comparing and applying four MKT methods to detect and quantify natural selection at the genome level

Jesús Murga, IBB-UAB

One of the most striking evidence of the power of natural selection is the characteristic footprints that it leaves on the patterns of genetic variation. The McDonald and Kreitman test (MKT)<sup>1</sup> is one powerful and robust methods to detect the action of natural selection at the molecular level. MKT can detect the action of recurrent positive selection by analyzing polymorphism and divergence data altogether. The main drawback of MKT is that it assumes that only neutral mutations contribute to polymorphism, but weak negative selection abounds in genomes, biasing downward the estimated adaptation values. Several methodological MKT extensions have attempted to correct for this bias by taking into account slightly deleterious polymorphism. Here, we perform a comparison of four different MKT methods: (i) the standard (original) MKT<sup>1</sup>; (ii) the Fay Wickoff and Wu correction<sup>2</sup>; (iii) the Extended MKT<sup>3</sup> and (iv) the asymptotic MKT<sup>4</sup>. Two population genomic data, real and simulated, are used to assess their performance for different datasets and evolutionary scenarios. Genome-wide DNA variation data come from Drosophila melanogaster and human populations, and simulated data was generated with the SLiM 2 evolutionary framework<sup>5</sup>. We test several conditions including geneto-gene vs gene concatenating analysis, and recombination effect to assess the power and bias of selection estimates of the different MKT methods. Furthermore, we developed iMKT (acronym for integrative McDonald and Kreitman test), a web-based service performing the four MKT methods. iMKT allows the detection and estimation of four selection regimes (adaptive, neutral, strongly deleterious and weakly deleterious). User's own population genomic data, and pre-loaded D. melanogaster and human sequences of protein-coding genes for 16 and 26 populations, respectively, can be analyzed. iMKT is a comprehensive reference site for the study of protein adaptation in massive population genomics datasets, especially in Drosophila and humans. iMKT is a free resource online at https://imkt.uab.cat.

- 1. McDonald, J. H. & Kreitman, M. Adaptive protein evolution at the Adh locus in Drosophila. *Nature* **351**, 652–654 (1991).
- 2. Fay, J. C., Wyckoff, G. J. & Wu, C.-I. Positive and Negative Selection on the Human Genome. *Genetics* **158**, 1227–1234 (2001).
- 3. Mackay, T. F. C. et al. The Drosophila melanogaster Genetic Reference Panel. Nature 482, 173–178 (2012).
- 4. Messer, P. W. & Petrov, D. A. Frequent adaptation and the McDonald-Kreitman test. *Proc. Natl. Acad. Sci.* **110**, 8615–8620 (2013).
- 5. Haller, B. C. & Messer, P. W. SLiM 2: Flexible, Interactive Forward Genetic Simulations. *Mol. Biol. Evol.* **34**, 230–240 (2017).

#### The potential of founder effect evaluated in reintroduced populations of Chelonia mydas

Anna Barbanti, Maria Turmo, Janice M. Blumenthal, Jack Boyle, Annette. C. Broderick, Lucy Collyer, Gina Ebanks-Petrie, Brendan J. Godley, Marta Pascual, Carlos Carreras. Department de Genètica, Microbiologia i Estadística and IRBio, Universitat de Barcelona, Av. Diagonal 643, 08028 Barcelona, Spain. Tel: 934024850. Email: anna.barbanti.es@gmail.com.

Shifts in distributions due to anthropogenic actions, such as global warming, or human mediated dispersal are currently causing the founding of new populations of many species worldwide. The study of the processes associated to the establishment of new populations can be challenging in long living and highly migratory species, such as marine turtles. The green turtle (Chelonia mydas) populations of Grand and Little Cayman were considered extinct in the 80s but in the last 20 years, the number of nests have been increasing progressively. A previous study has shown that most of the wild females captured in Grand Cayman were related to a reintroduction program that started in 1968 from captive breeding by the Cayman Turtle Center (CTC). This reintroduction program offers a unique opportunity to study the rise of these new populations to have a better understanding on how the evolutionary forces determine diversity and differentiation on founding processes on this species. We analysed 320 wild hatchlings sampled on Little and Grand Cayman in three consecutive nesting seasons using microsatellites and mtDNA D-Loop markers. We ran parentage and relatedness analysis against wild females and CTC breeding stock respectively using previously genotyped data, finding that 79% of Little Cayman hatchlings and 90% of Grand Cayman hatchlings were related to CTC individuals. We used parentage analysis to identify or infer parents of each nest. Only one nest per female was retained for population analysis. Both islands showed significant genetic differentiation from the CTC, when using nuclear markers while only Little Cayman showed significant differentiation from the CTC using the mtDNA. The genetic differentiation found was likely to be produced by genetic drift during the founding process. Moreover, we analysed nest site fidelity (NSF) of wild females comparing geographic distances between consecutive nests within a season, finding high degree of NSF. Finally, the sex ratio of breeding adults inferred from our parentage analysis did not show any significant shifting towards one sex, meaning that global warming did not affect the sex ratio of these adult populations.

#### The PIRENE project: a new genetic isolate in southern Europe

Iago Maceda Porto<sup>1</sup>; Miguel Martín Álvarez Álvarez<sup>2</sup>; Pedro Moral Castrillo<sup>2</sup>; Oscar Lao Grueso<sup>1</sup>.

<sup>1</sup> Population Genomics Group, Centre Nacional d'Anàlisi Genòmica, Centre de Regulació Genòmica (CRG-CNAG), Parc Científic de Barcelona, Baldiri Reixac 4, 08028 Barcelona, Catalonia, Spain.

<sup>2</sup> Anthropology Unit, Department of Evolutionary Biology, Ecology and Environmental Sciences, Faculty of Biology, University of Barcelona

We present a new dataset: PIRENE. This dataset is the result of deep sequencing 30 samples from 5 different valleys of the Catalan Pyrenees (Garrotxa, Pallars, Berga, Alt Urgell and Ripolles). We have found that this new dataset is a great example of genetic isolate, given the orography of the area where the samples were gathered. In order to find population substructure in a small geographical space, we decided to develop new tools to search for genetic clines and anisotropy independently of allelic model assumptions. We decided to use tools present in geostatistics coupled with a genetic algorithm for identifying this genetic barriers. We also explore the medical importance of this new dataset. We have found that this new dataset harbors a greater number of rare alleles, and potentially damaging, when compared with the general Iberian population. Also has signals of a bigger inbreeding when compared with the general population. To be able to understand the demographic history of this region we used a novel approach that couples Approximate Bayesian Computation with Deep Learning (ABC-DL), to estimate classic demographic parameters.

#### European Roma groups show complex West Eurasian admixture footprints and a common South Asian genetic origin

#### Font Neus Porterias

The Roma population is the largest transnational ethnic minority in Europe, characterized by a linguistic, cultural and historical heterogeneity. Comparative linguistics and genetic studies have placed the origin of European Roma in the Northwest of India. After their migration across Persia, they entered into the Balkan Peninsula, from where they spread into Europe, arriving in the Iberian Peninsula in the 15th century. Their particular demographic history has genetic implications linked to rare and common diseases. However, the South Asian source of the proto-Roma remains still untargeted and the West Eurasian Roma component has not been yet deeply characterized. Here, in order to describe both the South Asian and West Eurasian ancestries, we analyze previously published genome-wide data of 152 European Roma and 34 new Iberian Roma samples at a fine-scale and haplotype-based level, with special focus on the Iberian Roma genetic substructure. Our results suggest that the putative origin of the proto-Roma involves a Punjabi group with low levels of West Eurasian ancestry. In addition, we have identified a complex West Eurasian component (around 65%) in the Roma, as a result of the admixture events occurred with non-Roma populations between 1270 - 1580. Particularly, we have detected the Balkan genetic footprint in all European Roma, and the Baltic and Iberian components in the Northern and Western Roma groups, respectively. Finally, our results show genetic substructure within the Iberian Roma, with different levels of West Eurasian admixture, as a result of the complex historical events occurred in the Peninsula.

Reticulate evolution in eukaryotes: Origin and evolution of the nitrate assimilation pathway

Eduard Ocaña-Pallarès<sup>1</sup>; Sebastian R. Najle<sup>1, 2</sup>; Claudio Scazzocchio<sup>3, 4</sup>; Iñaki Ruiz-Trillo<sup>1, 5, 6</sup>

<sup>1</sup> Institut de Biologia Evolutiva (CSIC-Universitat Pompeu Fabra), Passeig Marítim de la Barceloneta 37-49, Barcelona 08003, Catalonia, Spain

<sup>2</sup> Instituto de Biología Molecular y Celular de Rosario (IBR) CONICET and Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario, Ocampo y Esmeralda s/n, Rosario S2000FHQ, Argentina

<sup>3</sup> Department of Microbiology, Imperial College, London, United Kingdom

<sup>4</sup> Institute for Integrative Biology of the Cell (I2BC), Gif-sur-Yvette, France

 <sup>5</sup> Departament de Genètica, Microbiologia i Estadística, Universitat de Barcelona, Avinguda Diagonal 645, Barcelona 08028, Catalonia, Spain
<sup>6</sup> ICREA, Pg. Lluís Companys 23, 08010 Barcelona, Catalonia, Spain

Genes and genomes can evolve through interchanging genetic material, this leading to reticular evolutionary patterns. However, the importance of reticulate evolution in eukaryotes, and in particular of horizontal gene transfer (HGT), remains controversial. Given that metabolic pathways with taxonomically-patchy distributions can be indicative of HGT events, the eukaryotic nitrate assimilation pathway is an ideal object of investigation, as previous results revealed a patchy distribution and suggested that the nitrate assimilation cluster of dikaryotic fungi (Opisthokonta) could have been originated and transferred from a lineage leading to Oomycota (Stramenopiles). We studied the origin and evolution of this pathway through both multi-scale bioinformatic and experimental approaches. Our taxon-rich genomic screening shows that nitrate assimilation is present in more lineages than previously reported, although being restricted to autotrophs and osmotrophs. The phylogenies indicate a pervasive role of HGT, with three bacterial transfers contributing to the pathway origin, and at least seven wellsupported transfers between eukaryotes. In particular, we propose a distinct and more complex HGT path between Opisthokonta and Stramenopiles than the one previously suggested, involving at least two transfers of a nitrate assimilation gene cluster. We also found that gene fusion played an essential role in this evolutionary history, underlying the origin of the canonical eukaryotic nitrate reductase, and of a chimeric nitrate reductase in Ichthyosporea (Opisthokonta). We show that the ichthyosporean pathway, including this novel nitrate reductase, is physiologically active and transcriptionally co-regulated, responding to different nitrogen sources; similarly to distant eukaryotes with independent HGT-acquisitions of the pathway. This indicates that this pattern of transcriptional control evolved convergently in eukaryotes, favoring the proper integration of the pathway in the metabolic landscape. Our results highlight the importance of reticulate evolution in eukaryotes, by showing the crucial contribution of HGT and gene fusion in the evolutionary history of the nitrate assimilation pathway.

The genome of a new filasterean parasite recovered from a metagenome provides insights into the unicelular ancestry of animals

<u>Konstantina Mitsi<sup>a,g</sup></u>, Ander Urrutia<sup>b,f,g</sup>, Michelle Leger<sup>a</sup>, Stephen W. Feist<sup>b</sup>, David Bass<sup>b,c</sup> and Iñaki Ruiz-Trillo<sup>a,d,e</sup>

<sup>a</sup> Institut de Biologia Evolutiva (CSIC-Universitat Pompeu Fabra), Passeig Marítim de la Barceloneta, 37-49, 08033 Barcelona, Spain.

<sup>b</sup> Centre for Environment, Fisheries and Aquaculture Science (CEFAS), Weymouth Laboratory, Barrack Rd, Weymouth, DT4 8UB, United Kingdom.

<sup>c</sup> Department of Life Sciences, Natural History Museum London, London, UK

<sup>*d*</sup> Departament de Genètica, Universitat de Barcelona, Avinguda Diagonal 643, 08028, Barcelona, Spain.

<sup>e</sup> Institució Catalana de recerca I Estudis Avançats (ICREA), Passeig Lluís Companys, 23, 08010 Barcelona, Spain.

<sup>f</sup> Res Ctr Experimental Marine Biology & Biotechnology (PIE-UPV/EHU) & Zoology & Animal Cell Biology Dept., (UPV-EHU) Plentzia 48080 Bilbao, Spain.

<sup>g</sup>These two authors contributed equally.

The eukaryotic group Holozoa comprises animals and their unicellular relatives, namely Choanoflagellates, Filasterea and Teretosporea (Ichthyosporea+Pluriformea). Unicellular holozoans hold a phylogenetic position that is key to addressing a long-standing open evolutionary question: the transition to animal multicellularity. To expand the extant holozoan genomic dataset, here we report the morphology, nuclear and mitochondrial genomes of Txikispora sp. . Txikispora sp. is known to infect at least two amphipod genera, Echinogammarus sp. and Orchestia sp. collected from the southwest coast of United Kingdom. It is the first confirmed filasterean parasite as it triggers host response in the form of granuloma formation and melanization, reducing host motility and general fitness. Phylogenomic reconstruction based on 85 single-copy protein domains and 23,526 aa positioned this novel unicellular holozoan species as an early-branching filasterean. The genome was acquired following a metagenomic pipeline, an approach that is commonly used to describe complex prokaryotic communities but is still in limited use for studies of eukaryotes. Comparative analysis revealed that the *Txikispora sp.* genome encodes most genes involved in the flagellar toolkit as well as with the majority of genes previously identified as the multicellular toolkit. The latter include the integrin adhesome and many developmental transcription factors. In addition, genes involved in meiotic recombination were identified. Overall, our results add to our understanding of the the genomic repertoire of the last unicellular common ancestor of animals, reinforce the current holozoan phylogeny by expanding the available dataset and provide insights into the mechanisms that facilitate a parasitic lifestyle in a filasterean.

#### Shared evolutionary footprints suggest mitochondrial oxidative damage underlies multiple Complex I losses

Miquel Àngel Schikora Tamarit

Comparative genomics lab, Life Sciences, Barcelona Supercomputing Center

Mitochondrial oxidative phosphorylation (OXPHOS) is among the most essential and conserved systems across the Tree Of Life. One of the cornerstones of this pathway is Complex I, which (surprisingly) has been lost multiple independent times in eukaryotes. This represents a recurrent phenomenon of convergent evolution, whose implications on cell physiology and behavior remain obscure. Understanding the evolutionary process that led to the loss may reveal novel features about this complex, which additionally plays roles in drug response, oxidative stress and pathogenesis. In this study we used a comparative approach to infer infer causes and consequences of Complex I loss. We identified 13 events of Complex I (CI) loss in eukaryotes, mostly in fungi. The focus was put on three recent fungal CI loss events, described here for the first time. We inferred the genomic changes convergently associated with CI loss, which may include increased mitochondrial antioxidants, higher fermentative capabilities, duplications of alternative dehydrogenases, loss of alternative oxidases and adaptation to antifungal compounds. We propose that the combination of previous compensatory mechanisms and exposure to environmental triggers of oxidative stress (such as hypoxia and/or toxic chemicals) induced the loss. Furthermore, we were able to predict novel CI related factors via gene co-loss. In summary, we provide the first comprehensive analysis about the genomic footprints underlying and following CI loss.

## Molecular and phenotypic characterization of *roo* elements inserted in a unique insertional cluster under different environmental challenges.

Miriam Merenciano and Josefa González

Institut de Biologia Evolutiva (CSIC-UPF), Barcelona

Transposable elements (TEs) play an important role in the capacity of organisms to deal with environmental challenges. Analysing 15 natural populations of Drosophila melanogaster from Europe, North America, and Africa, we previously discovered 20 independent roo solo-LTR insertions located in the promoter region of the stress related gene CG18446, which overlaps with the first intron of CG46338 gene. One of the identified insertions was associated with a cold-resistance phenotype and provides an alternative transcription start site to CG18446. We also found that this insertional cluster is unique: no other promoter region in the genome contains a similar number of roo insertions. In this work, we studied whether the two roo insertions found at higher population frequencies, FBti0019985 and roo.90 have any molecular or phenotypic effect beyond the already described cold-resistant phenotype. We found that flies containing FBti0019985 are associated with tolerance to ethanol exposure and to Pseudomonas entomophila infection. These functional changes are associated with changes in CG18446 expression. Moreover, in vivo enhancer assays suggested that FBti0019985 contains cis-regulatory elements that could be responsible for gene expression changes under infection and during embryonic development. Alternatively, flies containing roo.90 are more tolerant to low humidity levels than flies without this insertion, although no changes in CG18446 expression have been detected. Together, these two TEs are promising candidates for TE insertions that might lead to changes in organismal fitness. To definitively show a causal effect of the respective TE insertion, we are currently applying the CRISPR/Cas system to precisely delete FBti0019985 and roo.90 insertions in natural fly lines to establish unequivocal causal links between TE-adaptive mutations and fitness effects.

Chance and predictability in evolution: the genomic basis of convergent dietary specializations in an adaptive radiation

Joel Vizueta<sup>1</sup>, Nuria Macías-Hernández<sup>2, 3</sup>, Miquel A. Arnedo<sup>4</sup>, Julio Rozas<sup>1\*</sup> and Alejandro Sánchez-Gracia<sup>1\*</sup>

The coexistence of multiple eco-phenotypes in independently assembled communities makes island adaptive radiations the ideal framework to test convergence and parallelism in evolution. In the radiation of the spider genus *Dysdera* in the Canary Islands, species diversification occurs concomitant with repeated events of trophic specialization. These dietary shifts, to feed primarily on woodlice, are accompanied by modifications in morphology, behaviour and nutritional physiology. To gain insight into the molecular basis of this adaptive radiation, we performed a comprehensive comparative transcriptome analysis of five Canary Island Dysdera endemics representing two evolutionary and geographically independent events of dietary specialization. After controlling for the potential confounding effects of hemiplasy, our differential gene expression and selective constraint analyses identified a number of genetic changes that could be associated with the repeated adaptations to specialized diet of woodlice, including some related to heavy metal detoxification and homeostasis, the metabolism of some important nutrients and venom toxins. We uncovered specific genes, groups of genes with equivalent functions, and even particular amino acid positions as putative molecular substrates of convergent evolutionary changes. Our results shed light on the genomic basis of an extraordinary case of dietary shift convergence associated with species diversification.

# A Human Accelerated Region regulates forebrain expansion through the control of Foxg1 expression during neurulation

Sandra Acosta<sup>+1,7</sup>, Luciano Fiore<sup>1</sup>, Giovanni Iacono<sup>2</sup>, Isabel Rollán<sup>5</sup>, Alexander V. Misharin<sup>3</sup>, Nozomu Takata<sup>1</sup>, Martin Sikora<sup>6</sup>, Nikita Joshi<sup>3</sup>, Beisi Xu<sup>4</sup>, Eske Willerslev<sup>6</sup>, Miguel Manzanares<sup>5</sup>, Holger Heyn<sup>2,7</sup>, Guillermo Oliver<sup>+\*1</sup>

1. Centre for Vascular and Developmental Biology, Feinberg Cardiovascular Research Institute, Northwestern University, Chicago, IL 2. CNAG-CRG, Centre for Genomic regulation (CRG), Barcelona Institute of Science and Technology (BIST), Barcelona, Spain 3. Division of Pulmonary and Critical Care Medicine, Northwestern University, Chicago, IL 4. Bioinformatic Department, St. Jude Research Children's Hospital, Memphis, Tn 5. Centro Nacional Investigaciones Cardiovasculares (CNIC), Madrid, Spain 6.GeoGenetics Center, University of Copenhagen, Copenhagen, Denmark 7. Universitat Pompeu Fabra (UPF), Barcelona, Spain

+ Corresponding authors: S.A. (<u>Sandra.acosta@upf.edu</u>; <u>sacostav3@gmail.com</u>) and G.O. (guillermo.oliver@northwestern.edu)

How evolution impacted human forebrain development remains an intriguing question. Some of the molecular mechanisms implicated in the expansion of cortical progenitors have been deciphered; however, it is not yet known whether evolutionary events in genomic regions active during early stages of embryonic development, are responsible for the expansion of the human forebrain. Here, we identified an enhancer active at the onset of neurulation located in a human accelerated region (HAR) upstream of *Foxg1*, a key transcription factor implicated in forebrain development. *Foxg1* gain-of-function regulated by the mouse or human enhancer variant results in an increase in neural progenitors. Moreover, humanized forebrain organoids derived from HAR enhancer variant knock-in mouse ESCs are larger and dorsalized, as a consequence of an increased number of progenitors. These results suggest that human-specific mutations in critical regulatory elements controlling early brain development had a dramatic impact in the expansion and patterning of forebrain progenitors.

Gradual evolution of cell cycle regulation during the transition to animal multicellularity

Alberto Perez-Posada<sup>1</sup>, Omaya Dudin<sup>1</sup>, Eduard Ocaña-Pallarès<sup>1</sup>, Iñaki Ruiz-Trillo<sup>1,2,3</sup>, Andrej Ondracka<sup>1</sup>

<sup>1</sup> Institut de Biologia Evolutiva (CSIC-Universitat Pompeu Fabra), Passeig Marítim de la Barceloneta 37-49, 08003 Barcelona, Catalonia, Spain

<sup>2</sup> Departament de Genètica, Microbiologia i Estadística, Universitat de Barcelona, Av. Diagonal, 645, 08028 Barcelona, Catalonia, Spain

<sup>3</sup> ICREA, Passeig Lluís Companys 23, 08010, Barcelona, Catalonia, Spain

In animal cells, the progression through the cell cycle is coordinated by the activity of cyclins and cyclin-dependent kinases (CDKs). Temporal activity oscillations of specific cyclin-CDK complexes orchestrate other events, such as a temporal program of gene expression. In contrast to yeast, animals possess multiple members of the cyclin and CDK families. Despite our current knowledge of the cell cycle in other systems, how this regulation emerged in animals remains unknown. To shed light on the evolution of the cell cycle machinery, we characterized periodic expression of genes linked to cell-cycle regulation in a close unicellular relative of animals, the filopodiated amoeba Capsaspora owczarzaki. We performed RNA-seq in synchronized cell cultures, identifying a set of 801 periodic genes that grouped into five clusters of expression over time. Comparison with datasets from human cells and yeasts revealed that the periodic transcriptional program of *Capsaspora* is most similar to that of animal cells. Furthermore, we found that orthologues of cyclin A, B and E show the same temporal order of expression as in animals. The presence of one single ancestral CDK1-3 gene in Capsaspora suggests that this CDK is able to interact with cyclins A, B and E in the same temporal order as in animals, leading to a gradual evolutionary scenario where CDKs expanded and underwent functional specialization in the animal lineage.

# Estudio de los genes de la ruta piwi y la metilación de histonas en la desregulación de elementos transponibles en hibridos de Drosophila

Víctor Gámez Visairas<sup>1</sup>, Valeria Romero Soriano<sup>2</sup>, Joan Martí<sup>3</sup>, Cristina Vieira<sup>4</sup>, María Pilar García Guerreiro<sup>1</sup>

(1) Departament de Genètica i Microbiologia. Universitat Autònoma de Barcelona, 08193 Bellaterra (Barcelona), Spain.

(2) Institute of Integrative Biology. University of Liverpool. Liverpool L69 7ZB. United Kingdom

(3) Laboratory of clinical adn Epidemilogical virology Rega institute for Medical Research-Leuven

(4) Laboratoire de Biométrie et Biologie Evolutive, UMR5558, Université Lyon 1, Villeurbanne, France.

El estrés genómico causado por la hibridación interespecífica puede ocasionar inestabilidad genómica debido a la derepresión y amplificación de elementos transponibles (ETs) en el genoma de los híbridos. Estudios previos en híbridos entre las especies D. buzzatii y D. koepferae, realizados en nuestro grupo, mostraron alteraciones de los patrones de expresión de diferentes ETs, que no siempre estaban asociados a cambios en los niveles de los piRNAs encargados de su regulación. Con el fin de desentrañar los mecanismos implicados en la desregulación de ETs en híbridos, centramos nuestro estudio en los genes implicados en la ruta de síntesis de piRNAs así como los cambios en los patrones de metilación de las histonas a nivel genómico. Ambos estudios se llevaron a cabo en tejido germinal tanto en híbridos como en especies parentales. Los resultados señalaron, para algunos genes, un patrón de expresión complejo y diferente entre parentales e híbridos que no concordaba con un modelo aditivo. Dos de estos genes mostraban una sobreexpresión en híbridos respecto a ambos parentales, mientras que cuatro de ellos estaban sobre expresados respecto al menos uno de los parentales. Asimismo, observamos diferencias en la localización de los transcritos de uno de los genes dentro de las células germinales entre padres e híbridos. Por otra parte, el estudio de las marcas de metilación de las histonas, mediante la técnica de ChIP-seq, nos permitió detectar cambios en sus patrones de metilación en parentales respecto a híbridos En estos últimos se observaron zonas del genoma que están reprimidas mediante marcas de metilación y que estaban ausentes en los parentales. Estos resultados inducen a pensar en la existencia de mecanismos de desregulación extraordinariamente complejos en híbridos. El análisis minucioso de las secuencias del genoma afectadas está en curso y nos permitirá conocer que familias de ETs se encuentran afectadas, así como avanzar en el conocimiento de las bases moleculares de la inestabilidad híbrida y la esterilidad.

#### Repeat contribution to genome size ups and downs in family Asteraceae

Joan Pere Pascual-Díaz<sup>1\*</sup>, Daniel Vitales<sup>1\*</sup>, Teresa Garnatje<sup>1</sup>, Ales Kovarik<sup>2</sup>, Sònia Garcia<sup>1</sup>

<sup>1</sup>Institut Botànic de Barcelona, Consejo Superior de Investigaciones Científicas (IBB-CSIC)

<sup>2</sup>Institute of Biophysics, Czech Academy of Sciences (IBP-CAS)

(\*) Both authors contributed equally to this work.

**Introduction:** Angiosperms show one of the highest ranges of genome size (GS) variation, which may have significant evolutionary causes and consequences, including polyploidy and diversification. Most of the genome is composed by repetitive elements, including tandemly repeated DNA, such as satellite DNA, and dispersed DNA such as transposable elements, the latter accounting for the highest percentage of genome composition. Using as a model a wide representation of species from family Asteraceae, one of the most diversified and abundant of angiosperms, we aim to understand how GS varies through the most diversified tribes of the family by the detailed analysis of their repeat content.

**Methods:** We have analysed and compared the repetitive content of 15 tribes and 26 species from Asteraceae, through RepeatExplorer, a novel bioinformatics platform. In most cases (18), data has been specifically generated for this study by Illumina paired-end sequencing. For the remaining (8), data has been extracted from SRA in GenBank. Genome size of the species studied has been assessed by flow cytometry.

**Results:** Here we show the preliminary results indicating the repeat composition of the analysed species. Typically, LTR-retrotransposons *copia* (particularly SIRE) and *gypsy* (particularly Tekay and Athila) are the most abundant in most species (around 20%), while other transposable elements are specific of certain tribal, generic or specific levels. Tandemly arranged DNA such as rRNA genes account for around 0.5-1% of the genome.

**Discussion:** The comparisons of repeat abundance at the generic, tribal and subfamily levels allow us to infer the possible genomic contributors to the increased GS in tribes such as the Anthemideae, which is higher than most tribes in Asteraceae. In other tribes as the Gnaphalieae, the average GS is lower than the remaining tribes, and we detect which repetitive DNA elements are missing or particularly reduced in this group of lower GS.