S BAGE	PAGE 9	BAGE 53	40 -	46 BAGE
PROGRAM	SELECTED TALKS	SELECTED POSTERS	LIST OF PARTICIPANTS	S NOTES
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PRACTICAL INFO

COSMOCAIXA.

the Science Museum of "la Caixa" welfare service, opened on the 25th September of 2004. It occupies the facilities of which was the first interactive Science Museum in Spain (opened in 1981). Not only is it a great Museum, but also it pays special attention to Evolution. It is a must see for us and for our children.

NOTE FOR ASSITANTS:

A daily ticket will be hand by one of the organizers at the congres reception"

COSMOCAIXA BARCELONA Adress:c/ Isaac Newton, 26, 08022 Barcelona GPS coordinates: 41° 24' 47" N, 2° 7' 52" E



BY PUBLIC TRANSPORT



Ferrocarriles de la Generalitat (recomended) Ferrocarriles de la Generalitat de Catalunya Estación de Avinguda del Tibidabo



Bus

17, 22, 58, 73, 75, 60 y 196



PROGRAM

WEDNESDAY NOVEMBER 27TH

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09:00 09:30 Registration	09:00	09:30	Registration
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09:30 09:45 Welcome Address.

09:45 10:45 Opening Session.

Dan Graur. "How to Assemble a Human Genome? Mix generous amounts of Junk DNA and Indifferent DNA, add a Dollop of Garbage DNA and a Sprinkling of Functional DNA (Lazarus DNA optional)"

Session I. Evolutionary Systems Biology.

Chairs: Susana Manrubia & Juli Peretó.

09:45 11:30 Guest Speaker. Ricard Solé. "The major transitions: a Synthetic life Perspective"

11:30 12:00



Coffee Break and Poster Placement

Session I. Talks.

12:00	12:20	"toyLIFE: a toy Universe for gaining insight into evolution". Pablo Catalan
12:20	12:40	"Synteny in Bacteria: A Universal Law Shaped by Positive Selection". Ivan Junier
12:40	13:00	"A heuristic model on the role of plasticity in adaptive evolution". Ivan Gomez-Mestre
13:00	13:20	"Evolutionary study of metabolic pathways from a topological and functional network perspective". Ludovica Montanucci
13:20	13:40	"Neutral evolution and phenotypic entrapment". Jose A Cuesta

13:40 15:40



Lunch and Poster Session I

Session II. Evolutionary Medicine.

Chairs: Álvaro Daschner & María José Trujillo Tiebas.

15:40	16:25	Guest Speaker. Randolph Nesse. "The Smoke Detector Principle and Medical Decision Making"
16:25	16:45	"Craniosynostosis and The Evolution Of The Human Skull". Diego Rasskin-Gutman
16:45	17:05	"Anisakis simplex hemoglobin, evolution and allergy". Juan González-Fernández
17:05	17:25	"The role of social niche specialization in the evolution of cognitive syndromes". Pau Carazo
17:25	17:45	"A genome wide exploration of the pleiotropic theory of senescence. Are human disease and senescence the result of natural selection?" Juan Antonio Rodriguez
17:45	18:05	"Out-of-Africa migration and Neolithic coexpansion of Mycobacterium tuberculosis with modern humans". Iñaki Comas.
18:05	18:25	"Genome-wide analysis of wild-type Epstein-Barr virus genomes derived from healthy individuals of the 1000 Genomes Project". Gabriel Santpere.

THURSDAY NOVEMBER 28TH



Session III. Population Genetics and Genomics

Chairs: Francesc Calafell & Julio Rozas.

09:30 10:15 **Guest Speaker. Juliette de Meaux**. "Cis-regulatory divergence in the Arabidopsis genus"

10:15 10:45 Coffee Break and Poster Placement

10:45	11:05	"Estimating inbreeding coefficients from NGS data: impact on genotype calling and allele frequency estimation". Filipe Garrett Vieira.
11:05	11:25	"Population genomics and epidemiology of Legionella pneumophila outbreaks". Fernando Gonzalez-Candelas.
11:25	11:45	"Evolution of the Upstream Gene Regions: Evidence for Positive Selection in the Major Chemosensory Families". Pablo Librado.
11:45	12:05	"Detection of evidences of selection in human polymorphic inversions". David Castellano.
12:05	12:25	"Whole-exome sequencing reveals a rapid change in the frequency of rare functional variants in a founding population of humans". Ferran Casals.
12:25	12:45	"Great ape genetic diversity and population history". Javier Prado-Martinez.
12:45	14:00	Especial event. 3D Film. Selección Natural (Natural Selection). Charles Darwin trip on board of the HMS Beagle.

14:00 16:30 Lunch and Poster Session II

14:30 SESBE Assembly (simultaneous with lunch). Only for SESBE members

vative destabilizing mutations". Mario Fares.

Session IV. Functional Evolution.

Chairs: María Dolors Piulachs, Xavier Franch & Pedro Martinez.

16:30	17:15	Guest Speaker. Michael Akam. "Conservation and divengence in arthropod developmental mechanisms: insights from a centipede"
17:15	17:35	"Regulated aggregative multicellularity in a close unicellular relative of Metazoa". Arnau Sebé-Pedrós.
17:35	17:55	"Evo-devo contributions for understanding the forebrain". Loreta Medina.
17:55	18:15	"The evolution of androdioecism in Prockia krusei: evidences of the flower's development and structure". César Antonio Abarca-García.
18:15	18:35	"De novo sequencing and comparison of the inferred central nervous system transcriptomes of the solitary and gregarious Schistocerca gregaria". Rubén Martín-Blázquez.
10.70	10.00	"On the emergence of novel functions in microbes: unearthing the evolutionary trajectories of inno-

"DNA Uptake Sequences, Uptake Signal Sequences, DNA Uptake Enhancing Sequences, what are they anyway?". Mohammed Bakkali.

21:00 23:00 **Meeting Dinner.** Restaurant of Catalonia's History Museum (www.en.mhcat.cat).

FRIDAY NOVEMBER 29TH



Session V. Phylogeny and Systematics.

Chairs: Toni Gabaldón & José Castresana.

09:30	10:15	Guest Speaker. Martin Embley. "Disentangling the origins of eukaryotic cells: genes, trees and organelles"
10:15	10:35	"Life-history evolution and mitogenomic phylogeny of caecilian amphibians". Diego San Mauro.
10:35	10:55	"Striking functional and molecular differences among endosymbiotic lineages from five mealybug species". Sergio López Madrigal.

10:55	11:30		Coffee Break.
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11:30	19.00	Presentation of SESBE's Book "La Evolución Biológica: una reconstrucción darwinista".
	1.00	18:00

12:00	12:20	"Cryptic diversity and evolution of Australian Pseudotetracha tiger beetles". Alejandro López.
12:00	12:40	"The freshwater planarian Dugesia: A long history for a genus, from Gondwana to the present". Eduard Solà.
12:40	13:00	"Transcription factor evolution and the origins of multicellularity in eukaryotic lineages". Alex de Mendoza.
13:00	13:20	"Key innovations and island colonization as engines of evolutionary diversification: a comparative test with the Australasian diplodactyloid geckos". Joan Garcia-Porta.

SELECTED TALKS

SESSION I: EVOLUTIONARY S YSTEMS BIOLOGY.

Chairs: Susana Manrubia & Juli Peretó.



12:00 -12:20

TOYLIFE: A TOY UNIVERSE FOR GAINING INSIGHT INTO EVOLUTION.

Pablo Catalán,

Clemente Fernández-Arias and José A. Cuesta

Grupo Interdisciplinar de Sistemas Complejos (GISC),

Departamento de Matemáticas, Universidad Carlos III de Madrid

The existence of neutral mutations has been known since the middle of the 20th century. With the recent access to genome sequences, however, the relevance of neutrality has become more patent. Many models have attempted to study the effects of this neutrality on evolution. Usually, these models assume that every organism has a genotype and an associated phenotype. If an organism mutates, it changes into another genotype. but not necessarily into another phenotype. Genotypes that are associated to the same phenotype are said to be in the same neutral network. If a genotype can suffer many mutations without changing its phenotype, it is said to be robust. Models that study these phenomena define various kinds of "genotypes" - RNA, proteins, gene regulatory networks (GRNs) - and a corresponding "phenotype" - secondary structure in the case of RNA and proteins, and gene expression patterns, in the case of networks. Then, various properties of these neutral networks are studied. However, there are many levels of degeneracy that contribute to neutrality and are not taken into account in these models. Besides, it is difficult to define mutations on "genotypes" such as gene networks: if mutations affect the DNA, how are these changes translated into gene network structure? To solve these problems, we have developed a toy model that includes several levels of organization in order to study the effect of degeneracy on mutational robustness.

We present here toyLIFE, a new framework designed to study the evolution of organisms at various levels of organization. toyLIFE contains analogs of genes, aminoacids and proteins, which interact through well-defined physical laws to produce "toyGRNs". This simple framework allows us to study how the effects of mutation at the "toyDNA" level are carried to higher levels, leading to new insights on the evolution of these systems.

We studied the functioning of toyLIFE organisms, observing how its behavior strongly resembles the one we observe in real cells. We then used toyLIFE to study how mutations in toyGenes were translated into changes in protein structure, protein interactions and network behavior. We have seen that degeneracy accumulates between levels in a non-trivial way. We show that, for instance, it is not possible to deduce the structure of the GRN neutral network from the properties of the networks of protein structures. To correctly study the properties of a neutral network, all the lower levels of organization must be taken into account. Failure to account for these complexities may lead to erroneous conclusions about evolution.



12:20-12:40

SYNTENY IN BACTERIA: A UNIVERSAL LAW SHAPED BY POSITIVE SELECTION.

Ivan Junier¹ and Olivier Rivoire²

- ¹ Centre for Genomic Regulation (CRG) Dr. Aiguader 88, 08003 Barcelona, Spain;
- ² CNRS/Université Joseph Fourier Grenoble 1, Laboratoire Interdisciplinaire de Physique (LIPhy), UMR 5588, 38402 Saint Martin d'Hères, France

Genes are not located randomly along genomes. Synteny, the conservation of their relative positions in genomes of different species, reflects fundamental constraints on natural evolution. We present approaches to infer pairs of co-localized genes from multiple genomes, describe their organization, and study their evolutionary history.

In bacterial genomes, we thus identify synteny units, or "syntons", which are clusters of proximal genes that encompass and extend operons. These syntons are strongly correlated with experimentally determined genomic domains of protein occupancy, suggesting structural and regulatory properties that implicate nucleoid associated proteins. The size distribution of syntons partition them into two groups: large syntons, which correspond to fundamental macro-molecular complexes of bacteria, and smaller ones, which display a remarkable exponential distribution of sizes. This distribution is "universal" in two respects: it holds for vastly different genomes, and for functionally distinct genes.

Similar statistical laws have been reported in previous studies of bacterial genomes, and generally attributed to purifying selection or neutral processes. A parsimony-based analysis reveals here that the prevailing evolutionary mechanism behind the formation of small syntons is a selective process of gene aggregation. Altogether, our results imply a common evolutionary process that selectively shapes the organization and diversity of bacterial genomes.

1. I. Junier and O. Rivoire, Synteny in Bacterial Genomes: Inference, Organization and Evolution, submitted, arXiv:1307.4291



12:40-13:00

A HEURISTIC MODEL ON THE ROLE OF PLASTICITY IN ADAPTIVE EVOLUTION.

Ivan Gomez-Mestre and Roger Jovani

Estacion Biologica de Doñana, CSIC, Seville E41092, Spain

Environmental fluctuations are the rule rather than the exception in nature, and organisms have therefore usually evolved in heterogeneous environments. Environmental

heterogeneity, together with gene flow among subpopulations, is known to contribute to the maintenance of standing genetic variation within populations, required to fuel responses to selection imposed by rapidly changing environments. However, fluctuating conditions also favor the evolution of the ability to produce appropriate phenotypes under different environments, known as adaptive phenotypic plasticity. Here we present an individual-based heuristic model to compare the adaptive dynamics of populations composed of plastic or non-plastic genotypes under a wide range of scenarios where we modify environmental variation, mutation rate and costs of plasticity. The model illustrates how adaptive plasticity helps maintaining genetic variation within populations, reduces bottlenecks when facing rapid environmental changes, and confers an overall faster rate of adaptation.

Plasticity is favored by selection under fluctuating conditions. However, if the environment stabilizes and costs of plasticity are high, plasticity is reduced by selection leading to genetic assimilation, which could result in species diversification. More broadly, our model shows that adaptive plasticity is a common consequence of selection under environmental heterogeneity, and a potentially common phenomenon in nature. Adaptive plasticity may be critical in allowing populations to persist long enough until the required genetic variation necessary to cope with novel environments arises.



13:00-13:20

EVOLUTIONARY STUDY OF METABOLIC PATHWAYS FROM A TOPOLOGICAL AND FUNCTIONAL NETWORK PERSPECTIVE.

Ludovica Montanucci¹

Hafid Laayouni¹, Juli Peretó², Martino Colombo^{1,3}, Brandon M. Invergo¹, Kevin Keys¹ and Jaume Bertranpetit¹

- ¹ IBE Institute of Evolutionary Biology (CSIC Pomepu FabraUniversity),
- ² Institut Cavanilles de Biodiversitat i Biologia Evolutiva, *Universitat de València,*
- ³ University of Bern, Dept. Chemistry and Biochemistry

Relationships between evolutionary rates and gene properties on genomic, functional, pathway or system levels, are being explored to unravel the principles of the evolutionary process. In particular, network properties, both topological and functional, have been analyzed to recognize the constraints they may impose on the evolutionary fate of genes.

Topological properties have been analyzed to date, at a small scale, on a small number of specific metabolic pathways. Results show that a fraction of the variance in evolutionary rates of the enzyme-coding genes is indeed accounted for by their topological position within the metabolic network, however no general pattern has been identified. Here we undertake the study of the whole set of human metabolic pathways to derive a general picture of how selection is distributed over metabolic networks.

Functional network properties on the other hand have been loosely explored because of the lack of dynamical characterization for the most of the known systems and pathways. However, a specific metabolic system, the core metabolic network in human erythrocytes, is endowed with a comprehensive kinetic model that allows analyzing the relationship between the evolutionary rates of its genes and a relevant functional network

property: the metabolic flux distribution throughout it.

Our results show that while topology is a common determinant of evolutionary rates in human metabolic pathways, dynamical system-level properties also exert constraints on the evolution of the underlying genes. In particular we found that, in the erythrocyte core metabolic network, enzymes carrying high metabolic fluxes are more constrained in their evolution. The results demonstrate the importance of considering the dynamical functioning of gene networks when assessing the action of selection on system-level properties.



13:20-13:40

NEUTRAL EVOLUTION AND PHENOTYPIC ENTRAPMENT.

José A. Cuesta^{1,2,3} and Susanna Manrubia^{1,4}

- ¹ Grupo Interdisciplinar de Sistemas Complejos (GISC);
- Departamento de Matemáticas, Universidad Carlos III de Madrid, 28911 Leganés, Madrid (Spain);
- ³ Instituto de Biocomputación y Física de Sistemas Complejos (BIFI), Universidad de Zaragoza 5009 Zaragoza (Spain);
- ⁴ Centro de Astrobiología (CAB), CSIC-INTA, 28850 Torrejón de Ardoz, Madrid (Spain)

Large sets of genotypes give rise to the same phenotype because phenotypic expression is highly redundant. Accordingly, a population can accept mutations without altering its phenotype, as long as they transform its genotype into another one on the same set. By linking every pair of genotypes that are mutually accessible through mutation, genotypes organize themselves into genotype networks (GN). These networks are known to be heterogeneous and assortative. As these features condition the probability that mutations keep the phenotype unchanged—hence becoming blind to natural selection—it follows that the topology of the GN will influence the evolutionary dynamics of the population. We analyze this effect by studying the dynamics of random walks (RW) on assortative networks with arbitrary topology¹. We find that the probability that a RW leaves the network is smaller the longer the time spent in it—i.e., the process of phenotypic evolution is not Markovian. From the biological viewpoint, this "phenotypic entrapment" entails an acceleration in the fixation of neutral mutations, thus implying a non-uniform increase in the ticking rate of the molecular clock with the age of branches in phylogenetic trees. This effect is stronger the larger the fitness of the current phenotype relative to that of neighboring phenotypes.

¹http://arxiv.org/pdf/1307.0968v1.pdf

SESSION II: EVOLUTIONARY MEDICINE

Chairs: Álvaro Daschner & María José Trujillo Tiebas



16:25-16:45

CRANIOSYNOSTOSIS AND THE EVOLUTION OF THE HUMAN SKULL

Diego rasskin-Gutman¹ and Borja-Esteve-Altava¹

Theoretical Biology Research Group.

Institute Cavanilles for Biodiversity and Evolutionary Biology.

PARC CIENTIFIC. *University of Valencia*

Reduction in number of bones in the vertebrate skull is a macroevolutionary trend, known as Williston's Law, which occurs mainly due to two developmental processes: loss and fusion of bones. When fusion of bones happens prematurely during early human development, closure of cranial sutures occurs (craniosynostosis), which is a source of skull deformities, a medical condition whose incidence is about 3 to 5 in 10,000 births. The fact that a developmental process that causes evolutionary trends is also a source of a medical condition gives a unique opportunity to carry out a study on evolutionary medicine focused on organismic features.

Premature suture closure causes structural changes of the skull, shape malformations due to compensatory growth, and morphological novelties. These structural changes can be modeled and quantified using Network Analysis. Within this framework, skulls are modeled as a network, in which nodes and links of the network represent the bones and suture contacts of the skull bones, respectively. Using Topological Overlap as a measure of similarity we carried out a Multidimensional Scaling Analysis to predict bone shape deformation as a function of connectivity pattern. We show a preliminary analysis, comparing the skull network of a normal child at birth with paired frontals and occipital bones not fused, to network models for each of the following craniosynostosis conditions: (1) metopic, (2) sagittal, (3) left hemicoronal, (4) bicoronal, (5) lambdoidal, and (6) 'true' lambdoidal.

Our network models successfully predict the direction of bone malformation, showing how network models bring about new ways to study morphological integration and modularity in the human skull from an evolutionary and medical perspective.



16:45-17:05

ANISAKIS SIMPLEX HEMOGLOBIN, EVOLUTION AND ALLERGY.

Juan González-Fernández¹,

Alvaro Daschner², Natalie Nieuwenhuizen³, Carmen Cuéllar¹

- Departamento de Parasitología, Facultad de Farmacia, Universidad Complutense de Madrid, 28040 Madrid-Spain;
- ² Servicio de Alergia. Instituto de Investigación Sanitaria Hospital Universitario de La Princesa, 28006 Madrid-Spain.
- ³ Department of Immunology, Max Planck Institut für Infektionsbiologie, 10117 Berlin-Germany.

Globins are proteins commonly associated with oxygen transport in vertebrate blood. However invertebrate organisms display a wide variety of globin types. Their functions are mainly enzymatic and less frequently sensors. The transport of oxygen is a recently evolved function which has developed with the emergence of multicellular organisms [1]. Another well-known characteristic of hemoglobin is its role as allergen. In 1990, Mazur et al. characterised the inhalant allergenic hemoglobin of the midge *Chironomus thummi thummi* [2]. *Ascaris lumbricoides* and *A. suum* are cosmopolitan nematodes which parasitise humans and pigs, respectively and have a long history of host-parasite interaction. On the other hand Anisakis simplex is a parasite not adapted to humans but to marine mammals. *In vitro* experiments have shown that *Anisakis simplex* hemoglobin is a potent allergen which induces specific IgE antibodies, but unexpectedly these antibodies did not recognise haemoglobin of *Ascaris*, which belongs to the same family [3]. Our hypothesis is that different evolution in host-parasite interaction of both nematodes, have shaped hemoglobin proteins to display not only different known functions, but also different IgE recognition.

Hemoglobin sequences of *Ascaris suum*, *Homo sapiens*, *Anisakis pegreffi*, and *Chironomus thummi* were obtained from the NCBI protein database. Corresponding PDB structures were obtained from rcsb.org but *A. pegreffi* and *A. suum* hemoglobin were modeled using HHPred from www.proteinmodelportal.org. These models were evaluated using QMEAN server. The epitopes were predicted with Discotope 2.0, visualizing the results with PyMol. Different structure alignment software were tested. CLICK server, which offers to align 3D structures of biomolecules not restricted to any one type, was used for aligning in pairs. For multiple structure alignments, msTali was used. Both servers consider residue solvent accessible surface area, which is essential to observe the possible IgE interactions. Mega5.2 was used for constructing phylogenetic trees and GeneDoc for editing the alignments. Calculations of Area and electrostatic potential were obtained from Getarea 1.1 and APBS web server.

The electrostatic potential, relevant for antigen-antibody interactions [4], has been mapped on the molecular surfaces showing important differences in the *Anisakis* hemoglobin. Five epitopes were predicted in *A. simplex* hemoglobin. One of them seems to be specific for *Anisakis*. Aligning complementary epitopic surfaces of Chi t 1.01 (experimentally confirmed, [5]), Anisakis and Ascaris hemoglobin; we could construct a phylogenetic tree based on the fit of the epitopic surfaces.

This phylogenetic tree confirms the epitopic similarity related to IgE binding between Chi t 1 and Anisakis hemoglobin, as well as, the hypothesised differences between *Ascaris* and *Anisakis* ones. On the other hand, epitopic similarities between Ascaris and human hemoglobin were demonstrated according to the evolutionary history of both parasite and host. Therefore, our results show the usefulness of this methodology for predicting possible cross-reactivity to allergens.

- 2. Mazur G et al. Monogr Allergy. 28:121-37, 1990.
- 3. Cuéllar et al. Encuentro internacional de parasitólogos de España, Francia, Italia y Portugal. ISBN 10: 84-695-8471-5; ISBN 13: 978-84-695-8471-2. 1: 55, 2013.
- 4. van Oss CJ. Mol Immunol. 32:199-211, 1995. 5. van Kampen et al. Allergy 56: 118-125, 2001.



17:05-17:25

THE ROLE OF SOCIAL NICHE SPECIALIZATION IN THE EVOLUTION OF COGNITIVE SYNDROMES.

Pau Carazo^{1,2,} Daniel W.A. Noble², Martinand Martin J. Whiting²

- Edward Grey Institute, Department of Zoology, University of Oxford, Oxford OX1 3PS, UK;
- ² Department of Biological Sciences, Macquarie University, Sydney, New South Wales, Australia

Our understanding of animal personalities has advanced considerably, generating several adaptive models and hypotheses about the evolution of individual variation in non-cognitive behaviour [1]. In sharp contrast, studies have largely ignored the evolution and function of individual variation in cognitive performance [2]. Despite the existence of widespread intraspecific variation in cognitive performance, we remain ignorant about how it relates to ecology, selection and development at the individual level, and why. A recent proposal is that variation in cognition is functionally related to variation in personality by the existence of a shared risk-reward trade-off between fast-slow behavioural syndromes and speed-accuracy cognitive styles [3].

Here, we present a complementary scenario: the evolution of behavioural- cognitive syndromes by individual diversification/specialization into different social niches [4]. We suggest that behavioural-cognitive syndromes can result from disruptive selection on suites of behaviours/cognitive traits involved in divergent social roles and/or tactics. Importantly, these processes can give rise to personality- cognitive syndromes that cannot be explained by risk-reward trade-offs. In addition, we present data from a study exploring this possibility in the Eastern Water Skink (*Eulamprus quoyii*), where we examined associations between exploration, boldness and individual variability in spatial learning, a dimension of lizard cognition with important bearing on fitness.

In contrast to previous studies, we found a non-linear association between boldness and learning: both 'bold' and 'shy' behavioural types were more successful learners than intermediate males. Our results do not fit with recent predictions suggesting that individual differences in learning may be linked with behavioural types via high-low risk/reward trade-offs, but fit nicely with the possibility that differences in spatial cognitive performance may arise in lizards as a consequence of the distinct environmental variability and complexity experienced by individuals as a result of their sex and social tactics.

^{1.} Dingemanse, N. J., & Wolf, M. (2010) Recent models for adaptive personality differences: a review. Phil. Trans. Roy. Soc. B 365: 3947-3958.

^{2.} Thornton, A. and Lukas, D. 2012. Individual variation in cognitive performance: developmental and evolutionary perspectives. Phil. Trans. Roy. Soc. B 367: 2773-2783.

- 3. Sih, A. and Del Guidice, M. 2012. Linking behavioural syndromes and cognition: a behavioural ecology perspective. Phil. Trans. Roy. Soc. B 367: 2762-2772.
- 4. Bergmüller, R. and Taborsky, M. 2010. Animal personality due to social niche specialization. TREE 25: 504-511.



17:25-17:45

A GENOME WIDE EXPLORATION OF THE PLEIOTROPIC THEORY OF SENESCENCE. ARE HUMAN DISEASE AND SENESCENCE THE RESULT OF NATURAL SELECTION?.

Juan A Rodriguez ¹ and Arcadi Navarro ^{1,2,3,4}

- ¹ Institute of Evolutionary Biology (Universitat Pompeu Fabra-CSIC), PRBB, Doctor Aiguader 88, 08003, Barcelona, Catalonia, Spain;
- ² Centre de Regulació Genòmica (CRG). *Barcelona, Catalonia, Spain;*
- ³ National Institute for Bioinformatics (INB), *Barcelona, Catalonia, Spain;*
- ⁴ Institució Catalana de Recerca i Estudis Avançats (ICREA), Catalonia, Spain

The increasing global ageing of the World's population, has spurred the interest on the causes and mechanisms of senescence, the physical decay of organisms with age. Senescence has long been a mystery and, as of today, there is no single universally accepted theory that accounts for the ultimate evolutionary purpose of senescence (if indeed there is one). Perhaps the most popular of the evolutionary explanations proposed so far is the pleiotropic theory of senescence, suggested by G. Williams in 1957¹. This theory states that mutations conferring risk for traits that are damaging for the organism late in life (e.g. after the fertile stage) might be maintained in a population if they are advantageous early in life, when they can result in an increased reproductive success.

In humans, this theory is consistent with evidence coming from certain genes (*mTOR*, from specific conditions (*haemochromatosis*) or from the life-long reproductive patterns of a few animal models (swans and the fruit fly). Interestingly, recent genome wide association studies (*GWAS*) show that pleiotropy is common², with at least 17% of the genes and 4.6% of SNPs associated to a given disease being involved in 2 or more conditions. However, an exhaustive assessment of the impact of all these pleiotropic effects in the senescence of our species has not yet been carried out.

Using public metadata from Genome-Wide Association Studies (GWAS)³ we quantified the global extent and evolutionary implications of the kind of early-late age antagonistic pleiotropy defined in our species. Disease conditions were split in early or late onset conditions, based on several age thresholds. Pleiotropies were computed among the SNPs reported associated to the diseases. To gather data on SNPs, we used strategies based in its LD properties to increase sample size.

Our preliminary results are two-fold. First, they revealed some non-trivial antagonistic pleiotropies such as between bipolar disorder and osteoarthritis, or glioma and glaucoma, that may be relevant to diagnosis and treatment of age-related disease. Second, and more interestingly in evolutionary terms, we observed a significant excess of early-late antagonistic pleiotropy in our genomes.

At the time of this submission, we are examining the ancestral or derived state of the alleles involved in these pleiotropies and studying the potential signature of natural selection in the genomic regions harbouring these SNPs.

- 1. Hindorff, LA et al., (2009) NHGRI GWAS Catalog: https://www.genome.gov/26525384
- 2. Sivakumaran, S. (2011) Abundant pleiotropy in human complex diseases and traits.
- 3. Williams, G. (1957). Pleiotropy, natural selection, and the evolution of senescence.



17:45-18:05

OUT-OF-AFRICA MIGRATION AND NEOLITHIC COEXPANSION OF MYCOBACTERIUMTUBERCULOSIS WITH MODERN HUMANS.

Iñaki Comas^{1,2}, Qian Gao³, Stefan Niemann⁴, Julian Parkhill⁵, Douglas Young⁶, Sebastien Gagneux⁷

- ¹ Center for Public Health Research, CSISP-FISABIO, Valencia, S4pain;
- ² CIBER Epidemiology and Public Health, *Madrid*;
- ³ Fudan University, Shangai, China;
- ⁴ Research Center Borstel, *Borstel, Germany*;
- ⁵ Wellcome Trust Sanger Institute, Hixton, *United Kingdom*;
- ⁶ National Institute for Medical Research, London, United Kingdom;
- ⁷ Swiss Tropical and Public Health Institute, *Basel, Switzerland;*
- ⁸ University of Basel, *Basel, Switzerland*

Tuberculosis (TB) used to cause up to 20% of human deaths between the 17th and 19th centuries in Europe and North-America, and² remains a cause of high morbidity and mortality in much of the developing world. Recent data suggest human TB might predate the Neolithic revolution. Moreover, unlike most other typical crowd diseases, TB exhibits a characteristic latency period which can last for decades, a phenomenon thought to reflect adaptation to low host densities³. Here we applied massive genome sequencing to a global collection of 259 clinical isolates of human tuberculosis to study the origin of the disease and the population dynamics of the bacteria during the last millennia.

We used the Illumina platform to genome sequence a global collection of 220 isolates of the *Mycobacterium tuberculosis* complex (MTBC) plus 39 additional strains from China. We have used several phylogeographic approaches (RAST, BEAST) to infer the most likely location of the ancestor of extant MTBC strains. We have also compare MTBC phylogeny with more than 5,000 mtDNA genomes from diverse human populations. We have used BEAST to date the origin of the complex and to characterize changes of genetic diversity of the MTBC over time in a global and a regional (China) scale.

Here we show that the genome-based phylogeny clinical strains representing the global diversity of MTBC reveals striking parallels with a corresponding tree built from human mitochondrial genomes. Coalescent analyses suggest MTBC emerged 70 Kya and was ubiquitous in the first modern humans migrating out of Africa. We then tested the hypothesis that TB not only depends on host population sizes but also on host densities by looking at the population diversity changes of the bacilli at a global scale and also at a local scale by analyzing 76 East-Asian lineage genomes. In both cases bayesian skyline

plots shows parallel population expansions with humans associated to the Neolithic and agricultural revolutions. The most striking finding is that TB was able to maintain cycles of infection and to avoid its own extinction in small pre-Neolithic hunter-gathered populations. We hypothesize that the higher virulence associated with contemporary TB is a comparably recent phenomenon that evolved as a consequence of the increases in human hosts densities during the Neolithic and/or industrial revolutions³.

- 1. Wilson, L.G. Commentary: Medicine, population, and tuberculosis. Int. J. Epidemiol. 34, 521-4 (2005). 2. WHO, G. The Global Plan to STOP TB 2011-2015. WHO (2011).
- 3. Comas I, et al. Out-of-Africa migration and Neolithic co-expansion of Mycobacterium tuberculosis with modern humans. Nature Genetics 2013 In press.



18:05-18:25

GENOME-WIDE ANALYSIS OF WILD-TYPE EPSTEIN-BARR VIRUS GENOMES DERIVED FROM HEALTHY INDIVIDUALS OF THE 1000 GENOMES PROJECT.

Gabriel Santpere¹,

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Most people in the world (~90%) are infected by the Epstein-Barr virus (EBV), which establishes itself permanently in B-cells. Infection by EBV is related to a number of diseases including infectious mononucleosis, multiple sclerosis and different types of cancer. So far, only seven complete EBV strains have been described, all of them coming from donors presenting EBV-related diseases.

To perform a detailed comparative genomics analysis of EBV including, for the first time, EBV strains derived from healthy individuals we reconstructed EBV sequences infecting lymphoblastoid cell lines (LCLs) from the 1000 Genomes Project. Since strain B95-8 was used to transform B-cells to obtain LCLs, it is always present, but a specific deletion in its genome sets it apart from natural EBV strains. After studying hundreds of individuals, we determined the presence of natural EBV in at least 10 of them and obtained a set of variants specific to wild-type EBV. By mapping the natural EBV reads into the EBV reference genome (NC007605) we constructed wild-type viral genomes from three individuals.

Analysis of all the available sequences reveals a complex history of recombination among EBV strains and that latency genes harbour more nucleotide diversity than lytic genes. Six out of nine latency-related genes present the molecular signature of positive selection, suggesting rapid host-parasite co-evolution.

SESSION III: POPULATION GENETICS AND GENOMICS.

Chairs: Francesc Calafell & Julio Rozas



10:45-11:05

ESTIMATING INBREEDING COEFFICIENTS FROM NGS DATA: IMPACT ON GENOTYPE CALLING AND ALLELE FREQUENCY ESTIMATION

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Current NGS technologies produce short read sequences that are denovo assembled or mapped (aligned) to a reference genome and used for SNP or genotype calling. However, these data typically have high error rates due to multiple factors, from random sampling of homologous base pairs in heterozygotes, to sequencing or alignment errors. Furthermore, many NGS studies rely on low coverage sequence data (< 5× per site per individual), causing SNP and genotype calling to be associated with considerable statistical uncertainty. Recent methods rely on probabilistic frameworks to account for these errors and accurately call SNPs and genotypes, even at low depths (Li, 2011; Nielsen et al., 2012). These methods integrate the base quality score together with other error sources (e.g., mapping or sequencing errors) to calculate an overall "genotype likelihood". This likelihood function can be combined with a prior to calculate a posterior probability for the genotype. Most genotype calling methods for Next Generation Sequencing (NGS) data use priors based on allele frequencies under the assumption of HardyWeinberg Equilibrium (HWE). However, many organisms including domesticated, partially selfing or with asexual life cycles show strong HWE deviations. For such species, and specially with low coverage data, it is necessary to obtain estimates of inbreeding coefficients for each individual before genotype calling.

Here, we present two methods to estimate inbreeding coefficients from NGS data under a probabilistic framework based directly on genotype likelihoods. These estimates can then be incorporated into the genotype prior to provide improved calculations of genotype posterior probabilities. We demonstrate the accuracy of our method using simulation and show that the new method leads to increased accuracy in genotype calling and estimation of the Site Frequency Spectrum (SFS), specially on highly inbred individuals. Finally, we apply our method to a previously published rice dataset (Xu et al., 2011) and show marked improvements over previous methods.

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^{1.}Li H. 2011. A statistical framework for SNP calling, mutation discovery, association mapping and population genetical parameter estimation from sequencing data. Bioinformatics 27: 298793 2.Nielsen R, Korneliussen T, Albrechtsen A, Li Y, and Wang J. 2012. SNP calling, genotype calling, and sample allele frequency estimation from NewGeneration Sequencing data. PLoS One 7: e37558 3.Xu X, Liu X, Ge S, Jensen JD, Hu F, Li X, Dong Y, Gutenkunst RN, Fang L, Huang L, et al. 2011. Resequencing 50 accessions of cultivated and wild rice yields markers for identifying agronomically important genes. Nat Biotechnol 30: 105-11



11:05-11:25

POPULATION GENOMICS AND EPIDEMIOLOGY OF LEGIONELLA PNEUMOPHILA OUTBREAKS. DETECTION OF EVIDENCES OF SELECTION IN HUMAN POLYMORPHIC INVERSIONS.

Leonor Sánchez-Busó, Iñaki Comas and **Fernando González-Candelas.**

Joint Research Unit "Genomics and Health" FISABIO-University of Valencia. CIBERESP.

Legionella pneumophila is a strictly environmental, opportunistic pathogen and the main causing agent of legionellosis and Pontiac fever. It lives in aquatic environments and associated biofilms, from where it colonizes risk facilities to be disseminated by aerosols and infect susceptible persons. In the city of Alcoy (Spain), 18 legionellosis outbreaks, totaling 343 cases, were declared in the 1999-2010 period. These outbreaks were studied by traditional and molecular epidemiology methods. Now, we have used whole-genome sequencing to characterize strains related to legionellosis outbreaks in this area and in the nearby city of Calpe and to estimate their evolutionary and demographic dynamics.

We have analyzed 69 clinical and environmental *L. pneumophila* strains isolated during the epidemiological investigations of 13 different outbreaks produced in Alcoy and 6 from an outbreak produced in a hotel in Calpe in 2012. Most isolates from Alcoy corresponded to sequence type (ST)-578 (n=48) and ST1 (n=10), as determined by multilocus sequence typing (MLST), whereas those from Calpe mainly corresponded to ST23. We performed whole-genome sequencing (WGS) using SOLiD 5500XL technology, producing single-end 75 bp reads with an average coverage of 90X. The complete genome sequences were compared with 9 genomes of this species available from public databases. A reference genome was constructed by maximum-likelihood inference and it was used to derive the core and pangenome components of each genome. Ensuing phylogenetic, genetic variability and demographic reconstruction analyses were performed with the appropriate multiple alignments of the corresponding core genomes.

Genetic variability in Alcoy has increased through time and this is reflected in similar levels of variation within and among outbreaks. The demographic reconstruction indicates that two sublineages within ST578 have diverged in the Alcoy area since their initial establishment more than 20 years ago. The population dynamics of these lineages is also reflected at the epidemiological level and the genomic analysis has allowed us to ascertain the differential evolution of these two lineages. Similarly, demographic reconstruction of samples from the hotel in Calpe indicates that these strains likely colonized these premises at the time of its opening, in 2006, having evolved there ever since.

Results from this study lead to a change in the current view of legionellosis outbreaks as we reveal that they may not be clonal when analyzed by whole genome typing methods. The identification of a single source by low-resolution typing methods can be misleading when the actual genetic variability of *L. pneumophila* strains colonizing an area is not considered.



11:25-11:45

EVOLUTION OF THE UPSTREAM GENE REGIONS: EVIDENCE FOR POSITIVE SELECTION IN THE MAJOR CHEMOSENSORY FAMILIES.

Pablo Librado and Julio Rozas

Departament de Genètica and Institut de Recerca de la Biodiversitat (IRBio)

In insects, the peripheral chemosensory processes are mediated by proteins encoded in moderately-sized multigene families, including extracellular ligand-binding proteins such as odorant-binding proteins (OBPs) and chemosensory proteins (CheBs and CSPs), as well as membrane receptor proteins such as olfactory receptors (ORs), gustatory receptors (GRs) and ionotropic receptors (IRs). Since the ability to discriminate external chemical cues -and thus the individual fitness- depends on such proteins, chemosensory gene families may represent excellent candidates to gain insights into the role of positive selection in shaping transcriptional evolution.

Here, we use the functional annotation of the fly genome (modENCODE project), and the DNA sequence data of 158 D. melanogaster lines (DGRP project) from a single population (Raleigh, North Carolina) to perform a comprehensive analysis of the chemosensory upstream gene regions. In particular, we aim to infer the evolutionary forces underlying the patterns and levels of nucleotide variability and the turnover of cis-regulatory elements (CREs). To test for specific *D. melanogaster* CRE expansions, we implemented new models in our software BadiRate.

We determined that positive selection is shaping the upstream nucleotide diversity in 22 out of the 133 examined chemosensory genes, especially in ORs and GRs. Such analysis was conducted after controlling for the underlying demographic history of the Raleigh population. Remarkably, some upstream regions also exhibit accelerated CRE turnover rates in the lineage leading to *D. melanogaster*, highlighting the significance of chemical perception in adaptation to environmental changes.



11:45-12:05

DETECTION OF EVIDENCES OF SELECTION IN HUMAN POLYMORPHIC INVERSIONS.

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Chromosomal inversion polymorphism has been a cornerstone in the study of evolution all through the history of population genetics. Inversions are known to reduce and redistribute recombination, and thus they affect nucleotide variation levels. Apart from this descriptive effect of inversions, a clear and thorough understanding of population dynamics of inversions is needed for full comprehension of its evolutionary role in the

human genome. Inversions have been shown to have an adaptive value and the proposed mechanisms of selection that could affect them are numerous and varied. However, detecting selection in inversions is not trivial. There are clear evidences for at least two generation mechanisms of inversions in humans (associated maybe to different mutation rates): mediated and non-mediated by inverted repeats. It is therefore essential to assess the role of the main evolutionary forces (mutation, drift and selection) in the population behavior of these two families of inversions.

In this work, we analyzed population frequencies for 41 human polymorphic inversions in seven human populations and 20 fixed inversions between human and chimpanzee. For that, we took advantage of a large-scale genotyping effort of these inversions in 550 individuals and the nucleotide variation data from the 1000 Genomes Project. Inference of the recombination rates was performed by means of the coalescence-based algorithm implemented in the LDhat package, using the program rhomap. Measurements of nucleotide variation levels and populations structure were performed using PopGenome 1.2.5 (R statistical package) and Structure 2.3.4, respectively. Finally, we built mixed and generalized linear mixed models to predict how the frequency of inversions varies according to inversion features such as distance to closest gene, number of affected genes, inversion length, inverted repeats length and local recombination rate.

We were able to explain more than 30% of the variation in inversion frequencies in humans. Inversions affecting coding sequences are at significantly lower frequency than intergenic or intronic inversions. Among them, long inversions are even at lower frequency. Hence, these results indicate that human inversions are subject to purifying selection. Interestingly, the inverted repeats length is positively correlated with inversion frequency. The frequency of an inversion flanked by long inverted repeats is higher than the frequency of an equivalent inversion without or with shorter inverted repeats. Moreover, we found a few inversions that show clear signs of positive selection that deserve further investigation.



12:05-12:25

WHOLE-EXOME SEQUENCING REVEALS A RAPID CHANGE IN THE FREQUENCY OF RARE FUNCTIONAL VARIANTS IN A FOUNDING POPULATION OF HUMANS.

Ferran Casals^{1,2,}

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Whole-exome or gene targeted resequencing in hundreds to thousands of individuals has shown that the majority of genetic variants are at low frequency in human populations. Rare variants are enriched for functional mutations and are expected to explain an important fraction of the genetic etiology of human disease, therefore having a potential medical interest. In this work, we analyze the whole-exome sequences of French-Canadian individuals, a founder population with a unique demographic history that includes an original population bottleneck less than 20 generations ago, followed by a demographic explosion, and the whole exomes of French individuals sampled from France. We show that in less than 20 generations of genetic isolation from the French population, the genetic pool of French-Canadians shows reduced levels of diversity, higher homozygosity, and an excess of rare variants with low variant sharing with Europeans. Furthermore, the French-Canadian population contains a larger proportion of putatively damaging functional variants, which could partially explain the increased incidence of genetic disease in the province. Our results highlight the impact of population demography on genetic fitness and the contribution of rare variants to the human genetic variation landscape, emphasizing the need for deep cataloguing of genetic variants by resequencing worldwide human populations in order to truly assess disease risk.



12:25-12:45

GREAT APE GENETIC DIVERSITY AND POPULATION HISTORY

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Despite African great apes and orangutans are human's closest evolutionary relatives, the assessment of their genetic diversity has been systematically delayed in comparison to similar studies in our species. To overcome this limitation, we sequenced to high coverage a total of 79 great ape individuals representing all species and seven subspecies across the African continent and South East Asia. We discover ~86.5 million single nucleotide polymorphisms and report a three-fold range in nucleotide diversity among different ape populations. We find extensive inbreeding in almost all wild populations with Eastern gorillas being the most extreme population. Our analysis provides support for genetically distinct populations within each species, signals of gene flow, and the split of common chimpanzees into two distinct groups: Nigeria-Cameroon/Western and Central/Eastern populations. Using these data, we develop a framework to understand the recent evolutionary history of hominidae. This resource provides the first catalog of great-ape genome diversity to assist in better understanding our species and more effectively managing wild and captive great ape populations.

SESSION IV. FUNCTIONAL EVOLUTION.

Chairs: María Dolors Piulachs, Xavier Franch & Pedro Martinez



17:15-17:35

REGULATED AGGREGATIVE MULTICELLULARITY IN A CLOSE UNICELLULAR RELATIVE OF METAZOA.

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The evolution of metazoans from their unicellular protistan ancestors was one of the most important events in the history of life. However, which cellular and genetic changes in unicellular species ultimately led to the evolution of multicellularity is not known^{1,2}. By using electron microscopy and flow cytometry, we describe the life cycle of the unice-Ilular holozoan Capsaspora owczarzaki, including the existence of an aggregative multicellular stage. This represents the first of this kind in Holozoa (the clade that includes metazoans and their closest unicellular relatives). By comparative RNAseg analyses, we observe that the transitions in and out of this and other cell stages are tightly regulated at the transcriptomic level, impacting key functional categories, such as the integrin adhesome, extracellular matrix and their associated tyrosine kinase and G-protein signalling pathways. Furthermore, we observe striking transitions in regulated alternative splicing during the *C. owczarzaki* lifecycle, including extensive regulated intron retention and the deployment of an exon network associated with signalling, a feature of splicing regulation so far only observed in metazoan species3. In summary, our results reveal the existence of a highly-regulated aggregative stage and gene regulatory innovations in *C. owczarzaki* that bear hallmarks of muticellularity in metazoans. The results further suggest that features of aggregative cellular behaviour in an ancestral protist may have been co-opted to establish clonal multicellularity at the onset of Metazoa.

^{1.} King, N. The unicellular ancestry of animal development. Dev Cell 7, 313-25 (2004).

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^{3.} Han, H. et al. MBNL proteins repress ES-cell-specific alternative splicing and reprogramming. Nature 498, 241-245 (2013).



17:35-17:55

EVO-DEVO CONTRIBUTIONS FOR UNDERSTANDING THE FOREBRAIN.

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Institut de Recerca Biomèdica de Lleida (IRBLleida), Universitat de Lleida

The forebrain is the most complex region of the central nervous system, and includes centers that play a key role in complex cognitive functions and behaviors. This brain region has undergone divergence during vertebrate evolution, affecting in varying degrees all of its subdivisions (i.e. cerebral cortex/pallium, basal ganglia, amygdala, hypothalamus, thalamus), which likely relates to the ecological adaptations and variations between species in cognitive capabilities and behavior. Since evolution is the consequence of changes that took place in developmental mechanisms, evolutionary developmental (evo-devo) studies are essential if we want to unravel forebrain evolution, and its organization in different vertebrates. Based on this, during the last ten years our group has been using an evo-devo approach for trying to understand the organization and evolution of different forebrain centers, such as the cortex/pallium, the amygdala, and the basal ganglia. To that aim, we have compared the expression of orthologous developmental regulatory genes involved in patterning and morphogenesis in the embryonic brain of different vertebrate species.

We used *in situ* hybridization techniques to study the mRNA expression of a battery of developmental regulatory genes (such as those encoding the transcription factors Lhx2, Lhx9, Emx1, Tbr1, Pax6, Dlx2/5, Islet1, Nkx2.1, Otp) in mouse, chicken, the lacertid lizard *Psammodromus algirus*, and the pipid frog *Xenopus laevis*. We combined these results with experimental data from cell migration assays in mouse and chicken.

Our results on combinatorial gene expression patterns have allowed the identification of homologous progenitor divisions and subdivisions in the embryonic pallium and subpallium of different species. The gene expression patterns, combined with data from migration assays, have additionally allowed analysis of the derivatives of each progenitor zone, and have demonstrated a mosaic-like organization of many nuclei and areas, such as those of the amygdala and the basal ganglia. For example, the medial amygdala is formed by five different neuron subpopulations with distinct embryonic origin and characterized by expression of distinct transcription factors or other regulatory proteins. Moreover, these data are helping to understand the functional organization of these nuclei/areas, their variation between species, and their evolution.

Supported by a MINECO grant (BFU2012-33029).



17:55-18:15

THE EVOLUTION OF ANDRODIOECISM IN PROCKIA KRUSEI: EVIDENCES OF THE FLOWER'S DEVELOPMENT AND STRUCTURE.

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Androdioecy is the coexistence of individuals that produce male or hermaphrodite flowers and a possible origin of dioecy. Theoretically, such breeding system has many restrictions required for the invasion of males in co-sexual populations. Due to the rarity of androdioecy, it has received less attention than others forms of reproduction. Among angiosperms however, morphologically some species appear to be hermaphrodite but functionally are androdioecious.

Prockia krusei (Salicaceae) is a hermaphrodite species that presents two floral morphs well defined. One of them exhibits flowers with a reduction of its gynoecium and does not produce fruits. Theoretical models predict that the reduction of the female function in androdioecious species could positively affect male function. Therefore if *P. krusei* is an androdioecious species, we expected to detect flaws in female function during development of reduced gynoecium morph and an increase in the amount of resources for male function. To the contrary, we did not expect to find changes in the development of reproductive structures in the other morph. To test if *P. krusei* is an androdioecious species, we studied the development and morphology of gynoecium and androecium in both types of flower by scanning electron microscope and histological techniques. According to our expectations, we found different flaws during the development of female function in reduced gynoecium morph, such as collapsed cells that form the stigma or arrested ovules in the early stages of developmental. Finally, we are going to discuss the possible origin of dioecy from the androdioecy in the genus *Prockia*.

^{1.} Pannell, J. R. 1997. Widespread functional androdioecy in Mercurialis annua L. (Euphorbiaceae). Biological Journal of the Linnean Society 61: 95-116.

^{2.} Pannell, JR. 2002. The evolution and maintenance of androdioecy. Annual Review of Ecology and Systematics 33: 397-425.

^{3.} Webb, J.C. 1999. Empirical studies: evolution and maintenance of dimorphic breeding systems. In: Gender and sexual dimorphism in flowering plants. Geber, M.A; Dawson, T. E; Delph, L. F. (Eds.), Springer-Verlag, Germany.



18:15-18:35

DE NOVO SEQUENCING AND COMPARISON OF THE INFERRED CENTRAL NERVOUS SYSTEM TRANSCRIPTOMES OF THE SOLITARY AND GREGARIOUS SCHISTOCERCA GREGARIA.

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Locusts experiment an extreme biological change known as phase polyphenism that results in the occurrence of two phases, a solitary and a gregarious. Solitarty locusts tend to avoid each other whereas gregarious locusts tend to aggregate and form swarms. Although this phenotipic plasticity was reported in several taxonomic groups among Caelifera, the desert locust *(Schistocerca gregaria)* remains the paradigm species for studies on this subject.

Various stimuli and several hormonal pathways have been found to be involved in the development of the gregarious phase. However, the main genetic and molecular triggers of the shift towards the swarming phase remain unknown. In this study we report the results of a central nervous system (CNS) transcriptome RNA-seg analysis in adult individuals from solitary and gregarious S. gregaria. Five solitary and five gregarious adults were used to separately extract the mRNAs and sequence them using the Illumina Hi-Seg2000 Paired-end technology. After *De novo* assembly of the solitary and gregarious libraries, the resulting contigs were filtered then annotated. Reads were aligned to these contigs using and statistical analyses were performed to identify the differentially expressed genes. About 57k contigs were assembled, of which nearly 20k had significant matches in the protein and nucleotide sequence databases. This way we significantly contribute to the available set of *S. gregaria* expressed sequences. About a third (21k) of the assembled contigs showed significant differences in expression levels between the solitary and gregarious individuals. We interpret this as an indication of the huge complexity of the differences between the solitary and gregarious states which involve changes at almost every aspect of the animal's biology. Most of the differentially expressed contigs (19k) were over-expressed in the gregarious library indicating the probably more active transcriptional activity in the CNS of the gregarious animals than in the CNS of the solitary ones. Strikingly, the different isoforms of a same gene showed, in different instances, different gene expression patterns among phases, highlighting the role of the alternative splicing as one of the mechanisms underlying the molecular basis of this phase polyphenism.

GO analysis reveals that various biological processes are highly represented amongst the differentially expressed genes. Many of these corresponded to signal transduction, response to stress and response to stimuli (internal, external, biotic and abiotic) categories. Nonetheless, about 65 % of the assembled contigs correspond to unknown transcripts which leaves the doors wide open for gene-discovery and functional genetics studies.

As to individual genes, and apart for the contigs with no known annotation, our results highlight the cytochrome p450 6b29 (gregarious) and serine protease 17 precursor (solitary) among the genes that most differences in expression levels show between gregarious and solitary locusts.



18:35-18:55

ON THE EMERGENCE OF NOVEL FUNCTIONS IN MICROBES: UNEARTHING THE EVOLUTIONARY TRAJECTORIES OF INNOVATIVE DESTABILIZING MUTATIONS.

Mario A. Fares

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The emergence of novel functions is a recurrent and dynamic evolutionary process. Novel functions emerge through the modification of ancestral ones by mutations. Innovative mutations are, however, destabilizing as they compromise ancestral well-adapted functions, and thus the emergence of functional novelties is a slow process. Several mechanisms can buffer the deleterious effects of mutations and fuel evolution, chief between which is gene duplication and epistasis. Last years have seen an increase in our knowledge on the link between mutations and biological complexity. However, our understanding of the evolutionary paths underlying the emergence of novelties remains highly fragmented.

I here present some research avenues, which may provide opportunity for furthering our understanding on the evolutionary paths to biological innovation. Of these avenues the most promising are those based on the evolution of microorganisms under controlled experimental conditions that simulate particular biological and evolutionary scenarios. These approaches together with theoretical and bioinformatics treatment of data yields results which can be easily interpreted in the light of existing and new evolutionary theories.

Indeed, the evolution of the eukaryotic microbe *Saccharomyces cerevisiae* in the laboratory unearths two levels of evolution of functional novelties, including a re-shape of the functional interactions after gene duplication and the fixation of destabilizing mutations mediated by mutational robustness and compensatory evolution. Despite the bewildering nature of the evolutionary trajectories to functional innovations, our findings point to general mechanisms governing the fixation of such mutations and allowing leaps between adaptive picks in a fitness landscape.



18:55-19:15

DNA UPTAKE SEQUENCES, UPTAKE SIGNAL SEQUENCES, DNA UPTAKE ENHANCING SEQUENCES, WHAT ARE THEY ANYWAY?

Mohammed Bakkali

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Bacterial competence for transformation by spontaneous DNA uptake is one of the most interesting phenomena both at the fundamental as well as the applied levels. Among the naturally competent bacteria, those belonging to the Pasteurellaceae and Neisseriaceae families show an interesting bias towards uptake of con-specifics DNA. The reason behind this is a preference towards uptake of DNA fragments that contain sequence tags, referred to as DNA Uptake Sequences (DUS), Uptake Signal Sequences (USS) or DNA Uptake Enhancing Sequences (DUES). The high frequency of these sequences in the genomes of the abovementioned bacteria, added to the preference towards these tags, result in uptake bias towards the DNA coming from cells of the same species. The simple presence of a DUES in a ADN fragment then gives this latter an uptake advantage. Differences in the DUESs can thus result in barriers against horizontal DNA transfer, and DUESs similarity might be expected to favor homogenization throughout high levels of horizontal DNA transfer—together with the already famous epidemiological consequences of bacterial transformation.

This work was initially envisaged to tackle the surprisingly little information thus far available on the distribution and inter-specific diversity of these DUESs. Even more surprising is the lack of definitive data on the real nature of these sequences, which are not completely decided not even for pathogenic species of the caliber of *Haemophilus influenzae* (the first ever free-living genome to be sequenced) and *Neisseria gonorrhoeae* (a model species for studies on horizontal gene transfer). A bioinformatics analysis was carried out for all the complete and draft genome sequences available for members of the Pasteurellaceae and Neisseriaceae families. A sliding windows extraction of different word (sequence) sizes was carried out in each of those genomes. Frequency comparisons and statistical analyses were then applied to the sequence data.

Only two DUES variants were detected in the analyzed Pasteurellacean sequences. Whereas, for Neisseriaceae, the number of different DUESs was eight. Given the 'functional' implications of these sequences, one can therefore confidently infer a higher horizontal DNA flow between the Pasteurellaceae species than between the Neisseriaceae. As to the nucleotide composition of these DUESs, the results suggest that both Pasteurellaceae DUESs are of ten base pairs, instead of the currently admitted nine. Similarly, Neisseriaceae DUESs are larger than the currently accepted 12 bp and their length varies between 13 and 18 bp — suggesting a stronger divergence of these sequences in the Neisseriaceae than in the Pasteurellaceae. Finally the phylogenetic relationships between the DUESs of each family were explored —a not-so-obvious task in the absence of an outgroup for the just two Pasteurellacean DUESs.

SESSION V. PHYLOGENY AND SYSTEMATICS.

Chairs: Toni Gabaldón & José Castresana



10:15-10:35

LIFE-HISTORY EVOLUTION AND MITOGENOMIC PHYLOGENY OF CAECILIAN AMPHIBIANS.

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Caecilians (Gymnophiona) are one of the three orders of extant amphibians, frogs and salamanders being the other two. They are highly specialized with elongate, annulated, limbless bodies, and sensory tentacles on each side of the snout. Most of the 199 currently recognized species have a secretive fossorial lifestyle, but members of one family are secondarily adapted to aquatic habitats. Of the many evolutionary and ecological features that make caecilians so distinct, their great diversity of life history is among the most outstanding. They have a broad variety of reproductive strategies and types of parental care, matching frogs and salamanders in the main reproductive modes despite there being many fewer caecilian species than there are currently recognized species of salamanders (654) and frogs (6320). Caecilian reproductive strategies encompass oviparity with presence of free-living larva, oviparity with direct development, and viviparity. these combined with varying forms of parental care, including egg attendance and the recently discovered maternal dermatophagy in which hatchlings eat their mothers skin. Several studies have addressed life-history evolution and/or aspects of reproductive biology of caecilians but, thus far, no modern study has considered a broad sweep of the evolution of reproductive strategies within a phylogenetic framework.

We analyze mitochondrial genomes to reconstruct a robust phylogenetic framework for caecilian amphibians and use this to investigate life-history evolution within the group. Our study comprises 45 caecilian mitochondrial genomes (19 of them newly reported), representing all families and 27 out of 33 currently recognized genera, including some for which molecular data had never been reported.

Support for all relationships in the inferred phylogenetic tree is high to maximal, and topology tests reject all investigated alternatives indicating an exceptionally robust molecular phylogenetic framework of caecilian evolution. The phylogeny indicates that some genera are not monophyletic and are in need of further study, but is otherwise consis-

tent with current primarily morphology-based supraspecific classification. We used the mitogenomic phylogenetic framework to infer ancestral character states and assess correlation among three life-history traits (free-living larvae, viviparity and specialized pre-adult or vernal teeth), each of which is present only in some caecilian species. Our results provide evidence that an ancestor of the Seychelles caecilians abandoned direct development and re-evolved a free- living larval stage. This study yields insights into the concurrent evolution of direct development and of vernal teeth in an ancestor of Teresomata that likely gave rise to skin feeding (maternal dermatophagy) behavior and subsequently enabled the evolution of viviparity, with skin feeding possibly a homologous precursor of oviduct feeding in viviparous caecilians.



10:35-10:55

STRIKING FUNCTIONAL AND MOLECULAR DIFFERENCES AMONG ENDOSYMBIOTIC LINEAGES FROM FIVE MEALYBUG SPECIES.

Sergio López-Madrigal¹,

Aleixandre Beltrà², Serena Resurrección1, Sergio López-Olmos¹, Antonia Soto², Amparo Latorre^{1,3}, Andrés Moya^{1,3} and Rosario Gil¹.

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Mutualistic intracellular bacteria (endosymbionts) are needed to complement unbalanced insect host diets. Due to their obligate intracellular lifestyle, endosymbiont genomes undergo a reductive evolutionary syndrome. Because genomic degradation is progressive, recruitment of new endosymbionts sporadically happens, so that host survival gets warranted1. Mealybug *Planococcus citri* possess a nested endosymbiotic system where *Tremblaya princeps* (β-proteobacteria) harbors *Moranella endobia* (β-proteobacteria)², being both bacteria involved in essential amino acids (EAA) biosynthesis ³, ⁴. The detection of several prokaryote genes, acquired by horizontal gene transfer (HGT), in the host genome supports the idea of a tripartite nested symbiosis with an unprecedented level of metabolic complementation⁶. The recent genome sequencing of *T. phenacola* PAVE, single endosymbiont of *Phenacoccus avenae*, confirmed mealybugs' endosymbionts involvement in EAA provision⁶. In order to analyze EAA supply within unexplored *Tremblaya* lineages, we performed a genetic screening of genes involved in the late steps of EAA biosynthetic pathways on five mealybug species from several lineages of both subfamilies Pseudococcinae and Phenacoccinae.

Multiple alignments of homologous genes from a selected bacterial set were performed with ClustalW for the design of degenerate primers. PCR amplifications were performed on total DNA from adult mealybug females. Amplicons were cloned in pGEM®-T Easy and sequenced. We used Staden Package for reads assembly, and MEGA5 for global estimations on codon usage bias, nucleotides and amino acidic composition. Phylogenetic reconstructions were carried out by Maximum Likelyhood (ML) in RAxML. JModelTest was applied for proper evolutionary model selection.

In contrast to $\it{T. princeps}$, the molecular analysis of $\it{T. phenacola}$ genes suggests that this lineage is undergoing a typical endosymbiont genome AT-enrichment. Lineages from subfamily Pseudococcinae revealed great variability on $\it{\beta}$ - and $\it{\gamma}$ -endosymbionts metabolic coordination for amino acids biosynthesis. We also detected HGT events to be involved, at least, on the evolution of the tryptophan biosynthetic pathway in two $\it{T. phenacola}$ strains.

- 1. Gil et al., 2010. In: Hackstein JHP, ed. (Endo)symbiotic Methanogenic Archaea: Springer- Verlag. pp. 207-233.
- 2. von Dohlen et al., 2001. Nature 412:433-436.
- 3. McCutcheon & von Dohlen, 2011. Curr Biol 21:1366-1372.
- 4. Lopez-Madrigal et al., 2011. J Bacteriol 193:5587-5588.
- 5. Lopez-Madrigal et al., 2013. BMC Microbiology 13:74.1-74.12. 6. Husnik et al., 2013. Cell 153:1567-1578.



12:00-12:20

CRYPTIC DIVERSITY AND EVOLUTION OF AUSTRALIAN PSEUDOTETRACHA TIGER BEETLES

Alejandro López-López¹, Peter Hudson² and José Galián¹ ¹Área de Biología Animal. Departamento de Zoología y Antropología Física Universidad de Murcia. 30100, *Murcia (Spain).*

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The genus *Pseudotetracha* comprises 19 described species (McCairns et al., 1997; Sumlin, 1997) of big nocturnal tiger beetles (Coleoptera: Carabidae: Cicindelinae) distributed on salt lakes along Australia. Despite their wide range of distribution, big size and bright green coloration, they remain quite unknown because of the remoteness of their habitats. This unfamiliarity and their well structured populations makes them an ideal group for seeking unnoticed cryptic taxa and studying the processes that might have had an impact on their evolutionary history.

A phylogenetic analysis of 496 *Pseudotetracha* tiger beetles identified as 7 tentative species was carried out in BEAST 1.7.5 based on a concatenated matrix composed of two mitochondrial fragments: cytochrome oxidase III and rRNA 16S. A GMYC analysis was run using the obtained tree in order to identify potential independent entities corresponding to unknown cryptic taxa.

The Bayesian Inference tree divides the samples into three main groups corresponding to different species complexes. The GMYC subdivides these complexes into 51-58 putative independent entities, strongly correlated with their geographic distribution - ancient palaeorivers- but not with their morphology. Each of these clusters can represent a cryptic species, a fact that is supported in some cases by karyotypic differences. Although the entities are mainly specific of isolated lakes or ancient drainage basins, it is possible to conjecture some posterior events of colonization of adjacent or connected lakes. The main branches of the tree split in the second half of the Miocene, contemporaneous with

the last aridification event in Australia, when the salt lakes where this beetles live developed their present day structure, suggesting that this event may have had a significant role in the diversification of this group.

McCairns, R.F., Freitag, R., Rose, H.A., McDonald, F.J.D. (1997) Taxonomic revision of the Australian Cicindelidae (Coleoptera), excluding species of *Cicindela. Invertebrate Taxonomy* 11:599-687. Sumlin, W.D. (1997) Studies on the Australian Cicindelidae XII: additions to *Megacephala, Nickerlea* and Cicindela with notes (Coleoptera). *Cicindelidae: Bulletin of Worlwide Research* 4:1-56.



12:20-12:40

THE FRESHWATER PLANARIAN DUGESIA: A LONG HISTORY FOR A GENUS, FROM GONDWANA TO THE PRESENT.

Eduard Solà¹,

Renata Manconi², Giacinta Angela Stocchino², Abdul Halim Harrath³, Laia Leria¹, Marta Riutort¹

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- ³ Zoology Department, College of Science, King Saud University

Dugesia is a genus of freshwater flatworm best known because its regeneration capabilities and its triangle-shaped head, being frequently depicted in textbooks. It is also the most specious member of the Dugesiidae family with almost 80 known species, and there probably are many more to be discovered. Freshwater flatworms are supposed to be animals of low dispersal capabilities, depending on contiguous freshwater bodies to survive and disperse. However, *Dugesia* species present a wide distribution range, including Africa, Europe, Middle East, Oriental Region, Far East and Australasia. Some researchers have speculated that *Dugesia* has an African origin, placing it in a post- Gondwana scenario, when Africa and South America were split (130-100 Mya). However, the origin of this genus could be even older, taking into account that Madagascar, inhabited by three endemic *Dugesia* species, was split from Africa much before (160-130 Mya). After the fragmentation of Gondwana, *Dugesia* would have spread into Eurasia, possibly through the Arabian Plate or from the Indian subcontient.

Hitherto, the molecular phylogeographic studies of these animals have been limited to the Mediterranean Basin. Here we have expanded the range of study to different localities along its whole distribution range. We have carried out molecular phylogenetic analyses (Maximum Likelihood and Bayesian inference) and divergence time dating (BEAST software) in order to find out where and when Dugesia appeared and how their species have dispersed through all the present distribution.

The preliminary results suggest a very old origin of the genus, placing it in the supercontinent Gondwana during the Mesozoic. However, it is still unclear which was the dispersion route from Gondwana to Eurasia.



12:40-13:00

TRANSCRIPTION FACTOR EVOLUTION AND THE ORIGINS OF MULTICELLULARITY IN EUKARYOTIC LINEAGES.

Alex de Mendoza^{1,a,b,}

Arnau Sebé-Pedrós^{1,a,b,} Martin Sebastijan Šestakc, Marija Matejčićc, Guifré Torruellaa^b, Tomislav Domazet-Lošoc^{d,} Iñaki Ruiz-Trillo^{2,a,b,e}

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- ^C Laboratory of Evolutionary Genetics, Ruđer Bošković Institute, Bijenička cesta 54 HR-10000 Zagreb, Croatia;
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Independent transitions to multicellularity in eukaryotes involved the evolution of complex transcriptional regulation toolkits in order to control cell differentiation. By using comparative genomics we show that plants and animals required richer transcriptional machineries compared to other eukaryotic multicellular lineages. We suggest this is due to their orchestrated embryonic development. Moreover, our analysis study of transcription factor (TF) expression patterns during the development of both animals and plants reveal links between TF evolution, species ontogeny and the phylotypic stage.

We have analyzed the Transcription Factor repertoire for 71 eukaryotic genomes, and we have traced the evolutionary histories, diversification, architectural reconfiguration and ancestral composition across the eukaryotic tree of life. Moreover we have analyzed developmental expression datasets for TF activity in model species such as Danio rerio, Drosophila melanogaster, Arabidopsis thaliana.

Our results show that the most complex multicellular lineages (i.e., those with with embryonic development, Metazoa and Embryophyta) have the most complex TF repertoires, and that these repertoires were assembled in a step-wise manner. We also show that a significant part of the metazoan and embryophyte TF toolkits evolved earlier, in their respective unicellular ancestors. To gain insights into the role of TFs in the development of both embryophytes and metazoans, we analysed TF expression patterns throughout their ontogeny. The expression patterns observed in both groups recapitulate those of the whole transcriptome, but reveal important differences. We suggest that these differences are due to the difference between the determined and indetermined development of extant metazoans and embryophytes, respectively. Our comparative genomics and expression data re-shapes our view on how TFs contributed to eukaryotic evolution and reveals the importance of TFs to the origins of multicellularity and embryonic development.



KEY INNOVATIONS AND ISLAND COLONIZATION AS ENGINES OF EVOLUTIONARY **DIVERSIFICATION: A COMPARATIVE TEST WITH THE AUSTRALASIAN** DIPLODACTYLOID GECKOS

J. Garcia-Porta* & T. J. Ord†

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- Evolution and Ecology Research Centre, and the School of Biological, Earth and Environmental Sciences, University of New South Wales, Sydney NSW, Australia

A major challenge in evolutionary biology is understanding the main drivers that underlie morphological and species diversity. Ecological opportunity—access to new or previously inaccessible niches—has been classically identified as one of the most important drivers of both phenotypic and species diversification. This can arise from three main sources: (i) the extinction of ecological competitors that open up previously "filled" niches: (ii) exposure to new environments through dispersal (e.g. island colonization) or changes to existing environments through extrinsic forces that modify the environment (e.g., climate change); and (iii) the evolution of key innovations that allow taxa to use environments or resources in novel ways. Our study examined the latter two sources of ecological opportunity—specifically, the colonization of islands (in this case, New Caledonia and New Zealand) and the evolution of two putative key innovations (adhesive toepads and a snake-like phenotype)—and explored the extent these have driven diversification in a morphologically diverse and species rich vertebrate group: the Australasian diplodactyloid geckos.

To study this guestion, we developed a robust time-calibrated phylogeny of the whole radiation, and compiled body size data (our proxy to phenotype) for most of the species in it. We then applied a variety of recently developed comparative methods to test whether key innovations and island colonization were associated with accelerated rates of body size evolution and species diversification.

Our results show that island colonization has played the most prominent role in the evolutionary diversification of Australasian geckos, producing accelerated rates of phenotypic and species diversification. This is consistent with the expected scenario of a rapid niche-filling process coupled with high rates of speciation during the early stages of island colonization, when groups experience high levels of ecological opportunity. Regarding the two key innovations studied, only one of them, the snake-like phenotype, was associated to a pattern similar of that found for island colonization. Adhesive toepads, however, failed to show any direct impact on the total evolutionary diversification experienced by the group. This shows how key innovations, despite of allowing new interactions with the environment, not necessarily open the door to high rates of phenotypic and species diversification. Studies wishing to confirm the putative link between a key innovation and subsequent evolutionary diversification must therefore show that it has been the acquisition of an innovation specifically, not the colonization of new areas more generally, that has prompted diversification.

SELECTED POSTERS

TIPPING POINTS IN THE COMPOSITION OF POPULATIONS AT THE GENOTYPIC SCALE			
Aguirre Jacobo*, Susanna Manrubia.	*Centro de Astrobiología CSIC-INTA, Torrejón de Ardoz, Madrid. Grupo Interdisciplinar de Sistemas Complejos (G.I.S.C), Universidad Carlos III de Madrid.	S1	1
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Arribas María, Ester Lázaro*	*Centro de Astrobiología CSIC-INTA, Torrejón de Ardoz, Madrid. Grupo Interdisciplinar de Sistemas Complejos (G.I.S.C), Universidad Carlos III de Madrid.	31	U
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Capilla Laia*, Nuria Medarde, Alexandra Alemany-Schmidt, Maria Oliver-Bonet, Jacint Ventura, Aurora Ruiz-Herrera.	*Genome Integrity and Instability Group, Institut de Biotecnologia i Biomedicina (IBB), Universitat Autònoma de Barcelona, Campus UAB, 08193, Cerdanyola del Vallès, Spain; Departament de Biologia Animal, Biologia Vegetal i Ecologia, Universitat Autònoma de Barcelona, Campus UAB, 08193, Cerdanyola del Vallès, Spain	S1	11

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Capitán José A*, Susanna Manrubia.	*Centro de Astrobiología, INTA-CSIC. Ctra. de Torrejón a Ajalvir, km. 4. 28850 Madrid, Spain.		
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Garcia-Etxebarria Koldo*, Begoña M Jugo.	*Genetika, Antropologia Fisikoa eta Animalien Fisiologia Saila. Zientzia eta Teknologia Fakultatea. Euskal Herriko Unibertsitatea (UPV/EHU). 644 Postakutxa, 48080 Bilbao.	S 1	26
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Gomez-Mestre Ivan*, Robert Alexander Pyron, John J. Wiens.	*Ecology, Evolution and Development Group, Dept. of Wetland Ecology, Estación Biológica de Doñana, CSIC, Seville E41092, Spain;	S1	28
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Irene Hernando*	*Institut de Biologia Evolutiva (CSIC-UPF), Universitat Pompeu Fabra, 08003 Barcelona, Spain;	S1	33
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Lázaro Ester* , Kirina Kubota, María Arribas, Laura Cabanillas.	*Centro de Astrobiologia (INTO-CSIC), Ctra de Ajalvir Km 4, 28850 Torrejón de Ardoz, Madrid, Spain	S1	35
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Lozano Jesus*, Raúl Montañez, Xavier Bellés.	*Institut de Biologia Evolutiva (CSIC-UPF), Universitat Pompeu Fabra, 08003 Barcelona, Spain;	อเ	31

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Luisi Pierre*, David Alvarez-Ponce, Marc Pybus,	*Institute of Evolutionary Biology UPF-CSIC CEXS-UPF-PRBB;	S1	38
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