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PROTIST NEWS

Meeting Report: Minutes from EMBO: Ten Years of Comparative Genomics of Eukaryotic Microorganisms

The 2015 EMBO Conference on 'Exploring the genomic complexity and diversity of eukaryotes' had its origins 10 years ago with an ESF-EMBO Symposium on 'Comparative genomics of eukaryotic microorganisms: eukaryotic genome evolution, approaches with yeast and fungi' (Table 1). The initial symposium, organized by Jean-Luc Souciet and Ed Louis, along with Bernard Dujon and Claude Gaillardin, was focused on yeasts and filamentous fungi in general, as only a few other eukaryotic genomes were available at the time. The main reason for the meeting, however, was to provide a forum for the wider eukaryotic research community who didn't fit into the prokaryotic or multicellular model organisms genomics communities, and to share the tools that had been developed for the heavily populated yeast and other fungal groups. This desire has been highly successful. We have convinced molecular and cellular biologists that extending their interests from a few model organisms to protist groups that constitute the vast majority of the extant eukaryotic diversity, would be beneficial for everybody. At the same time, this EMBO meeting has increasingly attracted protistologists and evolutionary biologists to the eukaryotic genomics arena. Over the years the meeting has evolved, first with a second ESF-EMBO conference, and then two EMBO Conference series, such that the few talks on parasites and other protists among a plethora of yeast and fungal talks have now become the majority. There has been an overwhelming desire by the attendees to continue with this meeting and we have been fortunate enough to secure continued support from EMBO along with additional support from the Canadian Institute for Advanced Research (CIFAR).

As the topics evolve, so does the composition of attendees, yet there are some topics that return and many speakers and attendees make this a regular event. Indeed the organizer of the 2015 meeting, **Toni Gabaldón** (Centro de Regulacion Genomica, Barcelona, Spain) spoke at all 5 previous meetings, and **Marina Marcet-Houben** from his lab spoke about the origins of the whole genome duplication leading to the *Saccharomyces* yeasts, the topic of the very first talk in the first meeting by Ken Wolfe, who also spoke at the 2015 meeting. Marina demonstrated that the original duplicated genome, a tetraploid, was a hybrid between two different species rather than an autotetraploid.

The realization that eukaryotic diversity extends beyond the limits of classically studied lineages together with recent methodological advances, including the substantial decrease of sequencing costs and the development of cell-sorting and single-cell-based techniques, have certainly contributed to a more democratic distribution of whole genome and/or transcriptome projects across the eukaryotic tree. Thus, at the 2015 meeting, there was a palpable ambition to focus on uncultivable protists and divergent phylogenetic lineages discovered in oceans and other environments.

How fruitful the studies of protists can be was exemplified by the opening lecture of **Michael Gray** (Dalhousie University, Halifax, Canada) entitled "Mitochondrial genomes - anything goes". In his life-long passion for mitochondria and their evolution across the eukaryotic domain, Michael and his colleagues found virtually any imaginable (and sometimes even unimaginable) arrangement of the narrow set of mitochondrially-encoded genes. Even within a small clade of yeast, *Candida parapsilosis* and relatives, there is a myriad of mitochondrial genome structures as demonstrated by **Josef Nozek** (Comenius University, Bratislava, Slovakia). Josef and colleagues have found numerous linear mitochondrial genomes in addition to the circularly permuted

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Table 1. A brief history of the meeting – all held at Hotel Eden Roc, Sant Feliu de Guixols, Spain.

Year	Sponsor	Title	Organizer(s)
2005	ESF-EMBO	Comparative genomics of eukaryotic microorganisms: genome evolution, approaches with yeast and fungi	Jean-Luc Souciet Ed Louis
2007	ESF-EMBO	Comparative genomics of eukaryotic microorganisms: Eukaryotic genome evolution	Ed Louis Teun Boekhout
2009	EMBO	Comparative genomics of eukaryotic microorganisms: Eukaryotic genome evolution	Ed Louis Teun Boekhout
2011	EMBO	Comparative genomics of eukaryotic microorganisms: Understanding the complexity of diversity	Teun Boekhout Amparo Querol
2013	EMBO CIFAR	Comparative genomics of eukaryotic microorganisms: Complexity patterns in eukaryotic genomes	Amparo Querol Artur Scherf
2015	EMBO CIFAR	Exploring the genomic complexity and diversity of eukaryotes	Toni Gabaldón

forms, each with a different mechanism for maintaining their ends, the mitochondrial telomere. The seemingly limitless variations of mitochondrial genomes were further extended by **Uwe John** (Alfred-Wegener Institut, Helmholtz-Zentrum für Polar- und Meeresforschung, Bremerhaven, Germany), who convincingly showed that the parasitic marine dinoflagellate *Amoebophrya* retains cristae-carrying mitochondria, yet lost its mitochondrial genome altogether, the first such case known in a eukaryote.

Thanks to their small size, high copy number, and relative ease of their sequencing, mitochondrial genomes were in a way forerunners of current whole genome sequencing efforts of protists across accessible eukaryotic groups. However, the extensive sequencing ambitions have now been extended also to single cells. As paraphrased by **Patrick Keeling** (University of British Columbia, Vancouver, Canada), even uncultivable protists "matter" (they still represent an absolute majority of all described eukaryotic species), and they can now be accessed by single-cell genomics and transcriptomics, which was demonstrated as feasible even for miniscule and rare single cells. This approach turned out to be particularly useful in the genomic studies of the poorly known and highly diverse MAST (marine stramenopiles) groups as shown by **Ramon Massana** (Institute of Marine Sciences, Barcelona, Spain), and diplonemids, a group of virtually unknown marine euglenozoans that surprisingly emerged as the 3rd most diverse and 6th most abundant group of eukaryotes in the Tara Oceans barcoding data presented by **Patrick Wincker** (Genoscope, Evry, France). It was single-cell genomics by the Keeling lab that allowed sequencing individually collected protists, of which several turned out to be diplonemids, bridging the gap between morphological and sequence data for this elusive group for the first time. These morphologically inconspicuous cells indeed featured prominently at the meeting, as **Gertraud Burger** (University of Montreal, Montreal, Canada) described an unusually complex post-transcriptional unscrambling by *trans*-splicing and RNA editing in the diplonemid mitochondrion.

In parallel, some established protists of medical importance, such as *Plasmodium* spp. and *Toxoplasma gondii*, are being sequenced to ever increasing depth that according to **David Roos** (Pennsylvania University, Philadelphia, USA) already reached for the latter pathogen 10^{10} RNA seq reads. In the seq reads, up to 1.2 million introns have been reproducibly encountered, despite the fact that only about 45,000 of them have been annotated. If alternative splicing is implied, the number of possible transcripts in *T. gondii* can easily reach overwhelming numbers.

One gets the impression that at every meeting in St. Feliu de Guixols, the predicted LECA

(Last Eukaryotic Common Ancestor) is becoming increasingly complex. While **Laura Katz** (Smith College, Northampton, USA) provided some evidence that LECA might have had epigenetic mechanisms, **Inaki Ruiz-Trillo** (University of Barcelona, Barcelona, Spain) suggested that the last common ancestor of opisthokonts was already capable of controlling differentiation between its various stages. The idea that changes in regulation, rather than (only) gene innovation, lie at the origin of multicellularity led **Arnau Sebé-Pedrós** (Weizmann Institute of Science, Rehovot, Israel) to perform a variety of functional genomic assays in the holozoan *Capsaspora owczarzaki*. He was able to show that expression changes are associated with life cycle transitions (unicellular to colonial), thus reinforcing the hypothesis that genomic regulation already played a role at the origin of multicellularity. From his studies of lamin analogs and other nuclear envelope proteins in *Trypanosoma brucei*, **Mark Field** (University of Dundee, Dundee, UK) concluded that LECA also contained lamin-like proteins. Interestingly, although these flagellates have 10 times smaller nuclei than mammals, their lamin analogs are several times bigger, probably compensating for the absence of other components. Trypanosomes and related flagellates were strongly represented at the meeting, as **Marek Eliáš** (University of Ostrava, Ostrava, Czech Republic) described a surprising finding of a novel non-canonical genetic code in nuclear genes of trypanosomatids, while **Catarina Gadelha** (University of Nottingham, Nottingham, UK) presented an approach, by which she was able to identify surface components - 'a surfeome" of *T. brucei*, and for the first time followed defined patterns of their compartmentalization. In the same model protist, **Michael Ginger** (University of Lancaster, Lancaster, UK) explored the assembly of *c*-type cytochrome, which trypanosomatids perform in a manner distinguishing them from the rest of the eukaryotes. Trypanosomatids also differ from all other eukaryotes in their chromosome segregation machinery as discussed by **Bill Wickstead** (University of Nottingham, Nottingham, UK), where many of the canonical components are missing and other novel components have been discovered in genetic screens for chromosome loss and interacting partners.

In a unique study, **Debashish Bhattacharya** (Rutgers University, New Brunswick, USA) presented an effort to elucidate the origin and basis of halotolerance. Under strong selection and in a relatively short term, some green algae are capable of developing extreme halotolerance. This happens, he showed, by massive horizontal gene transfer from bacteria and other sources, and still the algae retain the most efficient photosynthesis. **Chris Lane** (University of Rhode Island, Kingston, USA) presented evidence that there are at least 100 known switches of red algae to a parasitic life style, which make this group particularly suitable for studying how and why these transitions occur. The observed heavily reduced expression of nuclear-encoded plastid-targeted genes is an expected step on this pathway which, however, seems to also include more surprising events, such as mitochondrion theft.

An unexpectedly large proportion of protein-coding genes in eukaryotes has a narrow phylogenetic distribution, being in fact often confined to a single species. By and large, these genes have been ignored, yet they got the attention of **Andrew Fraser** (University of Toronto, Toronto, Canada) who presented a view, based on studies of model organisms such as *S. cerevisiae* and *C. elegans*, according to which these genes tend to acquire essential functions by integrating into existing rapidly evolving machineries, such as chromosome segregation.

The availability of eukaryotic genomes from an increasingly wider taxonomic sampling facilitates the study of macroevolutionary aspects, which were very present in this EMBO meeting. Mitochondrial and eukaryotic evolution is fundamentally linked, such that, in principle, phylogenetic analyses of genes of bacterial origin in nuclear genomes might help to reconstruct major relationships among eukaryotic phyla including the root of the eukaryotic tree. This was discussed by **Sandra Baldauf** (Uppsala University, Uppsala, Sweden), who showed that many genes of alpha-proteobacterial ancestry have complex evolutionary histories that might confound large-scale phylogenomics. In an original approach, **Alessandro Pittis** (Center for Genomic Regulation, Barcelona, Spain) determined the timing of origin of proto-mitochondrial proteins in comparison with the rest of eukaryotic proteins. His analysis suggested that mitochondria were probably acquired late, arguing against mitochondria-early models for the origin of the eukaryotic cell. In a study aiming to refine the origin of the chloroplast within cyanobacteria, **Rafael Ponce** (Université Paris-Sud, Orsay, France) suggests that it emerged from early-branching cyanobacteria. Providing a nice example of evolutionary tinkering, **Jonathan Lombard** (University of Exeter, Exeter, UK) explored the origin of N-glycosylation in modern eukaryotes from pre-existing elements and new components.

Evolutionary and ecological aspects intermingled in the presentation of **Thomas Richards** (University of Exeter, Exeter, UK) who discussed the origin of osmotrophy in eukaryotes, a nutrition mode that required cell wall loss, the extracellular secretion of hydrolytic enzymes and the expansion of membrane transporters. Horizontal gene transfer of these transporters may have been instrumental for the development of osmotrophic lifestyles in two distantly related eukaryotic lineages, fungi (opisthokonts) and a group formed by oomycetes and several closely related stramenopiles. Phytoplankton diversity and genomics were integrated in a broad ecological and evolutionary framework by **Alexandra Worden** (Monterrey Bay Aquarium Research Institute, Moss Landing, USA), who unraveled aspects of green microalgal population dynamics in oceans. **Gwenael Piganeau** (Observatoire Océanologique, Banyuls-sur-Mer, France) also focused on the study of genomic variation in populations of tiny marine green algae belonging to the *Ostreococcus* species complex. On a more functional note, **Angela Falciatore** (Université Pierre et Marie Curie, Paris, France) presented deep insights on how marine diatoms regulate their responses to light in marine systems.

Among the yeast and fungal talks many dealt with mating type, sex and the associated genome dynamics. **Ken Wolfe** (University College Dublin, Dublin, Ireland) discussed the origins and evolution of reversible programmed DNA rearrangements for determination of cell mating type and its advantages over more common mechanisms of regulating mating type specific genes. The ability of a cell to be able to reversibly switch mating type can allow testing for improved environments from a spore state with a return to that state if the environment is not suitable. **Joe Heitman** (Duke University, Durham, USA) presented data on the mating type locus of the fungal pathogen *Cryptococcus neoformans* and related saprobic species. He showed that inter-centromeric recombination may have driven chromosomal translocations and the transition of an ancestral outcrossing saprobic state to a derived pathogenic bipolar configuration. **Cécile Fairhead** (Université Paris-Sud, Orsay, France) reported that *Candida glabrata* and related species, considered asexual yet having all the machinery for mating type switching, suffer lethality and gross chromosomal rearrangements when mating type switching is induced. In fungi where the mating type is not regulated by DNA rearrangements, the mating type loci are composed of several linked mating type specific regulators, pheromones, receptors and transcription factors, that are highly divergent between mating types. Repressed recombination between the “alleles” maintains this configuration. **Tatiana Giraud** (Université Paris-Sud, Orsay, France) demonstrated an extreme example of this in *Micobotryum* species where nearly the entire mating type chromosomes have diverged by extreme rearrangements, losses and transposable element insertions.

There were several talks on large-scale comparative genomics in yeasts and filamentous fungi. **Jason Stajich** (University of California, Riverside, USA) discussed the early branches of the fungal tree and the origins of various morphologies and life styles (filamentous, yeast, aquatic/terrestrial etc.). **Maitreya Dunham** (University of Washington, Seattle, USA) used comparative and functional genomics in the budding yeasts to study non-coding DNA elements, in particular origins of replication and centromeres. These elements, which are hard to identify based on sequence similarity, are being functionally confirmed after candidates have been identified through comparative genomics. **Cécile Neuvéglise** (INRA-AgroParisTech, Thiverval-Grignon, France) described the genome dynamics in hemiascomycete yeasts of the *Yarrowia* clade including reduction or expansion of genome size, horizontal gene transfers (HGTs), introgressions and transposable elements, and how the evolution of different lineages was influenced by different events. Other talks described some of these influences in specific clades: **Teun Boekhout** (CBS Fungal Biodiversity Center, Utrecht, The Netherlands) on speciation and hybrids in the genus *Malassezia*, an important component of the skin microbiome, **Gilles Fischer** (Université Pierre et Marie Curie, Paris, France) on the reconstruction of the genome history in the *Lachancea* clade, **Christophe d’Enfert** (Institut Pasteur, Paris, France) on the population genomics of *Candida albicans*, **Marcia David-Palma** (Universidade Nova de Lisboa, Caparica, Portugal) on molecular determinants of homothallic mating in *Phaffia rhodozyma*, and **Jackson Peter** (Université de Strasbourg, Strasbourg, France) on the 1002 genome project of *S. cerevisiae*.

HGTs and their influence were the subject of several talks. **Jason Slot** (Ohio State University, Columbus, USA) is reconstructing the history of HGTs among fungi, finding that many involve clusters of metabolic genes that evolve rapidly and may confer fitness advantages in certain environments. One example of this is the cluster of genes found in wine yeasts that provide an adaptive advantage and desired wine characteristics as

described by **Souhir Marsit** (INRA, Montpellier, France).

In short, the 2015 meeting was highly successful and addressed many comparative genomics aspects of an ever increasing diversity of lineages of eukaryote microorganisms. The future of this meeting is bright and we expect that discussions held at coming ESF-EMBO meetings (Table 1) on the subject will considerably improve our understanding of (genomic) diversification at deep and shallow time across eukaryotes. It is becoming increasingly clear that microbial eukaryotes play very important roles in many ecosystems, as producers, consumers and pathogens or as industrially important organisms.

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