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ITMO BIOLOGIE CELLULAIRE, DÉVELOPPEMENT ET ÉVOLUTION

ITMO GÉNÉTIQUE, GÉNOMIQUE ET BIOINFORMATIQUE

Colloque **Évolution : aujourd'hui et demain** | Colloquium **Evolution: Present and Future**

Illustration : Diversité morphologique et duplication globale chez les poissons téléostéens. ©Pauline Sémon et Marie Sémon (IGFL, UMR 5242 CNRS, École Normale Supérieure de Lyon)
Photo : *Astyanax mexicanus* : tête-à-tête entre morphotype de surface et morphotype cavernicole aveugle. © Sylvie Rétaux, CNRS UPR 3294, Gif-sur-Yvette

Les 28 (14 h) et 29 novembre 2013

CNRS, Campus Gérard Mégie
3 rue Michel-Ange, Paris 16e

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ITMO CELL BIOLOGY, DEVELOPMENT AND EVOLUTION

ITMO GENETICS, GENOMICS AND BIOINFORMATICS

November 28th and 29th, 2013

CNRS, Campus Gérard Mégie
3 rue Michel-Ange, Paris 16e

Colloquium Evolution: Present and Future

Thursday, November 28th, 2013

1:00 PM	**Reception - Coffee**
2:00 PM	**Introduction: Laurent Kodjabachian,** director of ITMO Cell biology, development and evolution; **Dominique Joly,** CNRS -Institute of ecology and environment; **Vincent Laudet,** Director of Institute of Functional Genomics of Lyon; **Thierry Galli**, deputy director of ITMO Cell biology, development and evolution
	SESSION 1: CELLULAR MECHANISMS OF DEVELOPMENT AND EVOLUTION **Chairman: Laurent Kodjabachian**
2:10 PM	How rapid evolution did reshape the ancestral chordate genome in tunicates (Oikopleura and other larvaceans), **Daniel Chourrout**, Bergen (Norway)
2:50 PM	Filamentous development in brown algae: alternative processes of multicellularity, **Bénédicte Charrier**, Roscoff
3:10 PM	Address of Pr **André Syrota**, President of Aviesan, Chairman and CEO of Inserm
3:20 PM	Clues about the origin and evolution of metazoan embryo polarity from studies in the cnidarian Clytia, **Evelyn Houliston**, Villefranche-sur-Mer
3:40 PM	Robustness and evolution of *C. elegans* vulva development, **Marie-Anne Félix**, Paris
4:00 PM	What studies in planarians reveal about animal centrosome structure and function, **Juliette Azimzadeh**, Paris
4:20 PM	**Coffee break**
4:40 PM	Regulatory mechanisms of emergence and diversification of morphological patterns, **Benjamin Prud'homme**, Marseille
5:00 PM	**Regenerating the body: old questions, new models**, **Michalis Averof**, Lyon
	SESSION 2: EVOLUTION AND PATHOLOGY **Chairman: Vincent Laudet**
5:20 PM	The capital economy in hominin evolution: body fat made us human**, Jonathan Wells**, London (UK)
6:00 PM	Cancer evolution and prevention, **Michael Hochberg**, Montpellier
6:20 PM	Population genetic tools to dissect immunity to infection in humans, **Lluis Quintana-Murci**, Paris

Friday, November 29th, 2013

SESSION 2: EVOLUTION AND PATHOLOGY (PART 2)
Chairman: Vincent Laudet

9:00 AM — Evolutionary thinking in medicine, **Michel Raymond**, Montpellier

9:20 AM — Biased gene conversion: the dark side of recombination, **Laurent Duret**, Lyon

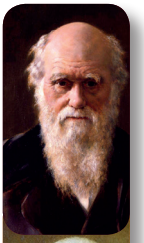
SESSION 3: ADAPTATION TO ENVIRONMENT
Chairman: Dominique Joly

9:40 AM — Address of **Stéphanie Thiebault**, Vice-president of AllEnvi, Director of the CNRS' Institute of ecology and environment (INEE)

9:50 AM — Tracing the genetic basis of adaptations in the house mouse, **Diethard Tautz**, Ploen (Germany)

10:30 AM — Coffee break

10:50 AM — The genetic basis of adaptation: molecular evolution of mimicry in butterflies, **Mathieu Joron**, Paris



11:10 AM — Metabolic evolution of a Drosophila fly adapted to its cactus host, **Virginie Orgogozo**, Paris

11:30 AM — Development and evolution of the brain in the blind cavefish *Astyanax mexicanus*: drift and selection, **Sylvie Rétaux**, Paris

11:50 AM — The dynamics of hybridization and speciation in forest trees, **Rémy Petit**, Bordeaux

12:10 PM — Rapid adaptive changes in morphology and function in natural population, **Anthony Herrel**, Paris

12:30 PM — Lunch break

2:00 PM — Round Table on future challenges in Evolutionary Biology led by **Michel Vervoort**

SESSION 4: NEW OUTLOOKS ON EVOLUTION
Chairman: Thierry Grange

2:40 PM — What have we learned from 25 years of molecular phylogenies of the animal kingdom? **Max Telford**, London (UK)

3:20 PM — Genetic and nongenetic inheritance: a current paradigm shift, **Etienne Danchin**, Toulouse

3:40 PM — Biodiversity and Evolution: the last refuge for basic research in Biology? **Jean-Michel Claverie**, Marseille

4:00 PM — How horizontal transfer shapes the biochemistry, genetics and behavior of bacteria, **Eduardo Rocha**, Paris

4:20 PM — A brief history of human evolution: are climates and geography the main driving forces? **Jean-Jacques Jaeger**, Poitiers

4:40 PM — End of colloquium

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ITMO CELL BIOLOGY, DEVELOPMENT AND EVOLUTION

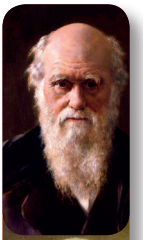
ITMO GENETICS, GENOMICS AND BIOINFORMATICS

28 et 29 novembre2013
CNRS, Campus Gérard Mégie
3 rue Michel-Ange, Paris 16e

Colloque Evolution: Aujourd'hui et demain

Jeudi 28 novembre 2013

13h00-14h00	**Accueil - café**
14h00-14h10	**Introduction** : **Laurent Kodjabachian**, directeur ITMO Biologie cellulaire, développement et évolution ; **Dominique Joly**, CNRS – Institut écologie et environnement ; **Vincent Laudet**, directeur de l'Institut de Génomique Fonctionnelle de Lyon; **Thierry Galli,** directeur adjoint ITMO Biologie cellulaire, développement et évolution.
	SESSION 1 : MÉCANISMES CELLULAIRES DU DÉVELOPPEMENT ET DE L'ÉVOLUTION **Modérateur : Laurent Kodjabachian**
14h10-14h50	Comment une évolution très rapide a modifié le génôme ancestral des chordés chez les tuniciers (Oikopleura et autres appendiculaires), **Daniel Chourrout**, Bergen (Norvège)
14h50-15h10	Existe-t-il des mécanismes originaux de la multicellularité chez les algues brunes ? **Étude du développement filamenteux du modèle Ectocarpus, Bénédicte Charrier**, Roscoff
15h10-15h20	Allocution du **Pr Syrota**, Président d'Aviesan, PDG de l'Inserm, Paris
15h20-15h40	L'origine et l'évolution de la polarité embryonnaire chez les métazoaires : leçons d'un cnidaire, **Evelyn Houliston**, Villefranche-sur-Mer
15h40-16h00	Robustesse et évolution du développement de la vulve de *C. elegans*, **Marie-Anne Félix**, Paris
16h00-16h20	Ce que l'étude des planaires nous apprend sur la structure et la fonction du centrosome animal, **Juliette Azimzadeh**, Paris
16h20-16h40	**Pause-café**
16h40-17h00	Mécanismes régulateurs de l'émergence et de la diversification des caractères morphologiques, **Benjamin Prud'homme**, Marseille
17h00-17h20	Régénération : anciennes questions, nouveaux modèles, **Michalis Averof**, Lyon
	SESSION 2 : ÉVOLUTION ET PATHOLOGIE **Modérateur : Vincent Laudet**
17h20-18h00	Économie du capital et évolution des hominidés: la graisse nous a rendu humains, **Jonathan Wells**, Londres (Royaume Uni)
18h00-18h20	Médecine préventive évolutionniste des cancers, **Michael Hochberg**, Montpellier
18h20-18h40	Génétique des populations humaines, immunité et maladies infectieuses, **Lluis Quintana-Murci, Paris**



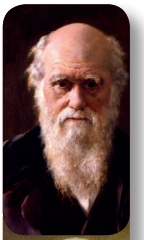
Vendredi 29 novembre 2013

SESSION 2 : ÉVOLUTION ET PATHOLOGIE (suite)
Modérateur : Vincent Laudet

9h00-9h20	L'approche évolutionniste en médecine, **Michel Raymond**, Montpellier
9h20-9h40	Conversion génique biaisée : la face cachée de la recombinaison, **Laurent Duret**, Lyon

SESSION 3 : ADAPTATION À L'ENVIRONNEMENT
Modérateur : Dominique Joly

9h40-9h50	Allocution de **Stéphanie Thiébault,** Vice-présidente d'AllEnvi, Directrice de l'Institut d'écologie et de l'environnement du CNRS, Paris
9h50-10h30	Tracer les bases génétiques des processus d'adaptation chez *Mus musculus*, **Diethard Tautz**, Ploen (Allemagne)
10h30-10h50	Pause-café
10h50-11h10	Bases génétiques de l'adaptation : l'évolution moléculaire du mimétisme chez les papillons, **Mathieu Joron**, Paris
11h10-11h30	Evolution métabolique chez une drosophile adaptée à son cactus hôte, **Virginie Orgogozo**, Paris
11h30-11h50	Développement et évolution du cerveau chez le poisson cavernicole aveugle *Astyanax mexicanus* : dérive et sélection, **Sylvie Rétaux**, Paris
11h50-12h10	Dynamique de l'hybridation et de la spéciation chez les arbres forestiers, **Rémy Petit**, Bordeaux
12h10-12h30	Changements rapides et adaptatifs de la morphologie et la fonction dans des populations naturelles, **Anthony Herrel**, Paris
12h30-14h00	Déjeuner-buffet
14h00-14h40	Table-ronde sur les défis futurs en biologie de l'évolution animée par **Michel Vervoort**



SESSION 4 : ÉVOLUTION : NOUVEAUX REGARDS
Modérateur : Thierry Grange

14h40-15h20	Qu'avons-nous appris en 25 ans de phylogénie moléculaire du règne animal ? **Max Telford**, Londres (Royaume Uni)
15h20-15h40	Hérédité génétique et non génétique, **Étienne Danchin**, Toulouse
15h40-16h00	Biodiversité et Evolution : dernier refuge de la recherche fondamentale en biologie ? **Jean-Michel Claverie**, Marseille
16h00-16h20	Comment le transfert horizontal façonne la biochimie, la génétique et le comportement des bactéries, **Eduardo Rocha**, Paris
16h20-16h40	Une brève histoire de l'évolution humaine : les climats et la géographie constituent-ils les moteurs principaux ? **Jean-Jacques Jaeger**, Poitiers
16h40	Fin du colloque

SESSION 1:
CELLULAR MECHANISMS OF DEVELOPMENT AND EVOLUTION

HOW RAPID EVOLUTION DID RESHAPE THE ANCESTRAL CHORDATE GENOME IN TUNICATES (OIKOPLEURA AND OTHER LARVACEANS)

Daniel Chourrout
Sars International Centre for Marine Molecular Biology, University of Bergen, Norway

Tunicates comprise several classes of chordates that are all marine and display rather simple anatomy. Considered for very long as best proxys of the chordate ancestor, tunicates now appear to be the result from a secondary and profound simplification process. This novel view is based on a variety of recent investigations, in large part conducted in the larvacean class. The genome of one cosmopolitan larvacean, Oikopleura dioica, has been thoroughly analysed and compared to those of other chordates and other metazoans. It shows remarkably divergent features, including ultracompaction, new sets of mobile elements, modified gene contents as well as profoundly remodelled syntenies and intron-exon structures. This alternative genome will be described in this talk, with rapidly evolving components illustrating the high level of genome plasticity and giving insight into fundamental mechanisms of genome evolution. New larvacean genomes were recently sequenced and their preliminary examination shows that accelerated evolution is a general trend, for at least the whole class. The nature of forces driving such a rapid evolution will be discussed.

FILAMENTOUS DEVELOPMENT IN BROWN ALGAE: ALTERNATIVE PROCESSES OF MULTICELLULARITY

Bénédicte Charrier
Morphogenèse des Macro-Algues, UMR7139 CNRS-UPMC « Végétaux Marins et Biomolécules », Station Biologique, Roscoff, France

While they are large photosynthetic multicellular organisms, brown algae are phylogenetically unrelated to land plants and other algae[1]. Actually, they display cellular[2] and molecular[3,4] features shared with metazoans. Mutant analysis[5] and single-cell transcriptomics performed on the filamentous brown algal model Ectocarpus allows to start deciphering the molecular factors involved in the establishment of tissue patterning in the early stages of development in these organisms. The talk will present to which extent these molecular factors together with the recently characterised biophysical features of Ectocarpus cells account for the concomitant polarised growth and cell differentiation processes taking place along the filament, in the context of the marine environment.

1. Charrier, B. et al. *Trends Plant Sci* 17, 468-477 (2012)
2. Katsaros, C. et al. *Ann. Bot* 97, 679–693 (2006)
3. Cock, J.M. et al. *Nature* 465, 617-21 (2010)
4. Billoud, B. et al. *Nucleic Acids Res*, doi: 10.1093/nar/gkt856 (2013)
5. Le Bail, A. et al. *Plant Cell* 23, 1666-1678 (2011)

CLUES ABOUT THE ORIGIN AND EVOLUTION OF METAZOAN EMBRYO POLARITY FROM STUDIES IN THE CNIDARIAN CLYTIA.

Evelyn Houliston
Cnidarian developmental mechanisms group, Laboratoire de Biologie du Développement de Villefranche-sur-mer (LBDV; CNRS UMR7009), Université Paris 6, Villefranche-sur-mer, France

Cnidarians, as a sister group to the Bilateria, can help us address how widely diverse animal forms are generated during development using a very similar "tool kit" of conserved developmental regulator genes. Over the last few years it has emerged that the basic cnidarian body plan, based on a single polarity axis and two germ layers, is directed by localised maternal determinants acting upstream of Wnt signalling and the expression of conserved metazoans transcription factors. Thus, mechanisms of primary axis and germ layer specification in cnidarians are more similar than previously thought to those known from bilaterian models, and may have been already employed in a common metazoan ancestor.
Work from of our group using the hydrozoan model *Clytia hemisphaerica*[1] has contributed to this new picture. In *Clytia*, embryonic polarity development is initiated by localised maternal mRNAs coding for a Wnt ligand and two Frizzled-family receptors[2,3]. These determinants restrict Wnt-ß catenin signalling to one side of the embryo, initiating transcription of many target genes including ones involved in polar identity and gastrulation. In parallel, morphogenesis to produce the elongated larva requires Strabismus–mediated planar cell polarity via the Fz-PCP pathway[4]. Our ongoing work is identifying genes acting downstream of Wnt signalling. These include not only metazoan conserved signalling pathway components and transcription factors, but also many novel cnidarian specific genes. Fundamental developmental processes in cnidarians may thus involve many "novel" genes as well as highly conserved ones.

References
1. E. Houliston, T. Momose, M. Manuel, Clytia hemisphaerica: a jellyfish cousin joins the laboratory, *Trends Genet*. 26, 159–167 (2010).
2. T. Momose, E. Houliston, Two oppositely localised frizzled RNAs as axis determinants in a cnidarian embryo, *PLoS Biol*. 5, e70 (2007).
3. T. Momose, R. Derelle, E. Houliston, A maternally localised Wnt ligand required for axial patterning in the cnidarian Clytia hemisphaerica, *Development* 135, 2105–2113 (2008).
4. T. Momose, Y. Kraus, E. Houliston, A conserved function for Strabismus in establishing planar cell polarity in the ciliated ectoderm during cnidarian larval development, *Development* 139, 4374–4382 (2012).

ROBUSTNESS AND EVOLUTION OF C. ELEGANS VULVA DEVELOPMENT

Michalis Barkoulas and **Marie-Anne Félix**
Team «Evolution of *Caenorhabditis*», IBENS, Department of Biology, ENS-CNRS-Inserm, Paris, France

Biological processes are generally studied in the laboratory under one environmental condition and in one reference genetic background. We try to widen this horizon to answer questions on the relationship between genetic and phenotypic evolution, by placing a paradigmatic model system in developmental biology, *C. elegans* vulval cell fate patterning, in its evolutionary context. We study properties of robustness, pattern of evolutionary variation and evolvability of this system. Using mutation accumulation lines, we showed that mutational effects may produce phenotypic trends, in the absence of selection.
Like many biological systems, the signaling network underlying vulval precursor cell fate patterning can perform reproducibly to generate invariant outcomes, despite external or internal noise. Although most of the key molecular factors underpinning vulval patterning have now been identified, still very little is understood in quantitative terms. Through pathway dosage modulation and single molecule FISH hybridisation, we investigated some quantitative aspects of developmental robustness and system behaviour by experimentally perturbing the two main pathways (EGF and Notch) involved in vulval patterning. Using comparative single molecule FISH hybridisation, we show that levels of lin-3 expression are conserved within *C. elegans* isolates and *C. briggsae*, and differ only slightly in more distant species such as *C. angaria* or *Oscheius tipulae*. We demonstrate that LIN-3 plays a key role in vulval induction in other *Caenorhabditis* species despite substantial evolution of some cis-regulatory elements required for anchor cell expression in the *C. elegans* context.

WHAT STUDIES IN PLANARIANS REVEAL ABOUT ANIMAL CENTROSOME STRUCTURE AND FUNCTION

Juliette Azimzadeh
Institut Jacques Monod, CNRS UMR7592/Université Paris-Diderot, Paris, France

The centrosome is the main organizer of the microtubule cytoskeleton in animal cells. The centrosome is a membrane-free organelle formed by cylinder-shaped centrioles surrounded by a protein matrix that anchors microtubule-nucleating complexes. Duplication of the centrioles at each cell cycle ensures the reproduction of the centrosome and the assembly of a bipolar spindle during mitosis[1]. The older centriole within the centrosome can also template the assembly of a primary cilium, a sensory organelle found on nearly every cell in the human body[2].
We found that, unlike the rest of animals, freshwater planarians of the genus Schmidtea completely lack centrosomes[3]. Planarians do form centrioles but only in terminally differentiating ciliated cells to trigger the assembly of cilia. This pathway for centriole assembly, called acentriolar pathway, is also found in multiciliated cells from human tracheal and ependymal epithelia and is distinct from centriole/centrosome duplication in proliferating cells. Centrioles are never present in planarian proliferating cells, supporting that these animals are devoid of centrosomes. This unique characteristic allowed us to identify a large set of conserved proteins required for centriole assembly in animals, as well as the centrosome signature proteins missing from the planarian genome. Our work uncovers the molecular architecture and evolutionary history of the animal centrosome. It also suggests that the evolution of the centrosome is not linked to its cellular functions, such as chromosome segregation or intracellular trafficking, but is linked to its functions in development.

1. J. Azimzadeh, W. F. Marshall, Building the centriole. *Current biology* : CB 20, R816 (Sep 28, 2010).
2. H. Ishikawa, W. F. Marshall, Ciliogenesis: building the cell's antenna. *Nature reviews. Molecular cell biology* 12, 222 (Apr, 2011).
3. J. Azimzadeh, M. L. Wong, D. M. Downhour, A. Sanchez Alvarado, W. F. Marshall, Centrosome loss in the evolution of planarians. *Science* 335, 461 (Jan 27, 2012).

REGULATORY MECHANISMS OF EMERGENCE AND DIVERSIFICATION OF MORPHOLOGICAL PATTERNS

Benjamin Prud'homme
IBDML, CNRS UMR 7288, case 907, Parc scientifique de Luminy, 13288 Marseille cedex 9, France

The typical pattern of morphological evolution associated with the radiation of a group of related species is the emergence of a novel trait and its subsequent diversification. From butterfly eyespots and their various colorful rings to the diversity of shapes assumed by vertebrate teeth, seashells or horn beetles, this pattern of emergence-diversification holds for countless characters across most animal groups. Yet the genetic mechanisms associated with these two evolutionary steps are poorly characterized.
We're studying the evolution of wing pigmentation patterns in flies to address from a gene regulatory perspective how morphological novelties (rarely) emerge and how they (often) diversify.
We're also studying the function of wing pigmentation patterns in mating behavior in order to identify the possible selective mechanisms underlying the evolution of this morphological trait.

REGENERATING THE BODY: OLD QUESTIONS, NEW MODELS

Nikolaos Konstantinides and **Michalis Averof**
Institut de Génomique Fonctionnelle de Lyon, 32-34 avenue Tony Garnier, 69007 Lyon, France

Many animals have the ability to regenerate amputated or damaged body parts, but it is unclear to what extent different taxa use similar strategies to achieve this. For instance, planarians and vertebrates – members of the Lophotrochozoa and Deuterostomes, respectively – use different cells to replace missing tissues; in planarians all tissues can regenerate from a common pool of pluripotent progenitor cells, whereas in vertebrates different cell types arise from distinct progenitors. In most animals we lack the experimental tools needed to determine the origin of regenerated tissues. It is thus not known if similar types of progenitor cells exist across phyla and which regeneration strategy is most ancient. I will present a genetically tractable model for limb regeneration, the crustacean Parhyale hawaiensis, which belongs to the third major clade of bilaterian animals, the Ecdysozoa. Adult Parhyale can fully regenerate their limbs within two weeks. Using transposon insertions as cell lineage markers, we find that limb regeneration involves distinct progenitor cells for the ectoderm and mesoderm, residing locally in the amputated stump. No progenitors contribute to both ectodermal and mesodermal cell types. In addition, we identify a population of mesodermal cells that express Pax3/7 and resemble satellite cells, adult muscle progenitors previously described only in chordates. We show that Parhyale satellite-like cells proliferate during regeneration, participate in the regeneration blastema and contribute to regenerated muscle. Our results suggest that satellite-like muscle precursors also exist in arthropods, arguing for a common cellular basis of muscle regeneration in animals as diverse as vertebrates and arthropods.

SESSION 2:
EVOLUTION AND PATHOLOGY

THE CAPITAL ECONOMY IN HOMININ EVOLUTION: BODY FAT MADE US HUMAN

Jonathan CK Wells
Childhood Nutrition Research Centre, University College London Institute of Child Health, London, United Kingdom

Evolutionary anthropologists have long assumed that the physical traits most evident in the fossil record – bipedal locomotion, free hands and large brains – were those that defined human evolution. Recently, anthropologists have begun to ask how these traits were favoured by selection. Using the robust framework of life history theory, we can ask how organisms invest energy in different organs or tissues. Clearly, the genus Homo has invested in large brains, but this organ is metabolically costly, so how did early hominins manage to meet these extra costs? I propose that the answer to this question is linked to the evolutionary history of another organ, body fat. Storing energy temporarily in adipose tissue (physical capital) allows greater coherence in life history strategy, and the subsequent investment of energy in other organs and tissues. Cooperative behavior is a similar strategy, allowing individuals to store energy temporarily in relationships of reciprocity (social capital). Intriguingly, many other primates show similar traits, indicating that hominins merely developed these existing trends to a greater degree. I suggest that early hominins were exposed to volatile environments and that enhanced body fat stores and social cooperation aided in resolving this ecological stress. With greater control of energy metabolism, it then became possible to invest in expensive traits such as large brains, and to adapt to diverse ecological niches, which drove the global colonization of the Homo genus. While not preserved in the fossil record, body fat may prove to be a key factor in the evolution of our species.

CANCER EVOLUTION AND PREVENTION

Michael Hochberg
CNRS, Institut des Sciences de l'Evolution, UMR5554, Université Montpellier II, Place E Bataillon, 34095 Montpellier, France

Since the mid 1970s, cancer has been described as a process of Darwinian evolution, with somatic cellular selection and evolution being the fundamental processes leading to malignancy and its many manifestations (neoangiogenesis, evasion of the immune system, metastasis, and resistance to therapies). Historically, little attention has been placed on applications of ecology and evolutionary biology to understanding and controlling neoplastic progression and to prevent therapeutic failures. This is now beginning to change, and there is a growing interest in the interface between ecological and evolutionary theories and cancer therapies. I describe fronts where the ecological and evolutionary perspective is most developed, in particular, that cancer generates substantial levels of phenotypic diversity, which makes it a challenge to control even when discovered in early stages. I present an analysis supporting the notion that major advances in 'winning the war' against cancer will require preventive approaches, and in particular ultra-low impact treatments and/or life-style changes for people at high risk of developing the disease.

POPULATION GENETIC TOOLS TO DISSECT IMMUNITY TO INFECTION IN HUMANS

Lluis Quintana-Murci
Unit Human Evolutionary Genetics, CNRS URA3012, Institut Pasteur, Paris, France

Infectious diseases have been paramount among the threats to health and survival throughout human history, so natural selection is expected to act strongly on host defence genes. This is particularly expected for innate immunity genes, as they represent the first line of host defence against pathogens. In the past years, we have initiated an evolutionary dissection of genes and pathways involved in innate immunity in humans. We have focused on major families of innate immunity receptors, such as TLRs, RLRs and NLRs, and other molecules involved in the signalling pathways triggered by them, such as adaptors and effectors molecules. I will present different cases of how some of these genes and the pathways they trigger have been targeted by natural selection, in its different forms and intensities. I will also illustrate how these findings are helping to delineate genes that are important for host defence, with respect to those exhibiting higher immunological redundancy, and to increase our understanding of how past selection has had an impact on disease susceptibility in modern populations. Finally, I will discuss how changes in human lifestyle and modes of subsistence – e.g. the transition from hunter-gathering to farming – may affect the demographic and adaptive history of human populations. More generally, I will illustrate how adopting an evolutionary genetics approach is an indispensable complement to clinical and epidemiological approaches for identifying functionally important genes involved in host immunity to infection and disease outcome.

EVOLUTIONARY THINKING IN MEDICINE

Michel Raymond
Equipe de Biologie Evolutive Humaine, Institut des Sciences de l'Evolution (ISEM, UMR CNRS 5554), Université de Montpellier II, Montpellier, France

Our body is not perfect: it is susceptible to diseases, it senesces during ageing, etc. Medicine aims to extend our longevity by correcting and compensating these caveats; however, a fair understanding of the mere existence of these imperfections is certainly required. Built by natural selection during our evolutionary past, like every other animal, our body has been optimized for reproduction (and not directly for an extended longevity), with tradeoffs between the other life-history traits (e.g. pathogen resistance, metabolism, and obviously longevity). Evolutionary biology theory could thus provide interesting cues to accelerate the improvement of the medical knowledge and practice, and this will be illustrated with several examples.

BIASED GENE CONVERSION: THE DARK SIDE OF RECOMBINATION

Laurent Duret
Laboratoire Biométrie et Biologie Evolutive, UMR CNRS 5558, Université Lyon 1
43 Bld du 11 Novembre 1918, 69622 Villeurbanne cedex, France

Recombination is typically thought as a symmetrical process resulting in large-scale reciprocal genetic exchanges between homologous chromosomes. Recombination events, however, are also accompanied by short-scale, unidirectional exchanges in the neighborhood of the initiating double-strand break: gene conversion. A large body of evidence suggests that gene conversion is GC-biased in many eukaryotes, including mammals and human. AT/GC heterozygotes produce a larger amount of GC- than AT-gametes, thus conferring a population advantage to GC-alleles in high-recombining regions. This apparently unimportant feature of our molecular machinery has strong evolutionary consequences. Structurally, GC-biased gene conversion explains the spatial distribution of GC-content in mammalian genomes - the so-called isochore structure. Functionally, GC-biased gene conversion promotes the «undesired» segregation and fixation of deleterious AT->GC mutations, thus increasing our genomic mutation load. I will review the recent evidence for a GC-biased gene conversion process in mammals, its consequences on genomic landscapes, molecular evolution, and human functional genomics.

SESSION 3:
ADAPTATION TO ENVIRONMENT

TRACING THE GENETIC BASIS OF ADAPTATIONS IN THE HOUSE MOUSE

Diethard Tautz
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Although the house mouse is a well-established model system for biomedical research, it has received much less attention by evolutionary biologists so far. However, there are many aspects that make it particularly suitable for studying evolutionary questions. It has a well-defined history of population expansions and colonization of new habitats, ranging from desert climates to sub-Antarctic islands. Several colonizations have occurred during historic times, which allow studying the earliest phases of evolutionary adaptations. The mouse has also a broad behavioral repertoire making it suitable for analyzing social communication and mate choice. In the past years, we have build up a large collection of samples and animals from natural populations. I will report on the experimental approaches that we are using to better understand the genetics of adaptation and population differentiation. We can make full use of the genomic resources that were developed for the laboratory mouse, allowing us to do genome scans for adaptive trait genes and to map the genetic basis for complex traits, such as the unusual growth of mice on some islands. We find evidence that adaptive introgression of alleles from other populations plays a larger role in shaping the genomes than previously considered.

THE GENETIC BASIS OF ADAPTATION: MOLECULAR EVOLUTION OF MIMICRY IN BUTTERFLIES

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The response of populations to natural selection, a process called adaptation, is at the heart of modern biology. However, we know relatively little about the nature of genetic and ecological changes associated with adaptation, highlighting the need for study systems where both genetic approaches and good ecological knowledge can be combined. The butterflies are great models for ecological genomics because they show diverse wing phenotypes associated with clear ecological processes, and are amenable to molecular genetic investigation, allowing to link genomic variation with known selection regimes. In the tropical Heliconius butterflies, wing patterns are selected for their protective role in warning predators of their toxicity, and show remarkable convergent evolution between species, a widespread process called mimicry bringing survival benefits to convergent species. Mimicry is an example of radical morphological changes evolving under natural selection in distant lineages. We have pinpointed the genomic regions controlling mimicry, and the genes and structural variants underlying distinct wing patterns are being characterised using population and functional approaches. Now, genomic data on population genetic variation at these loci allow a better understanding of the mechanisms of wing pattern evolution. We showed that hybridisation and introgression are widespread phenomena strongly influencing adaptation. Mimicry alleles can cross the species boundary and facilitate instant resemblance between closely related species. In contrast, more distant species evolve true convergence via independent, parallel evolution at the same genes. The data shows that genomic regions under selection can have radically different evolutionary trajectories than the genomes and populations harbouring them.

METABOLIC EVOLUTION OF A DROSOPHILA FLY ADAPTED TO ITS CACTUS HOST

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Most living species exploit a limited range of resources. However, little is known about how tight associations build up during evolution between such specialist species and the hosts they use. We examined the dependence of Drosophila pachea on its single host, the senita cactus. Several amino acid changes in the Neverland oxygenase rendered D. pachea unable to transform cholesterol into 7-dehydrocholesterol (the first reaction in the steroid hormone biosynthetic pathway in insects) and thus made D. pachea dependent on the uncommon sterols of its host plant. The neverland mutations increase survival on the cactus's unusual sterols and are in a genomic region that faced recent positive selection. This study illustrates how relatively few genetic changes in a single gene may restrict the ecological niche of a species.

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DEVELOPMENT AND EVOLUTION OF THE BRAIN IN THE BLIND CAVEFISH ASTYANAX MEXICANUS: DRIFT AND SELECTION

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We use the emerging fish model *Astyanax mexicanus* to understand genetic and cellular mechanisms involved in morphological and behavioral evolution. Within this species, there are populations of river-dwelling surface fish ("normal fish") and populations of blind cavefish inhabiting the darkness of caves. The latter have undergone some striking losses (eyes, pigmentation) but have also undergone some probably adaptive gains, such as more taste buds, more neuromasts, larger jaws, more teeth, modified hypothalamus and larger olfactory structures. Their physiology and behavior is also very different from their surface counterparts.
We use developmental biology approach (evo-devo)[1,2], molecular evolution tools[3], and behavioral analyses [4,5] to understand the evolutionary forces at work during cavefish brain evolution and its adaptation to cave life [6].
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THE DYNAMICS OF HYBRIDIZATION AND SPECIATION IN FOREST TREES

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The botanist Edgar Anderson[1] once made the rather extreme claim that in the plant species he was studying, "all the readily detectable variation can be ascribed to introgression". This is just one example of the (fluctuating) opinions on the role of interspecific genetic exchanges in evolution. Trees have played a notable role in this debate. Charles Darwin[2] used the familiar oaks in the Chapter 2 of his Origin book to express his views on the fuzziness of species. Subsequently, Leigh Van Valen[3] also used the oaks to defend his view on the failure of the biological species concept and to push forward his ecological species concept. Currently, forest trees such as oaks, poplars, and several conifers remain important models for studies of hybridization, introgression and ecological speciation. I will illustrate some of the main findings of this research front. In particular, I will present results from extensive genetic surveys of diversity in species-rich tropical tree communities and from more classical population genetic surveys of introgression in trees. Ongoing studies have started to rely on population genomic approaches or on detailed parentage analyses in mixed species stands[4-7]. All these studies contribute without exception to the growing recognition that the perimeter of genetic exchanges often extends beyond species boundaries, to the point that it is no longer safe to assume that species within genera evolve genetically largely independently from each other.

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RAPID ADAPTIVE CHANGES IN MORPHOLOGY AND FUNCTION IN NATURAL POPULATION

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Although rapid adaptive changes in morphology on ecological time scales are now well documented in natural populations, the effects of such changes on whole-organism performance capacity are often unclear. We present data on a study system where lizards have rapidly evolved differences in head morphology, bite strength, and digestive tract structure after experimental introduction into a novel environment resulting in a change in diet. Despite the short time scale (~36 years) since this introduction, the changes in morphology and performance parallel those typically documented among species and even families of lizards in both the type and extent of their specialization. We present novel data on the seasonality of the observed changes in morphology, performance, and diet suggesting an important role for plasticity in driving some of the observed changes. Finally we document changes in intestinal tract structure and function that underwrite the importance of the microbial gut community in allowing lizards to switch to an herbivorous diet. These data provide a compelling example of how the invasion of a novel habitat can drive variation on morphology through selection on function.

SESSION 4:
NEW OUTLOOKS ON EVOLUTION

WHAT HAVE WE LEARNED FROM 25 YEARS OF MOLECULAR PHYLOGENIES OF THE ANIMAL KINGDOM?

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25 years ago, the first small subunit ribosomal RNA based phylogeny of the animal kingdom was published by Katherine Field and co-authors. This landmark paper kick-started the pursuit of an accurate molecular based phylogeny of the animal phyla. I will look back at the progress towards this goal that has been made over the past two decades. I will look at the major unexpected relationships that have been uncovered, what technical innovations these discoveries were based on and what our new understanding of phylogeny means for interpretations of animal evolution at the levels of morphology, genes and genomes. The surprises have inevitably arisen where the molecules are in conflict with our prejudices regarding morphological evolution. The real novelty of the modern tree of animal relationships are these unexpected distributions of morphological characters such as though guts, ciliated larvae, ecdysis, segmentation and body cavities. Some of these characters, once thought insignificant, now define groups (e.g. ecdysis and the Ecdysozoa) but others formerly believed to define clades (coeloms and the Coelomata) are now seen to have a patchy distribution. These patchy characters are of particular interest in terms of understanding adaptation as they have either been evolved multiple times or been lost repeatedly. I will also talk about deuterostome phylogeny and the contentious issue of the position of *Xenoturbella* and the Acoelomorpha.

GENETIC AND NONGENETIC INHERITANCE: A CURRENT PARADIGM SHIFT

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Several biologists are calling for the modernization of the current modern synthesis of evolution[1-4]. We usually consider that biological information is transmitted across generations through the sole DNA sequence. However, evidence is accruing that both genetic and nongenetic inheritance, as well as their interactions, concur in producing heredity, which has momentous implications on population functioning and evolution[5, 6]. Moreover, non genetic heredity is likely to be particularly prevalent in humans, and it is urgent to include nongenetic inheritance in all our medical approaches. After briefly reminding the fundamentals of natural selection I will present the case of the missing heritability, one of the major enigmas of current molecular biology[7]. I will then define the various components of genetic and nongenetic heredity and illustrate the latter process with an example involving behavioral and epigenetic inheritance. Nongenetic inheritance has momentous implications in agronomy, conservation biology and more specifically in medicine where it should drastically influence therapeutic research strategies on supposedly genetic disorders[8, 9]. Missing heritability, as well as many other pieces of evidence, suggest that we should abandon the prevailing genocentrism and adopt a broader perspective including nongenetic inheritance into an inclusive evolutionary synthesis. France is clearly at the forefront of this current paradigm shift towards another vision of living organisms.

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BIODIVERSITY AND EVOLUTION: THE LAST REFUGE FOR BASIC RESEARCH IN BIOLOGY?

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According to modern epistemologists, what defines Science and what produces significant progress in scientific knowledge is either (or both) the falsification of well-established conservative theories and/or the experimental confirmation of novel risky hypotheses. One does not recognize those attributes in most of today's fundable research projects that rather emphasize predefined goals to be reached within a well delimited framework of knowledge, an activity that could be righteously considered the exact opposite of a valid «research program» (sensus Lakatos). In that sense, looking for a drug or a vaccine only provide valuable scientific information when it fails. Conditioning the funding of scientists to their (apparent) interest in solving practical societal challenges is thus self-contradictory and the promises of a long term scientific stagnation. Exploring the edge of a field or plowing it are clearly different activities requiring people with different skills. The question then becomes: do we know enough of biology to justify today's exclusive priority given to «translational» research? I think not. As an example, the recent discovery of a whole new world of giant DNA viruses[1-3] demonstrates that, even after 150 years of «modern» microbiology (dated from the death of the «spontaneous generation»), all the **types** of microbial life forms have not yet been discovered on our planet, not mentioning the secret of their origin or a plausible mechanisms for their evolution. Translational research should wait a little longer, just enough to check whether solutions to our problems might not be found within the biology we yet don't know.

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HOW HORIZONTAL TRANSFER SHAPES THE BIOCHEMISTRY, GENETICS AND BEHAVIOR OF BACTERIA

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Evolutionary processes are typically described as the result of mutation, descent and selection. Many microbes lack sexual reproduction but have the ability to acquire genetic information from very distantly related organisms. Horizontal gene transfer allows the instantaneous acquisition of new complex adaptive traits and their transmission to subsequent generations. This speeds up evolutionary processes as exemplified by the acquisition of virulence traits in emerging infectious agents and by antibiotic resistance in most human bacterial pathogens. In bacteria, horizontal gene transfer is much more frequent than gene duplication and affects different types of functions. This shapes the population genetics of bacteria and blurs species' definitions. Rapid spread of genes encoding social traits also has the potential to drive social interactions in bacterial communities. Hence, horizontal gene transfer drives the evolution of bacterial cells and bacterial communities in many ways.

A BRIEF HISTORY OF HUMAN EVOLUTION: ARE CLIMATES AND GEOGRAPHY THE MAIN DRIVING FORCES?

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Human evolution, since its beginning in Asia, and until the origin of modern man in Africa, always occurred in a tropical environment. But this last environment should not be confused with the «lost paradise» of the Bible. It corresponded to a tropical climate but with many periods of instability, being sometimes characterized by strong seasonality or by periods of cooling. Numerical climatic models have been recently developed who allow quantified reconstructions of the prevalent climates of the past, including those of the late Tertiary. They can be used in conjunction to vegetation models to reconstruct vegetation cover of the past and their modifications, to reconstruct potential ecological niches of past hominoids and hominids and therefore to understand the influence of climatic changes in the course of human evolution and dispersion. However, this huge improvement of the analysis of the paleoclimates has led to underestimate the other major factors like predation and community composition changes, which are in fact more difficult to analyze, due to the lack of data. Some examples are given here illustrating the difficulties to identify the main factors which have driven morpho-anatomic changes during some critical periods of human evolution.