

The Origins Of Genome Architecture

The Topological Model of Genome and Evolution Evolutionary Feedbacks Between Population Biology and Genome Architecture The Origins of Genome Architecture Evolution of Genome Architecture Bioinformatics of Genome Regulation, Volume I, 2nd Edition Mechanisms Driving Karyotype Evolution and Genomic Architecture Nuclear, Chromosomal, and Genomic Architecture in Biology and Medicine The Evolution of Organelle Genome Architecture Analysing the various layers of genome architecture using a high-throughput single-molecule technique DNA Rearrangements by Default Or Design? Impacts of Genome and Nuclear Architecture on Molecular Evolution in Eukaryotes The Analysis of Genome Structure and Transcription in *Dictyostelium Discoideum* Using Three Recombinant Plasmids Chromosome Biology as a Key to Understand Disease Mechanisms, Genome Architecture and Evolution Genomic Architecture Handbook Experimental Evolution of Genome Architecture and Complexity in an RNA Virus Genome Structure of Human Cytomegalovirus Genome Chaos Characterization of the Interplay Between the Genome Architecture and Gene Co-expression Genome Research The Evolutionary Feedback Between Genetic Conflict and Genome Architecture Pradeep Chhaya Tariq Ezaz Michael Lynch Rebeca Campos Sanchez Yuriy L. Orlov Aurora Ruiz-Herrera Małgorzata Kloc David R. Smith Jonas Huber Christine J. Shaw Xyrus Maurer-Alcalá Karen Linnea Kindle Hartsuyker Anja Weise Paloma Young Anouk Willemsen Joyce C. Tamashiro Henry H. Heng Audrey Baguette Adrian Young

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this book deals with the missing link in the domain of functional genomics viz genomic architecture it begins with a deconstruction of the darwinian paradigm using the proposed model of modified involuted manifolds it recasts the process of natural selection as a process of information transfer using a topological model this book outlines a new genomic architecture the key argument for this proposed model is that some such structuralism has always been implicit in genomics the proposed model fits very well with the known genomic characteristics and allows to separate the regulatory genome from the transcriptive genomes the model is capable of discerning modular architecture of genomes with different genomic functionalities existing in hierarchical relationships and demonstrates that genomes act as units of selection and as the environment for the individual genes which act as competing species towards the end the book also examines the role of genomic evolution in cancer and the principles of natural selection and evolution of the genotype the regulatory genome is also discussed with an emphasis on its evolution and natural selection it is a valuable source for researchers working in functional genomics mathematical modeling in biology and evolutionary genomics

this ebook presents all 10 articles published under the frontiers research topic evolutionary feedbacks between population biology and genome architecture edited by scott v edwards and tariq ezaz with the rise of rapid genome sequencing across the tree of life challenges arise in understanding the major evolutionary forces influencing the structure of microbial and eukaryotic genomes in particular the prevalence of natural selection versus genetic drift in shaping those genomes additional complexities in understanding genome architecture arise with the increasing incidence of interspecific hybridization as a force for shaping genotypes and phenotypes a key paradigm shift facilitating a more nuanced interpretation of genomes came with the rise of the nearly neutral theory in the 1970s followed by a greater appreciation for the contribution of nonadaptive forces such as genetic drift to genome structure in the 1990s and 2000s the articles published in this ebook grapple with these issues and provide an update as to the ways in which modern population genetics and genome informatics deepen our understanding of the subtle interplay between these myriad forces from intraspecific to macroevolutionary studies population biology and population genetics are now major tools for understanding the broad landscape of how genomes evolve across the tree of life this volume is a celebration across diverse taxa of the contributions of population genetics thinking to genome studies we hope it spurs additional research and clarity in the ongoing search for rules governing the evolution of genomes

the availability of genomic blueprints for hundreds of species has led to a transformation in biology encouraging the proliferation of adaptive arguments for the evolution of genomic features this text explains why the details matter and presents a framework for how the architectural diversity of eukaryotic genomes and genes came to arise

the topic of genome architecture is of great interest to evolutionary biologists small to large chromosome rearrangements have been reorganizing the genome information including genes and heterochromatic regions such as centromeres and telomeres transposable elements are an essential component of the genomes of all life forms studied until now not only because of their abundance but also because of their

influence on reshaping the genome architecture multiple studies have provided evidence that tes are located in particular regions of the genome e g gc rich regions for alus or at rich regions for l1s here using abundant genomic data and statistical methods as diverse as pair wise non parametric tests multiple linear regression multiple negative binomial regression multiple logistic regression interval testing procedure itp and functional logistic regression flr we addressed two questions about te biology 1 how do alus dna transposons and endogenous retroviruses 2s neighboring regions reflect integration site preferences and fixation processes for these tes what genomic features are associated with their presence genome wide 2 can we capture integration site preferences alone using data from young polymorphic or ex vivo integrations the results from the te analyses contributed to our understanding of fixation and integration site preferences genome wide providing abundant information from diverse genomic features this information is of great importance to direct studies of insertional mutagenesis and gene therapy additionally we provided a set of statistical tools to analyze complex genomic datasets moreover we explored the genes on the y chromosome of gorilla we performed this by first generating y specific transcripts from testis rnaseq data second by evaluating their structure in the y chromosome assembly third by using these transcripts to scaffold the y chromosome assembly finally we predicted novel genes from the assembly that could have been transposed from other chromosomes this project allowed us to create a workflow to assemble y transcripts from testis samples this protocol will be applied in future studies in addition we proved the usefulness of transcriptome data to scaffold genomes

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understanding of the origin of species and their adaptability to new environments is one of the main questions in biology this is fueled by the ongoing debate on species concepts and facilitated by the availability of an unprecedented large number of genomic resources genomes are organized into chromosomes where significant variations in number and morphology are observed among species due to large scale structural variants such as inversions translocations fusions and fissions this genomic reshuffling provides in the long term new chromosomal forms on which natural selection can act upon contributing to the origin of biodiversity this book contains mainly articles reviews and an opinion piece that explore numerous aspects of genome plasticity among taxa that will help in understanding the dynamics of genome composition the evolutionary relationships between species and in the long run speciation

this volume reviews the latest research on the functional implications of nuclear chromosomal and genomic organization and architecture on cell and organismal biology and development and progression of diseases the architecture of the cell nucleus and non random arrangement of chromosomes genes and the non membranous nuclear bodies in the three dimensional 3d space alters in response to the environmental mechanical chemical and temporal cues the changes in the nuclear chromosomal or genomic compaction and configuration modify the gene expression program and induce or inhibit epigenetic modifications the intrinsically programmed rearrangements of the nuclear architecture

are necessary for cell differentiation the establishment of cell fate during development and maturation of tissues and organs including the immune muscle and nervous systems the non programmed changes in the nuclear architecture can lead to fragmentation of the nucleus and instability of the genome and thus cause cancer microbial and viral infections can lead to a clustering of centromeres telomeres and ribosomal dna and alter the properties of the nuclear membrane allowing large immobile macromolecules to enter the nucleus recent advances in next generation sequencing technologies combined with nucleus chromosome conformation capture super resolution imaging chromosomal contact maps methods integrative modeling and genetic approaches are uncovering novel features and importance of nuclear chromosomal and genomic architecture this book is an interesting read for cell biologists researchers studying the structure and function of chromosomes and anyone else who wants to get an overview of the field of nuclear chromosomal and genomic architecture

the traditional view of genomes suggests that they are static entities changing slowly in sequence and structure through time e g evolving over geological time scales this outdated view has been challenged as our understanding of the dynamic nature of genomes has increased changes in dna content i e polyploidy are common to specific life cycle stages in a variety of eukaryotes as are changes in genome content itself these dramatic genomic changes include chromosomal deletions i e paternal chromosome deletion in insects goday and esteban 2001 ross et al 2010 developmentally regulated genome rearrangements e g the v d j system in adaptive immunity in mammals schatz and swanson 2011 and the specialization of a distinct somatic genome through epigenetically regulate dna elimination during development found in protists and some animals coyne et al 2012 prescott 1994 wang and davis 2014 wyngaard et al 2011 what likely allows genomes to be highly flexible is the separation of germline i e heritable and somatic i e functional material even in the context of a single nucleus germline soma distinctions have been best described and most easily seen in lineages of multicellular eukaryotes e g plants animals and fungi due to obvious sexual structures germline genomes of these taxa are restricted to specialized cells e g gametes for example pollen grains eggs and spores and remain undifferentiated and often transcriptionally inactive whereas the somatic cells e g skin leaves hyphae provide the basis for ensuring organismal survival to reproductive life stages sequestered germline and somatic genomes are not restricted to these well known multi cellular lineages but are also well described among ciliates the focus of this dissertation and some foraminifera however in these protists germline and somatic genomes are not isolated into distinct cells and tissues but rather are isolated into distinct nuclei that share a common cytoplasm ciliates are a diverse and ancient clade of eukaryotes 1 1 2 gya old and their study has led to the discovery of broad uniting eukaryotic features such as telomeres blackburn and gall 1978 and self splicing rnas kruger et al 1982 as in the microbial eukaryotes the somatic genome macronucleus mac is transcriptionally active transcribing all the genes necessary to maintain the cell while the germline genome micronucleus mic remains transcriptionally inactive during the asexual portions of the life cycle while the germline chromosomes in ciliates are physically similar to other traditional eukaryotic chromosomes e g being multi mbp with centromeres the physical structure of the somatic chromosomes is highly variable for example in the model ciliate *tetrahymena thermophila* the somatic genome is composed of 225 unique chromosomes most of them being 200 400kbp with each at approximately 45 copies whereas *oxytricha trifallax* s somatic genome is composed of 16 000 gene sized chromosomes 2 3kbp with each chromosome at its own independent copy number average copy number 2

000 despite dramatic differences in somatic genome architecture in ciliates the development of a new somatic genome involves for all ciliates studied to date this metamorphosis from traditional germline chromosomal architecture to the incredibly variable somatic genome architecture includes large scale genome rearrangements and dna elimination this transformation involves the epigenetically guided retention of somatically destined dna from the background germline genome while genomic rearrangements in most other eukaryotes are often fatal and are symptoms of well known diseases e g some cancers this traditionally catastrophic event is a fundamental part of ciliate life cycles although studies of ciliate germline genomes have largely been restricted to only a few genera there appear to be broad similarities in gene organization that may be phylogenetically conserved ciliate germline genome architecture has been categorized as either non scrambled or scrambled where non scrambled architectures are often defined as possessing macronuclear destined sequences mdss soma that are separated by germline limited dna and remain in consecutive order e g 1 2 3 4 figure 3 1a and figure 4 4a scrambled germline architectures are highly variable but are broadly defined as mdss being maintained in non consecutive order e g 1 3 4 2 and or on opposing strands of dna figure 3 1 b d and figure 4 4b the germline genomes of chilodonella uncinata the main focus of this dissertation possess a combination of scrambled and non scrambled architectures before my thesis work only those ciliates with gene sized chromosomes have been demonstrated to have scrambled germline loci interestingly previous work has implicated somatic genome architecture impacting the observable accelerated rates of protein evolution in ciliates where the proteins of those ciliates possessing gene sized chromosomes experience the greatest evolutionary rates these observations highlight the need for further work exploring the evolutionary impacts of different germline genome architectures as the germline structure itself has direct impact on the development of the somatic genome while this dissertation aims to elucidate some aspects of the evolution of germline soma distinctions and the impact of genome and nuclear architecture chapters 2 4 there remain several fundamental questions that we can start addressing for instance in this work we observe that the most expanded gene families in chilodonella uncinata are composed of genes that are disproportionately found at scrambled germline loci chapter 3 a major step future step will be to explore the functional implications of this increased paralog diversity through forward and reverse genetics techniques similarly it will be incredibly valuable to better understand the nuclear architecture of the differing genomic contents of the three distinct nuclei present during ciliate development i e the degrading parental mac the new mic and the developing mac there may be observable compartmentalization that is exploitable or critical to the accurate rearrangement of the germline genome into a functional somatic genome finally with the increasingly apparent utility of single cell omics techniques which we use in chapters 3 and 4 there is opportunity to probe into taxonomic groups where physical germline soma separations exist which will provide a far more expansive understanding of the evolutionary and functional impacts of harboring multiple distinct genomes inside of a single cell organism

this topic has been realized and is in collaboration with dr constanze pentzold post doctoral researcher at the institute of human genetics university hospital jena

a genome includes all of the genetic information of an organism it is made up of the nucleotide sequences of dna the complete set of non

random arrangements of functional elements within the genome is known as the genomic architecture the architecture of the genome is crucial in gene regulation utilizing high throughput techniques for 3d interaction mapping and chromatin profiling produces extensive experimental data sets that describe the structure and dynamics of the genome the study of genomic architecture is currently a very prominent area of research that has significant applications in the study of processes such as cell development differentiation and carcinogenesis this book explores all the diverse aspects of genomic architecture it presents researches and studies performed by experts across the globe the extensive content of this book provides the readers with a thorough understanding of the subject

genome chaos rethinking genetics evolution and molecular medicine transports readers from mendelian genetics to 4d genomics building a case for genes and genomes as distinct biological entities and positing that the genome rather than individual genes defines system inheritance and represents a clear unit of selection for macro evolution in authoring this thought provoking text dr heng invigorates fresh discussions in genome theory and helps readers reevaluate their current understanding of human genetics evolution and new pathways for advancing molecular and precision medicine bridges basic research and clinical application and provides a foundation for re examining the results of large scale omics studies and advancing molecular medicine gathers the most pressing questions in genomic and cytogenomic research offers alternative explanations to timely puzzles in the field contains eight evidence based chapters that discuss 4d genomics genes and genomes as distinct biological entities genome chaos and macro cellular evolution evolutionary cytogenetics and cancer chromosomal coding and fuzzy inheritance and more

the relation between the structure of the genome and gene regulation is critical to normal and disease development but the molecular details of how they are interconnected are still unknown chromatin conformation capture hic studies discovered several layers of chromatin organization however the way those structures impact or are impacted by regulation is unclear we thus wanted to clarify the links between chromatin architecture and transcription regulation in this study we use two types of domains one having a structural definition and the other a functional definition and compare them to find their differences and similitudes topologically associating domains tads have been selected to represent the genomic architecture they have a more static nature and their boundaries have been suggested to limit the spread of regulatory signals co expression domains cods were chosen to represent the aspects of gene regulation cods are defined as domains within which genes have correlated expression by definition cods are thus very dynamic and more likely to change from cell to cell in this study we analyze the effect of tad boundaries on nearby genes here we show that tads and cods have distinct functions and are delimited by different boundaries we confirm that tad boundaries disrupt co expression we also characterize cod boundaries and find that they seem to be marked by a switch of strand on which genes are located and they are independent of structural proteins we use expression quantitative trait loci eqtl data to confirm the observations and find that genes affected by the same eqtl are preferentially located on the same strand and are less likely to be separated by barriers such as tad boundaries we thus propose a model for human cells in which the gene conformation impacts gene co regulation we suggest that strand position of genes affects their co expression probability and the introduction of barrier elements further

disrupts it that model would serve as a simple principle to which more complex mechanisms may rely

the advent of separate sexes set the stage for dramatic evolutionary innovation across a wide range of taxa much of this innovation is attributable to divergent evolutionary interests between now distinct sub populations of males and females trade offs inherent to these divergent life histories coupled with a common genome conspire to limit natural selection s ability to simultaneously maximize the fitness of both sexes such conflict between the sexes has therefore largely shaped the history of the genomes of sexual taxa however various aspects of the genomic environment including genes spatial distributions abilities to regulate their expression and rates of recombination also feed back to influence future sex specific evolutionary trajectories using various genomic resources and transcriptome sequences for the lab mouse i test several theoretical predictions regarding this feedback between genetic conflict and features of genomic organization

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