Sexual Development
Genetics, Molecular Biology, Evolution, Endocrinology, Embryology and Pathology of Sex Determination and Differentiation
An evolutionary perspective

Sex Determination and Differentiation in Insects

Editors

Eveline C. Verhulst
Louis van de Zande

Three conditions are essential for evolution: variation, heredity and time. Most animal species transmit genetic information through sexual reproduction in order to meet the first two conditions. The consequence for sexual reproduction is the need for (at least) two sexes with different reproductive roles. Consequently, evolutionary issues arise, such as differences in morphological and behavioral attributes between the sexes, which are reflected in the plethora of animal sex-determining systems. Indeed, a transition to asexual development may occur, sometimes induced by microbial endosymbionts. All these aspects are represented in the insect sex-determining system, which is the focal topic of this issue of Sexual Development.

Sex Determination and Differentiation in Insects is recommended to scientists interested in the evolution of sex determination in particular and developmental pathways in general.

Contents

- Evolutionary Transitions between Sex-Determining Mechanisms: A Review of Theory: van Doorn, G.S.
- Sex Determination in Insects: Variations on a Common Theme: Bopp, D.; Saccone, G.; Beye, M.
- Sex Determination Mechanisms in the Calliphoridae (Blow Flies): Scott, M.J.; Pimsler, M.L.; Tarone, A.M.
- Phylogenetic Distribution and Evolutionary Dynamics of the Sex Determination Genes doublesex and transformer in Insects: Geuverink, E.; Beukeboom, L.W.
- Thelytoky and Sex Determination in the Hymenoptera: Mutual Constraints: Vorburger, C.
- Manipulation of Arthropod Sex Determination by Endosymbionts: Diversity and Molecular Mechanisms: Ma, W.-J.; Vavre, F.; Beukeboom, L.W.
- Genomic Imprinting and Maternal Effect Genes in Haplodiploid Sex Determination: van de Zande, L.; Verhulst, E.C.
- Sex-Determining Mechanisms in Insects Based on Imprinting and Elimination of Chromosomes: Sánchez, L.
- Lepidopteran Sex Determination: A Cascade of Surprises: Nagaraju, J.; Gopinath, G.; Sharma, V.; Shukla, J.N.
- Practical Applications of Insects’ Sexual Development for Pest Control: Koukidou, M.; Alphey, L.

Author Index

The easiest way to order: www.karger.com/sxd

Karger – Medical and Scientific Publishers
CH-4009 Basel, Switzerland
orders@karger.com; Tel. +41 61 306 12 34
www.karger.com
Guidelines for Authors

Aims and Scope
Recent experimental and clinical research have led to impressive advances in our knowledge of the genetic and environmental mechanisms governing sex determination and differentiation, their evolution as well as the mutations or endocrine and metabolic abnormalities that interfere with normal gonadal development. The new journal Sexual Development aspires to provide a unique forum for this rapidly expanding field. Its broad scope will cover all aspects of genetics, molecular biology, embryology, endocrinology, evolution and pathology of sex determination and differentiation in humans and animals. It will publish high-quality original research manuscripts, review articles, short reports, case reports and commentaries. Sexual Development is a modern journal managed by an internationally renowned and multidisciplinary editorial team of three Chief Editors and ten prominent scientists serving as Section Editors, supported by a distinguished panel of editorial board members. They are committed to ensuring fast and author-friendly editorial processing and peer reviewing. Contributions from the scientific community are invited to make Sexual Development the long-awaited and viable forum for basic and medical research on sex determination and differentiation.

Sexual Development
Publishes high-quality original reports and reviews covering all biological and clinical aspects of human and animal sexual determination and differentiation.

Categories of publications in conventional issues
Original Articles are full reports in the following areas • Genetics • Molecular Biology • Evolution • Endocrinology • Embryology • Pathology of Sex Determination and Differentiation. Other categories closely related to the above topics could be considered by contacting the editors for approval.

Reviews covering a timely topic in the field are either invited by the Editors or may be submitted for consideration.

Short Reports must present results of sufficient importance to justify accepted acceleration. They should take up no more than 3 printed pages in the journal and include a maximum of 2 figures, 1 table and 20 references. One printed text page corresponds to about 1,050 words or 5,700 characters.

Case Reports are for de novo observations of single cases with clinical or scientific significance. Reports of single mutations at genes, endocrine or metabolic abnormalities which have already been documented will be published only if they are of unusual clinical or biological interest. Brevity and clarity are always likely to enhance the chance of a manuscript being accepted for publication.

Abstracts
A forum for observations, opinions and comments outside the realm of conventional scientific papers. They should not be longer than 2 printed pages. Original data, and a maximum of 1 illustration and 1 table may be included. One printed text page in the journal corresponds to about 1,050 words or 5,700 characters.

Single topic issues
The journal will publish a series of thematic issues. For these volumes we are soliciting the assistance of one or more expert investigators to act as Guest Editor(s) in the area that is particularly interesting and/or in which there is a need for thorough overview. The Guest Editors invite top researchers to contribute original research reports or reviews on a topic that is in their main area of interest. These papers are peer reviewed in the same way as those received for the conventional issues. Proposals clearly outlining a theme and nominating potential Guest Editors are welcome.

Special requirements
Studies involving human subjects: Sexual Development requires that investigations performed on human subjects have prior approval of the institutional committee on human experimentation. Authors are required to submit a signed statement concerning the date and details of the appropriate review. In countries where such mechanisms for approval do not exist, authors are required to submit a signed declaration that the research was carried out in accordance with the Helsinki Declaration.

Consent of patients: If there is any chance that a patient may be identified from an illustration, we ask for the written consent of the patient for publication (or where appropriate from his/her relatives or guardian). This will be so even if all the identifying details of the patient are removed. Data relating to anonymous tissue and other samples will not normally be considered to be personal information relating to a particular patient and publication of research findings connected with such samples does not require patient consent.

Studies involving animals: A statement is required to document that animal experimentation was performed under circumstances that conformed to the guidelines established by the animal care committees in the respective countries and/or institutions.

Submission
Papers should be submitted online at: www.karger.com/sxd

Should you experience any problems with your submission, please contact the editorial office: claus.steinlein@biozentrum.uni-wuerzburg.de

Claus Steinlein
Department of Human Genetics
University of Würzburg
Biozentrum, Am Hubland
D–97074 Würzburg (Germany)
Tel. (+49) 931 318 8901
Fax (+49) 931 888 4058

Authors should indicate which Section Editors they feel would be most appropriate for their report, and may also suggest up to three reviewers together with their e-mail addresses.

All manuscripts are subject to editorial review. The editors are committed to ensuring a fast turnaround time of 3 weeks for the review process. The editors reserve the right to improve style and, if necessary, return the manuscript for rewriting to the authors. The editorial office reserves rights to reject manuscripts based on priorities and space availability in the journal.

Arrangement
Papers must be prepared strictly in accordance with the style of this journal. The order in the paper must be: Title page, Abstract, Introduction, Materials and Methods, Results, Discussion, Acknowledgements, References, Figure legends, Figures, Tables.

Title page: The title page should give the full names of the authors and their affiliations, as well as full postal address, phone and fax numbers and the e-mail address of the corresponding author.

Abstracts with a maximum length of 250 words should be provided for all Original Articles and Reviews, and with 100 words for Short Reports and Case Reports.

Figures: Digital illustrations should be sharp with good contrast and color rendition. Resolution for all graphics should be at least 300 dots per inch. We request that all illustrations be in a common format such as jpg (.jpeg), tif (.tiff), eps or .ptt.

Tables must be in Word format. Please use Microsoft Word Table > Insert > Table commands from the menu bar to make tableture.

Literature cited: References should be quoted in the text as follows: single author: Jones (1999); two authors: Jones and Smith (2000); more than two authors: Jones et al. (2002). The reference list should be alphabetically arranged according to the first author’s surname. Examples of citations are as follows: (1) Jones A, Smith B: The sex determining gene of Tyrannosaurus rex. J Ext Rept 7:1–5 (2002). (2) Jones A: Pathology of Sex Determination in Parrots (Fantasy Press, London 1999). (3) Smith B: Evolution of the Mullerian duct, in White M, Black N (eds): Sex Differentiation in Kangaroos (Outback Press, Sydney 2003). Papers published in electronic format exclusively should list authors, title and journal as above followed by the journal’s URL.

Agreement between text citations and the reference list should be checked carefully, and the latter checked for accuracy. If many errors are found, the manuscript will be returned for corrections which may cause considerable delay in publication.

Supplementary data may be submitted together with the manuscript, and will appear in their original form in the online version of the journal. The authors must refer to these data in their articles.

Gene/protein nomenclature: Authors must use officially approved gene/protein designations and check out every single gene/protein name before placing them in their papers.

Human gene symbols: Only official gene symbols of the International System for Genome Nomenclature (ISGN) are accepted. Authors must obtain or verify the official gene symbol of the gene(s) and indicate that they have done so in the submitted paper. This can be accomplished for human genes by contacting Dr. Sue Pourry (HUGO Gene Nomenclature Committee), Department of Biology, University College London, Wolfson House, 4 Stephenson Way, London, NW1 2HE (UK); Tel. +44 20 7679 7410; Fax +44 20 7387 3496; E-Mail: nomen@alton.galton.ac.uk; URL: www.gene.ucl.ac.uk

Animal gene symbols: Authors submitting material on mouse and rat genetics should obtain correct genetic nomenclature before publication. Contact Lois Maltais, MGD Nomenclature Coordinator, The Jackson Laboratory, 600 Main Street, Bar Harbour, ME 04609 (USA); Tel. +1 207 288 6429; Fax +1 207 288 6132; E-Mail nomen@informatics.jax.org; MGD home-page: www.informatics.jax.org. Guidelines set forth by the International Committee on Standardized Ge...
Electronic Proofs
Unless indicated otherwise, proofs will be e-mailed to the corresponding author.

Reprints of the articles are available against payment. Order forms listing prices are provided with the proofs. If no reprints are desired this should be indicated on the order form. Orders submitted after the issue has gone to press are subject to higher prices.

Supplementary Material
Supplementary material is restricted to additional data that are not necessary for the scientific integrity and conclusions of the paper. Please note that all supplementary files will undergo editorial review and should be submitted together with the original manuscript. The Editors reserve the right to limit the scope and length of the supplementary material. Supplementary material must meet production quality standards for Web publication without the need for any modification or editing. In general, supplementary files should not exceed 10 MB in size. All figures and tables should have titles and legends and all files should be supplied separately and named clearly. Acceptable files and formats are: Word or PDF files, Excel spreadsheets (only if the data cannot be converted properly to a PDF file), and video files (.mov, .avi, .mpeg).

Author’s Choice™
Karger’s Author’s Choice™ service broadens the reach of your article and gives all users worldwide free and full access for reading, downloading and printing at www.karger.com. The option is available for a one-time fee of CHF 325.00, which is a permissible cost in grant allocation. More information can be found at www.karger.com/authors_choice.

Page Charges
There are no page charges for articles of 6 or less printed pages (including tables, illustrations and references). Each additional complete or partial page is charged to the author at CHF 325.00. 1 printed page is equal to approximately 3 manuscript pages.

NIH-Funded Research
The U.S. National Institutes of Health (NIH) mandates under the NIH Public Access Policy that final, peer-reviewed manuscripts appear in its digital database within 12 months of the official publication date. As a service to authors, Karger submits the final version of your article on your behalf to PubMed Central. For those selecting our premium Author’s Choice™ service, we will send your article immediately upon publishing, accelerating the accessibility of your work without the usual embargo. More details on NIH’s Public Access Policy is available at http://publicaccess.nih.gov/policy.htm

Self-Archiving
Karger permits authors to archive their pre-prints (i.e. pre-refereeing) or post-prints (i.e. final draft post-refereeing) on their personal or institution’s servers, provided the following conditions are met: Articles may not be used for commercial purposes, must be linked to the publisher’s version, and must acknowledge the publisher’s copyright. Authors selecting Karger’s Author’s Choice™ feature, however, are also permitted to archive the final, published version of their article, which includes copyediting and design improvements as well as citation links.

‘A collection of extraordinary essays’

GOTTFRIED SCHATZ
A MATTER OF WONDER
What Biology Reveals about Us, Our World, and Our Dreams

Where do we come from? Is our destiny determined by the genes we inherit? In this book Gottfried Schatz, the world-renowned biochemist and co-discoverer of mitochondrial DNA, gives lucid – albeit often surprising – answers to universal questions and takes the reader on a fascinating journey of discovery across the boundaries of scientific disciplines. With passion and a keen sense of wonder he draws on philosophy, cultural history and art to formulate his reflections on the mysteries of life. His essays will appeal not only to scientists but to all inquisitive minds, regardless of educational and professional background.

G. Schatz (Basel)
A Matter of Wonder
What Biology Reveals about Us, Our World, and Our Dreams
Translated by A. Shields
XII + 190 p., 2 color fig., hardcover, 2011
CHF 29.– / EUR 21.50 / USD 29.00

More information and sample essays at www.karger.com/schatz
Contents

See the journal website for contents
CECE 2014

27th Conference of European Comparative Endocrinologists
Rennes (France) August 25–29, 2014

On behalf of the European Society for Comparative Endocrinology, we are pleased to invite you to participate in the 27th Congress of European Comparative Endocrinologists.

http://cece2014.org

Confirmed speakers
Bon-chu Chung (Academia Sinica, Taiwan)
Silvia Zanuy (CSIC, Spain)
Dick R. Nässel (Stockholm University, Sweden)
Luiz Renato de França (Belo Horizonte, Brazil)
Charles Tyler (University of Exeter, UK)
Shlomo Melmed (UCLA, California)
Ilpo Huhtaniemi (London, UK)
Wei Ge (Macau, China)
Julien Sebag (Nashville, USA)
Pierre Léopold (Nice, France)
Valérie Simonneaux (Strasbourg, France)
Manuel Tena-Sempere (Córdoba, Spain)
Yvette Taché (Nashville, USA)
Pierre Léopold (Nice, France)
Valérie Simonneaux (Strasbourg, France)
Manuel Tena-Sempere (Córdoba, Spain)
Yvette Taché (Nashville, USA)

Aki Takahashi (Kanagawa, Japan)
Horst-Werner Korf (Frankfurt, Germany)
Etienne Challet (Nouzilly, France)
Li F. Chan (London, UK)
Jean-Louis Nahon (Nice, France)
Jan Deussing (München, Germany)
José Miguel Cerdá-Reverter (Torre de la Sal, Spain)
Serge Luquet (Paris, France)
Nicholas Bernier (Guelph, Canada)
Annika Herwig (Hamburg, Germany)
Gary Ankley (US EPA, USA)
Robert J. Denver (Ann Arbor, Michigan)
Björn Thrandur Björnsson (Göteborg, Sweden)

Michael Schumacher (Le Kremlin-Blicêtre, France)
Vance L. Trudef (Ottawa, Canada)
Anne-Simone Parent (Liège, Belgium)
François Brion (INERIS, France)
Robert Dores (Denver, USA)
Bas Zwaan (Wageningen, The Netherlands)
Xavier Bellés (Barcelona, Spain)
Shireen Davies (University of Glasgow, Glasgow, UK)

Florian Raibé (Vienna, Austria)
Reinhard Predel (University of Cologne, Germany)
Pierre Grève (Poitier University, France)
Gerd Gade (University of Cape Town, South Africa)
Stacia Sower (University of New Hampshire, USA)

Dan Larhammar (University of Uppsala, Sweden)
Samantha J. Richardson (Victoria, Australia)
Bruno Quérat (Université Paris Diderrt, France)
Patrick Balaguier (INSERM, Montpellier, France)
Séverine Mazot-Guittot (IRSET, Rennes, France)
Shogo Haraguchi (Waseda University, Japan)
Jean-Paul Paluzzi (York University, Canada)
Anna Di Cosmo (Federico II University, Naples, Italy)
Shinji Kanda (University of Tokyo, Japan)
Erik Hrabovszky (Budapest, Hungary)
Eric Pailhoux (INRA, Jouy-en-Josas, France)
Amaury Herpin (Wurzburg University, Germany)

Ching-Fong Chang (Keelung University, Taiwan)
Hubert Vaudry (INSERM, Rouen, France)
Nicolas Dietel (U. St. Denis, Saint-Denis, La Réunion)
Thierry Charlier (University of Ohio, Athens, USA)
Monique Vallée (INSERM, Bordeaux, France)

Information:
cece2014@univ-rennes1.fr
Understanding disease by focusing on genome-mediated somatic cell evolution

Genetic Heterogeneity and Human Diseases

Editor
Henry Heng

The contribution of karyotype heterogeneity to human diseases is a crucial but overlooked issue. Recent genomic research has revealed high levels of genetic/epigenetic heterogeneity, in particular karyotypic heterogeneity and somatic mosaicism associated with many complex but common human diseases. These important findings challenge the current gene-based concept of many common diseases. To frame this new emerging field, this publication presents pertinent examples linking karyotype heterogeneity to diseases and identifying it in the general population. Specifically, a few key topics essential to understanding karyotypic heterogeneity are discussed, including genomic instability, non-clonal chromosome aberrations, previously unreported/ignored types of chromosome aberrations, cell death heterogeneity and somatic mosaicism. These subjects are discussed with an emphasis on determining the biological implications of genomic heterogeneity and synthesizing these implications into the frameworks of systems biology and genome theory.

Contents
Preface: Heng, H.H.Q.

- Genomic Heterogeneity in Acute Leukemia: Paulsson, K.
- Somatic Cell Genomics of Brain Disorders: A New Opportunity to Clarify Genetic-Environmental Interactions: Iourov, I.Y.; Vorsanova, S.G.; Yurov, Y.B.
- Trisomy 21 Mosaicism: We May All Have a Touch of Down Syndrome: Hultén, M.A.; Jonasson, J.; Ivarsson, E.; Uppal, P.; Vorsanova, S.G.; Yurov, Y.B.; Iourov, I.Y.
- Never in Neutral: A Systems Biology and Evolutionary Perspective on how Aneuploidy Contributes to Human Diseases: Pavelka, N.; Rancati, G.
- The Hypergenome in Inheritance and Development: Sgaramella, V.

Author Index

The easiest way to order: www.karger.com/crg

Karger – Medical and Scientific Publishers
CH-4009 Basel, Switzerland
orders@karger.com, T +41 61 306 12 34
www.karger.com
Rare Diseases: From Bench to Bedside to Public Health

Guest Editor
Domenica Taruscio

Contents

Editorial: Taruscio, D.

• New and Evolving Rare Diseases Research Programs at the National Institutes of Health:
  Groft, S.C.; Rubinstein, Y.R.

• The European Union Policy in the Field of Rare Diseases:
  Montserrat Moliner, A.; Waligóra, J.

• EUROPLAN: A Project to Support the Development of National Plans on Rare Diseases in Europe:

• The Current Situation and Needs of Rare Disease Registries in Europe:
  Taruscio, D.; Gainotti, S.; Mollo, E.; Vittozzi, L.; Bianchi, F.; Ensini, M.; Posada, M.

• A Model for the European Platform for Rare Disease Registries:
  Vittozzi, L.; Gainotti, S.; Mollo, E.; Donati, C.; Taruscio, D.

• EU Pancreas: An Integrated European Platform for Pancreas Cancer Research – from Basic Science to Clinical and Public Health Interventions for a Rare Disease:

• Biomarkers in Rare Diseases:
  Ferlini, A.; Scotton, C.; Novelli, G.

• Clinical Trial Transparency and Orphan Drug Development:
  Recent Trends in Data Sharing by the Pharmaceutical Industry:
  So, D.; Joly, Y.; Knoppers, B.M.

Author Index / Subject Index

Dear Librarian
I have reviewed this publication and would like to recommend it for our library.
Recommended by:

Department:

Date:

Signature:

Orders may be placed with any bookshop, subscription agency, directly with the publisher or through a Karger distributor.

The easiest way to order: www.karger.com/phg

Karger – Medical and Scientific Publishers
CH-4009 Basel, Switzerland
orders@karger.com, f: +41 61 306 12 34
www.karger.com
Original Articles

139 Congenital Adrenal Hyperplasia, Ovarian Failure and Ehlers-Danlos Syndrome due to a 6p Deletion

146 No Mutations in the PSMC3IP Gene Identified in a Swedish Cohort of Women with Primary Ovarian Insufficiency

160 A Lack of Association between Polymorphisms of Three Positional Candidate Genes (CLASP2, UBP1, and FBXL2) and Canine Disorder of Sexual Development (78;XX; SRY-Negative)
Salamon, S.; Nowacka-Woszuk, J.; Szczepański, I. (Poznań); Dzimira, S.; Nizanski, W.; Ochota, M. (Wrocław); Swiłonski, M. (Poznań)

166 A Dual Role for SHH during Phallus Development in a Marsupial

178 Gene Expression of Chicken Gonads Is Sex- and Side-Specific

Case Report

151 46,XY Disorder of Sex Development in a Sudanese Patient Caused by a Novel Mutation in the HSD17B3 Gene
Ellaithi, M. (Khartoum/Omdurman); Werner, R. (Lübeck); Riepe, F.G. (Kiel); Krone, N. (Birmingham); Kulle, A.E. (Kiel); Diab, T. (Khartoum); Kamel, A.K. (Cairo); Arlt, W. (Birmingham); Holterhus, P.-M. (Kiel); Sabir, O. (Khartoum); Hiort, O. (Lübeck)

Short Report

156 A Child with a Novel de novo Mutation in the Aristaless Domain of the Aristaless-Related Homeobox (ARX) Gene Presenting with Ambiguous Genitalia and Psychomotor Delay