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Steroid Hormones and Receptors in Health and Disease:

A Research Conference Co-Organized by FASEB and the International Committee on Rapid Responses to Steroid Hormones (RRSH), May 25–27, 2021

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Keywords

aldosterone; estrogen; estradiol; VDR; MR; GR; glucocorticoids; androgens; progesterone; vitamin D; thyroid hormone; nuclear receptors

Steroid hormone effects have been reported for almost 140 years^{1–3}. Research over the past 50 years has led to the discovery of steroid hormone receptors that act via both genomic and nongenomic (“rapid”) mechanisms. Steroids are involved in physiology and disease, mediating endocrine, cardiovascular, and reproductive functions and play a role in cancer, neurological, metabolic, renal, and cardiovascular diseases.^{4–7} Over the past decades, both the Federation of American Societies for Experimental Biology (FASEB) and the International Committee on Rapid Responses to Steroid Hormones (RRSH) have held meetings presenting the newest science on steroid hormone biology and receptor signaling^{8–26} (Tables 1 and 2). Previously, both FASEB^{8–14} and RRS^{15–26} organized their own conferences, usually in alternating years, and in 2018, decided to organize their first joint conference to be held in the United States. Initially, the organizers of this joint conference (i.e., authors of this manuscript) had selected West Palm Beach, FL, as the venue for the conference, which was to be held July 12–17, 2020. However, when the COVID-19 pandemic hit earlier that year, plans were put on hold. Hoping for early control of the pandemic, the organizers prepared for a 4-day in-person meeting to be held in Puerto Rico, USA. However, as COVID-19 continued to be a global health concern, challenging societies, scientists, and science around the world, in late 2020, the organizers took the

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AUTHOR CONTRIBUTIONS

M. Barton conceived and wrote the manuscript; D. E. Frigo, Z. Madak-Erdogan, F. Mauvais-Jarvis, and E. R. Prossnitz contributed and/or edited content.

decision to hold the conference as a virtual meeting. The conference was ultimately held online as a 3-day meeting on May 25–27, 2021. It represented the 10th occurrence of the FASEB Science Research Conferences (SRCs) on Steroid Hormones with Daniel E. Frigo (University of Texas M. D. Anderson Cancer Center, Houston, TX, USA), Zeynep Madak-Erdogan (University of Illinois, Urbana, IL, USA) and Franck Mauvais-Jarvis (Tulane University, New Orleans, LA, USA) as chairs, and the 12th International Meeting on Rapid Responses to Steroid Hormones (RRSH 2020) with Matthias Barton (University of Zurich, Zurich, Switzerland) and Eric R. Prossnitz (University of New Mexico, Albuquerque, NM, USA) as chairs.

The FASEB and RRSB conferences are usually well received by the scientific community since many presentations and discussion topics include unpublished, cutting-edge research. The joint conference brought together scientists and clinicians from all areas of biology and medicine, covering a broad range of topics related to steroid hormone and steroid hormone receptor function in physiology and human health. The program included one keynote speaker, 38 scheduled invited speakers, 18 short talks (“lightning presentations”) and 28 virtual poster presentations. The conference drew a record attendance of 110 participants, reflecting an increasing interest in steroid hormone signaling in the scientific community. In terms of diversity, women constituted over 55% of attendees and over 40% of all invited speakers. Early career scientists (defined as faculty with <10 years of experience, postdoctoral associates, and graduate students) were also well represented, comprising 55% of all conference attendees.

The welcome address was given by Daniel E. Frigo on behalf of FASEB, and Eric R. Prossnitz on behalf of RRSB, who, together with other organizers, led the program. Keynote speaker Donald McDonnell (Duke University School of Medicine, Durham, NC, USA) set the stage of the conference with his intriguing lecture “If we knew then what we know now, what would we have done differently to exploit nuclear receptors as drug targets?”. Dr. McDonnell, who discovered several mechanisms that led to drug treatments for hormone-responsive cancers, provided the audience with a lifetime view of his work, also looking back at the beginnings of field, which he and others pioneered. His lecture was followed by the first session of the day on nuclear steroid receptor regulation of metabolism, led by Sayeepriyadarshini Anakk (University of Illinois, Urbana-Champaign, IL, USA). A series of lectures by Adriana Maggi (University of Milan, Milan, Italy), Carolyn Cummins (University of Toronto, Toronto, ON, Canada), Andrea Hevener (University of California, Los Angeles, CA, USA), Sheng Wu (Johns Hopkins University, Baltimore, MD, USA), Brian Feldman (University of California, San Francisco, CA, USA), Wen Xie (University of Pittsburgh, Pittsburgh, PA, USA), and Warren Thomas (Royal College of Surgeons in Ireland, Dublin, Ireland) presented updates on metabolic functions of estrogen, androgen, and glucocorticoid receptors, as well as evidence for functional roles for estrogen sulfotransferase and steroid sulfatase in energy metabolism, and how aldosterone regulates renal Na⁺ reabsorption through novel protein kinase D isoforms. The lectures were followed by lively discussions moderated by the session chairs, even though the meeting was held online. Following the first session, Dr. Yvette Seger, FASEB Director of Science Policy, introduced the science policy of FASEB and moderated a round table discussion on the subject.

The second half of the first day of the conference was dedicated to clinical aspects of therapies targeting steroid hormone receptors. The session was chaired by Jay Gertz (University of Utah, Salt Lake City, USA) and Martin Wehling (University of Heidelberg, Heidelberg, Germany). Lectures addressed many areas of clinical medicine and disease, including mineralocorticoid receptor function in the treatment of cardiovascular disorders, thyroid receptor signaling in cancer, and membrane progesterone receptor function in the uterus, as well as epigenetics and cistromics in cancer and clinical trials. Lectures were presented by Iris Jaffee (Tufts University, Medford, MA, USA), James Pru (University of Wyoming, Laramie, WY, USA), Paul Davis (Albany Medical College, Albany, NY, USA), Wilbert Zwart (Netherlands Cancer Institute, Amsterdam, The Netherlands), and Mathieu Lupien (University of Toronto). Following the clinical session, a number of young investigators (Florian Le Billan, University of Toronto; Alicia Arredondo Eve, University of Illinois; Ximena Calle Chalco, University of Chile, Santiago, Chile; Innocence Harvey, Pennington Biomedical Research Center, Baton Rouge, LA, USA; and Jia Xu Li, University of Toronto), presented 3-minute poster abstract summaries, which were part of the subsequent virtual poster session presented the same afternoon and well received by the online audience.

The second day of the conference began with the morning session focusing on systems biology approaches to interrogate nuclear steroid receptor functions, and was chaired by Andrea Cignarella (University of Padova, Padua, Italy) and Lindsey Trevino (City of Hope, Duarte, CA, USA). Topics presented in this session included glucocorticoid receptor-dependent transcription in single cells and individual genes (Trevor Archer, National Institute of Environmental Health Sciences, Durham, NC, USA), imaging of nuclear receptor actions at the single cell level (Fabio Stossi, Baylor College of Medicine, Houston, TX, USA), subcellular localization of estrogen receptor (ER) and cardiometabolism (Pierre Gourdy, University of Toulouse, Toulouse, France), mechanisms of ER enhancer function (Lee Kraus, University of Texas Southwestern Medical Center, Dallas, TX, USA), and steroid G protein-coupled receptor (GPCR)-mediated renal fibrosis in *Drosophila* (Marc Tatar, Brown University, Providence, RI, USA). Lectures were again followed by talks given by young investigators (Eriko Katsuta, Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; Ayca Mogol, University of Illinois; Qianying Zuo, University of Illinois; and Kendall Langsten, Wake Forest School of Medicine, Winston-Salem, NC, USA) and by a career development workshop entitled “Presenting your science to the public,” by Mila Becker, Chief Policy Officer of the Endocrine Society. The afternoon session was chaired by Martin Kelly (Oregon Health and Science University, Portland, OR, USA) and included a number of presentations of different aspects of steroid functions in the brain. Gabriele Rune (University of Hamburg, Hamburg, Germany) presented insights into the sex-dependent effects of neurosteroids in the hippocampus; Charlotte Cornil (University of Liège, Liège, Belgium) discussed nuclear and membrane-actions of neuroestrogens in the control of male sexual behavior, and Margaret Mohr (University of California, Los Angeles) provided an update on estradiol-induced hypothalamic progesterone synthesis during pubertal development. In the second half of the session, Kevin Sinchak (California State University, Long Beach, CA, USA) discussed how neuroprogesterone and progesterone receptor regulate the lutenizing hormone surge, John Meitzen (North Carolina State University,

Raleigh, NC, USA) gave a talk on how estradiol rapidly modulates excitatory synapse properties in the nucleus accumbens, and Karyn Frick (University of Wisconsin, Madison, WI, USA) discussed ER β activation as a potential treatment for alleviating menopausal symptoms, such as hot flashes. The second day ended with a third lightning round, with 4 short talks given by young investigators (Michael Saikali, University of Toronto; Dominik Awad, M. D. Anderson Cancer Center; Ashlie Santaliz Casiano, University of Illinois; and Cameron Leyers (Medical University of South Carolina, Charleston, NC, USA), summarizing their poster presentations.

The last day of the conference was dedicated to novel roles of steroids and steroid receptors in neoplastic and other diseases. The morning session, “Novel functions of steroid receptors in cancer,” was chaired and moderated by Christy Hagan (University of Kansas, Lawrence, KS, USA) and Stephen Hammes (University of Rochester, Rochester, NY, USA). The session was opened by Rosamaria Lappano (University of Calabria, Rende, Italy), who spoke about the role of the membrane receptor G protein-coupled estrogen receptor (GPER) in breast cancer, followed by Carol Lange (University of Minnesota, Minneapolis, MN, USA), who discussed signaling properties of progesterone receptor and glucocorticoid receptors in stemness, and Marina Holz (New York Medical College, Valhalla, NY, USA), who presented new data on estrogen/mTOR crosstalk in lymphangioleiomyomatosis and breast cancer. These lectures were followed by Matt Sikora (University of Colorado, Anschutz, CO, USA) who shared recent progress on the role of ERs in the therapy response and resistance in lobular mammary carcinoma and by Scott Tomlins (Strata Oncology, Ann Arbor, MI, USA), who gave a talk on high-throughput -omics to identify driver mutations and gene fusions in cancer. The session also featured short talks from five young investigators, presenting data from their virtual posters (Anasuya Das Gupta, University of Illinois; Sarah El Kharraz, KU Leuven, Leuven, The Netherlands; Asmaa El-Kenawi, Moffitt Cancer Center, Tampa, FL, USA; Wanting Han, University of Massachusetts Boston, Boston, MA, USA; and Thu Truong (University of Minnesota).

In the first afternoon session of day 3 of the conference, Donald DeFranco (University of Pittsburgh) and Ellis Levin (University of California, Irvine, CA, USA) moderated a series of lectures on new mechanisms and approaches of how to target steroid receptors. Elahe Mostaghel (Fred Hutchinson Cancer Center, Seattle, WA, USA) discussed how prostate cancer and how adrenal androgens and AR axis inhibition may contribute to therapy resistance and serve as predictors of the therapeutic response. Douglas Kojetin (Scripps Research Florida, Jupiter, FL, USA) then presented evidence on how to use nuclear magnetic resonance spectroscopy to visualize ligand-induced peroxisome proliferator-activated receptor γ (PPAR γ) repression. Edward Filardo (University of Iowa, Iowa City, IA, USA) discussed dual specificity proteolysis-targeting chimeras (PROTACs) targeting GPER and ERs, and John Katzenellenbogen (University of Illinois) presented recent evidence from his laboratory demonstrating ER β -mediated effects in response to very low affinity ER ligands. All talks were followed by questions from the online audience, with lively and engaging discussions moderated by the chairs.

The subsequent afternoon session, which concluded the conference, was chaired by Kristy Brown (Weill Cornell Medicine, New York, NY, USA) and Subhamoy Dasgupta (Roswell

Park Comprehensive Cancer Center). The session focused on mechanisms of crosstalk between nuclear steroid receptors and metabolic pathways. Ian Mills (Queens University Belfast, Belfast, UK) discussed how androgens regulate metabolism in prostate cancer, and Rebecca Riggins (Georgetown University, Washington, DC, USA) presented evidence for novel functions of ER-related receptor β (ERR β) in the pathogenesis of glioblastoma. Giorgia Zadra (National Research Council of Italy) reported data on the modulation of intra-tumor lipid metabolism via androgen receptor. Erik Nelson (University of Illinois) then discussed how cholesterol, ER, and liver X receptors (LXRs) modulate the tumor microenvironment in breast cancer, and Philip Shaul (University of Texas Southwestern Medical Center) closed the meeting presentations with data from his and other laboratories on endothelial ER signaling and its effects on cardiometabolic health and disease.

Despite the challenges imposed by COVID-19 and the virtual character of the conference, all sessions saw lively discussions and participation from the online audience. Results from the feedback evaluation were very positive regarding the organization of the meeting and the selection of topics. More than 90% of attendees who provided feedback gave favorable comments regarding the general sessions, poster sessions, and the scientific content of the conference. However, there were a few who noted issues with how quickly attendees could access desired on-demand content. Regardless, essentially all respondents of the feedback evaluation indicated that they plan to attend the next meeting, which will be held next year, and that they recommend attending this meeting to other researchers in the field. Many of the speakers and presenters have agreed to write a contribution on the topic of their talks for the conference proceedings, which, as for the last 20 years,^{9–15, 18–27} will be published in the journal *Steroids* as a Virtual Special Issue in 2022.

The organizers express their gratitude to FASEB and to the numerous sponsors of the meeting, which are listed in the Acknowledgments, especially the U.S. National Institutes of Health (NIH) for providing funding to sponsor young investigator travel awards. These awards helped to recognize the contributions of students and postdoctoral trainees in the difficult times of the COVID-19 pandemic, resulting in an increased attendance at the meeting by junior researchers. Indeed, with the support of NIH/National Institute of Diabetes and Digestive Diseases, young investigator travel awards were awarded to every student or postdoc who expressed interest in attending the online conference. The next conference (in the form of the 13th International Meeting on Rapid Responses to Steroid Hormones, RRSB 2022) will be held in September 2022 in Paris, France, at the historic venue of the Sorbonne Université, which reaches back to the year 1257 and is one of the oldest and most prestigious universities in the world.²⁸ The organizers hope to welcome scientists active in all fields of steroid hormone research and medicine in Paris next year.

Acknowledgments

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Abbreviations

ER	estrogen receptor
GPER	G protein-coupled estrogen receptor
FASEB	Federation of American Societies for Experimental Biology
RRSH	Rapid Responses to Steroid Hormones
SRC	Science Research Conference

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Table 1.

History of the FASEB Science Research Conferences on Steroid Hormones

Year	Conference chairs	Location
1999	Cheryl Watson, Peter Blackmore, Ilka Nemere	Copper Mountain, CO, USA
2002	Ilke Nemere, Peter Blackmore, Richard Pietras	Snowmass, CO, USA
2004	Richard A. Pietras, Ellis Levin, Mary C. Farach-Carson	Tucson, AZ, USA
2006	Carol A. Lange, Paul Davis, Jeffrey Bender	Tucson, AZ, USA
2008	Paul Davis, Jeffrey Bender, Carol A. Lange	Carefree, AZ, USA
2010	Stephen R. Hammes, Joyce Slingerland, Martin Kelly	Snowmass, CO, USA
2012	Joyce Slingerland, Martin Kelly, Stephen R. Hammes	Snowmass, CO, USA
2015	Donald B. DeFranco, Paul Micevych, Nancy L. Weigel	Big Sky, MT, USA
2017	Carol A. Lange, Ellis R. Levin, Stephen R. Hammes, Donald B. DeFranco	Snowmass, CO, USA
2020	Daniel E. Frigo, Zeynep Madak-Erdogan, Franck Mauvais-Jarvis	Puerto Rico, USA ^a

^aHeld as a virtual meeting with RRSB in 2021.

Table 2.

History of the International Meetings on Rapid Responses to Steroid Hormones

Year	Conference chairs	Location
1998	Martin Wehling	Mannheim, Germany
2001	Anthony W. Norman	Denver, CO, USA
2003	Elisabetta Baldi	Florence, Italy
2005	Anthony W. Norman	San Diego, CA, USA
2007	Brian Harvey	Dublin, Ireland
2009	Angel Nadal	Elche, Spain
2011	Elias Castanas	Crete, Greece
2013	Jack D. Caldwell	Erie, PA, USA
2015	Eileen Jea Chien	Taipei, Taiwan
2016	Barbara Boyan, Jerry Strauss	Richmond, VA, USA
2018	Brian Harvey	Dublin, Ireland
2020	Matthias Barton, Eric R. Prossnitz	Puerto Rico, USA ^a

^aHeld as a virtual meeting with FASEB in 2021.