Alcohol 46 (2012) 101−105

ALCOHOL

Proceedings of the 2009 annual meeting of the Fetal Alcohol Spectrum Disorders Study Group

Feng C. Zhou[a,*], Cynthia J.M. Kane[b], Susan M. Smith[c]

[a]*Department of Anatomy and Cell Biology, Indiana University School of Medicine, Indianapolis, IN, USA*
[b]*Department of Neurobiology and Developmental Sciences, University of Arkansas for Medical Sciences, Little Rock, AR, USA*
[c]*Department of Nutritional Sciences, University of Wisconsin-Madison, Madison, WI, USA*

Received 6 November 2010; received in revised form 26 November 2010; accepted 22 December 2010

Abstract

The annual meeting of the Fetal Alcohol Spectrum Disorders Study Group (FASDSG) was held on June 20, 2009 in San Diego, CA, as a satellite of the Research Society on Alcoholism Meeting. The FASDSG membership includes clinical, basic, and social scientists who meet to discuss recent advances and issues in Fetal Alcohol Spectrum Disorders research. The main theme of the meeting was "Epigenetics and Development." Two keynote speakers, Dr. Randy Jirtle and Dr. Michael Skinner, addressed the role of epigenetics and environmental inputs, including alcohol, during critical stages of development and their potential critical and long-lasting effects. Members of the FASDSG provided new findings through brief "FASt" data reports, and national agency representatives provided updates on activities and funding priorities. Scientific presentations were made by recipients of the Student Research Merit Award and Rosett Award.

Keywords: Fetal alcohol syndrome; Fetal development; Organization on fetal alcohol spectrum disorders; Epigenetics; Alcoholism; FASDSG

The 2009 Fetal Alcohol Spectrum Disorders Study Group (FASDSG) met on June 20, 2009, in San Diego, CA, as a satellite of the Research Society on Alcoholism Meeting. The 2008−2009 FASDSG officers, *Feng Zhou* (President), *Cindy Kane* (Vice-President), and *Susan Smith* (Secretary-Treasurer) organized the meeting. The FASDSG membership includes clinical, basic, and social scientists who meet to discuss recent advances and issues in fetal alcohol spectrum disorders (FASD) research. More than 161 individuals attended the study group, including more than 100 FASDSG professionals and approximately 60 students. Attendees were largely from the United States and included researchers from Canada, South Africa, Norway, Spain, Brazil, Russia, New Zealand, and Israel. In this meeting, a new logo (Fig. 1, right panel) was adopted to represent FASDSG, and a Web page for the Study Group was introduced in the beginning of the meeting (www.FASDSG.org; Fig. 1).

Keynote speech

The main theme of the meeting was "Epigenetics and Development." There is growing awareness that gestational alcohol exposure might alter fetal epigenetic programming, potentially affecting both developmental sensitivity to alcohol and gestational outcome. The first keynote speaker was Dr. Randy Jirtle, PhD, Professor and Director of the Epigenetics and Imprinting Laboratory at Duke University Medical Center. The title of the presentation was "*Epigenetics and the fetal origins of disease susceptibility.*" In linking environmental input, epigenetics, and developmental disorder, Dr. Jirtle first posed the questions: "Why do we vary in our susceptibility to diseases?" And, "why do identical twins vary in their susceptibility to diseases and disorders if the only thing that really matters is the genetic variation?" Dr. Jirtle pointed out that slight variations in the environment in the womb can create susceptibility variations later in life (Jirtle and Skinner, 2007). He explained that epigenetics, "above genetics," refers to the study of heritable changes in gene function during cell replication that occur without a change in the DNA sequence itself. The two basic mechanisms associated with epigenetics are DNA methylation and histone modifications. The two together alter chromatin structure. He used an analogy that the genome is comparable to the hardware of a computer, whereas the epigenome is comparable to the software of a computer, that is, telling the computer how, when, and where to work. Two groups of epigenetic genes were introduced: metastable epiallele genes (genes with unusual characteristics of variable expressivity in the absence of genetic heterogeneity) and

---

* Corresponding author. Department of Anatomy and Cell Biology, Indiana University School Medicine, Indianapolis, IN 46032, USA. Tel.: +1-317-274-7359; fax: +1-317-278-2040.

E-mail address: imce100@iupui.edu (F.C. Zhou).

0741-8329/$ - see front matter
doi: 10.1016/j.alcohol.2010.12.008

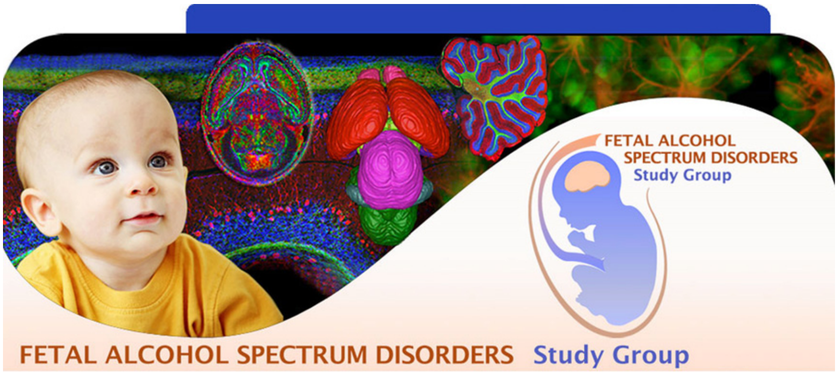

Fig. 1. The web page of FASDSG "www.FASDSG.org". The logo is shown in the lower right panel.

genomically imprinted genes. He used the *Agouti* gene model to pose questions about the effects of the womb environment. For example, exposure to dietary supplements was linked to phenotypic and disease susceptibility changes in adulthood and offspring through the mechanism of DNA methylation rather than genomic mutations. This indicates the prominence of nurture over nature. Furthermore, epigenetically induced changes in disease susceptibility, for example, via food, really are important components in medicine. To some degree, humans might be what their mothers ate while they were in the womb. Addressing the second group of epigenetic genes, Dr. Jirtle said that all genes are equal, but some are more equal than others, meaning those genes that are more equal are genomically imprinted genes because they are expressed from one, paternal or maternal, allele. Misrepresentation of DNA methylation on these genes from parental allele may alter gene expression and subsequently introduce disease. He explained theories of how and why these imprinted genes evolved and how imprinted genes influence gene expression. He cited the intragenomic conflict theory of evolutionary biologist, David Haig. This theory posits that genomic imprinting and parent–offspring conflict are remnants of a genetic battle between male and female parents to control nutrient utilization and the growth of offspring (Haig, 1997). An animal model of imprinted genes demonstrated differentially methylated imprinted regulatory elements affecting expression of the genes. He concluded his presentation discussing the characteristics of epigenetic involvement, including imprinted genes and their linkage to diseases, such as cancer and developmental syndromes.

The second keynote speaker was **Michael Skinner, PhD**, Professor at the Center for Reproductive Biology at the School of Molecular Biosciences at Washington State University. The title of the presentation was "*Epigenetic transgenerational actions of endocrine disruptors on reproduction and disease: The ghosts in your genes*." Dr. Skinner began by explaining how epigenetics play a role in environmentally mediated adult onset diseases and in transgenerational phenomena. He stressed that the individual is exposed to the environmental factor, but so too is the subsequent progeny. For example, in his published work, the environmental compounds, methoxychlor (a pesticide and replacement for DDT) and vinclozolin (a fungicide), can bind to hormone receptors and are pathogenic through more than one generation (Anway et al., 2005, 2006). His research identified a paternal allele that was transgenerational or permanently reprogrammed in subsequent generations. Transgenerational effects of environmental toxicants (e.g., endocrine disruptors) significantly amplified the impact and health hazards of these compounds. One of the most sensitive periods to exposure is during embryonic gonadal sex determination when the germ line is undergoing epigenetic programming and DNA remethylation. Endocrine disruptors can affect embryonic testis development and subsequently cause an increase in spermatogenic cell apoptosis in the adult. Interestingly, this spermatogenic defect is transgenerational (F1, F2, F3, and F4 generations) and hypothesized to be because of a permanent alteration of DNA methylation in the germ line. This appears to involve the induction of new imprinted DNA methylation sites that regulate transcription distally. Regions of differential DNA methylation were identified with chromatin immunoprecipitation-Chip analysis in F3 generation sperm. The expression of more than 200 genes was altered in the embryonic testis, and surprisingly, this altered transcriptome was similar for all generations (F1–F3). All tissues that were examined had a transgenerational transcriptome effect that was tissue specific. In addition to the detection of the male testis disorder, transgenerational effects on other disease states were observed as the animals aged, including tumor development, prostate disease, kidney disease, and immune abnormalities. Recent observations suggest transgenerational effects on behaviors, such as sexual selection and anxiety. Therefore, the transgenerational epigenetic mechanism appears to involve the actions of an environmental compound at the time of sex determination. This, in turn, alters the epigenetic (i.e., DNA methylation) programming of the germ line permanently and alters the transcriptomes of developing organs to induce disease development transgenerationally