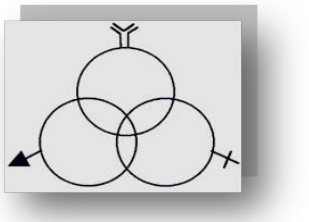
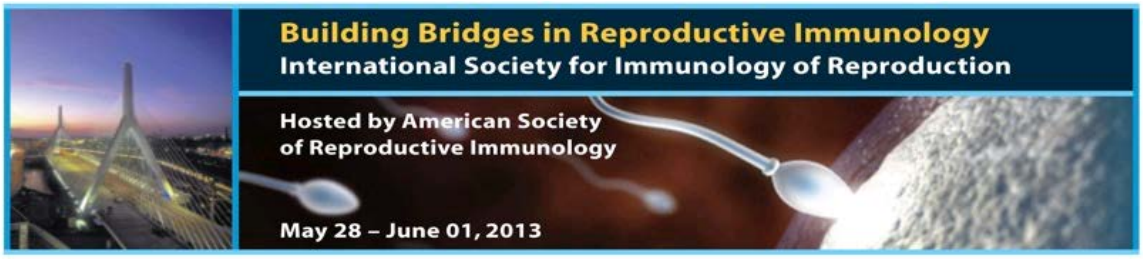


INTERNATIONAL SOCIETY FOR IMMUNOLOGY OF REPRODUCTION

Newsletter 2013

UPDATE ON:

12th INTERNATIONAL CONGRESS OF REPRODUCTIVE IMMUNOLOGY



Dear Colleagues,

The International Society for Immunology of Reproduction (ISIR) and the American Society for Reproductive Immunology (ASRI) cordially invite you to submit your abstract to the pre-eminent meeting on Reproductive Immunology:

ISIR2013
Building Bridges in Reproductive Immunology
May 28 – June 01, 2013
Boston Park Plaza Hotel
Boston, Massachusetts

Submit your abstract today! The submission deadline is February 01, 2013. Abstracts will be published in the May edition of the American Journal of Reproductive Immunology (AJRI).

ASRI is proud to promote participation of Young Investigators with special events and will provide travel awards and opportunities to present at plenary sessions. Also the 6th Annual Post-Graduate Workshop "How to Study Immune Cells in the Reproductive Tract" will take place May 28-29 prior to the main meeting.

A special pre-meeting HIV Workshop "Hormone Regulation of the Mucosal Environment in the Reproductive Tract and the Prevention of HIV Infection" will also take place May 28-29, registration is limited, so plan now to attend.

To view the full program, register and book your accommodations, please go to:
http://www.regonline.com/ISIR2013

Join or renew your membership to take advantage of the lowest available registration rates.
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Please forward this to your colleagues and students.

Chuck Wira

ISIR President-Elect
Co-Chair, Program Committee

Stress during pregnancy, epigenetics and identification of potential biomarkers

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Pregnancy is perhaps one of the most complicated stress tests that a woman may take during her life; with many compounding factors contributing to a successful pregnancy. Despite the advances in our understanding about the biological mechanisms regulating reproductive processes, we still witness high numbers of maternal and fetal pre- and peri-natal complications worldwide. Looking for new and more accurate biomarkers to predict deleterious outcomes of the pregnancy has become a challenge in many research fields.

In recent years, evidence has grown regarding stressful psychological and adverse environmental insults on pregnancy disorders and fetal complications. Maternal exposure to stress during pregnancy is associated with an increased risk for pregnancy failure such as preterm birth, reduced birth weight and preeclampsia[1,2]. Additionally, adverse programming of offspring health such as cardiovascular[3], metabolic and psychiatric disorders[4] has been shown implicating long term consequences involving alterations in the Hypothalamus-Pituitary-Adrenal (HPA) axis[5].

Stress responses are usually related to and measured by the levels of hormones of the HPA axis; especially glucocorticoids. Cortisol for example, increases in concentration during stressful events enabling the characteristic fight or flight response[6,7]. However the use of this hormone as a stress biomarker during pregnancy is not a straightforward relationship, since in pregnancy, the HPA axis shows a general state of activation with physiological hypercortisolism[5,7]. Moderate anxiety in pregnant women has been associated with increments of serum cortisol and progesterone, and linked with increased frequency of gestational and peri-natal complications for the mother but not for the neonate[8].

As pregnancy progresses, plasma corticotropin and corticotropin releasing hormone (CRH) levels rise reaching their highest levels at term and falling after delivery. CRH is secreted from

the placenta and is not affected by the negative feedback that cortisol has on the hypothalamus; on the contrary, cortisol increases the production of placental CRH[9]. The enzyme 11-hydroxysteroid dehydrogenase type 2 (11β HSD2) controls the access of cortisol to its nuclear receptor within the placenta. The 11β HSD2 enzyme converts cortisol to its inactive metabolite cortisone, protecting the fetus from hydrocortisone excesses [9,10].

Adrenal hormones contribute to fetal programming, especially in brain development early in embryogenesis and to lung maturation in late pregnancy. However, the impact of excessive concentrations of cortisol due to any stress insult and/or malfunctioning in its receptors or the 11β HSD2 enzyme in the placenta is less recognized. Some authors have found that in preeclampsia, high concentrations of cortisol contribute to the detrimental growth of the placenta. Further, in cultures of the human first trimester trophoblast cell line HTR-8/SV neo and primary human trophoblast cells treated glucocorticoids, proliferation was inhibited in a dose dependent manner[10]. Other authors hypothesized that high levels of cortisol resulting from psychological stress during pregnancy may increase a woman's vulnerability to developing preeclampsia by elevating lymphoid cell exposure to cortisol, altering lymphocyte sensitivity to glucocorticoids and promoting the pro- inflammatory state seen in preeclampsia[2].

The placenta connects maternal and fetal physiology and recently it was shown that expression of 11β HSD2 was lower in placentas from rats exposed to chronic restraint stress and this was accompanied by increased DNA methylation of the gene promoter. The DNA methylation status was correlated between the placenta and fetal cortex[11].

The research group of Dr. Tracy Bale demonstrated, in a rat model, the effects of stress can be sex biased in neurodevelopmental disorders such as schizophrenia and autism. In many neuropsychiatric syndromes, symptoms are present after a stressful event in life and sex-based differences exist in risk and/or the response to the treatment. The programming mechanisms altered due to stress are mainly changes in the epigenetic patterns of some genes important to sex determination (Sry for instance)[12].

Animal data strongly suggest alterations of the offspring(s)' HPA axis due to maternal stress, however translation of these findings to humans lags. Researchers on gestational stress must be aware of the limitations of the present instruments to measure stress in humans. Improved, more comprehensive methods are needed to validate different psychosocial stresses or environmental effects on mothers and offspring. Maternal medications will be complications and long term

clinical outcomes will need to be followed to evaluate learning, cognition behavior, risk of psychiatric disorders in people who suffered stress during their prenatal life. In this regard, the recent findings on DNA methylation patterns of certain genes in the placenta raise the possibility to finding new epigenetic biomarkers able to predict programming consequences for the newborn. Further studies are needed to explore this fascinating area of human reproduction.

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