

## MARCH 2016 NEWSLETTER

### ENDOMETRIAL CANCER IN PCOS

This issue is dedicated to possible mechanisms influencing the development of endometrial cancer in women with PCOS.

Enrico Carmina M.D., Professor of Endocrinology at the University of Palermo, Executive Director of AEPCOS and Editor of the Newsletter, has interviewed William Atiomo, M.D., about his study on endometrial cancer in women with PCOS. William is Associate Professor of Obstetrics and Gynecology at the University of Nottingham, United Kingdom and member of AEPCOS Society from 2012.

The updated program of next Boston AEPCOS Update meeting and some information regarding 14th AEPCOS Annual Meeting that will be held in Lorne, near Melbourne, Victoria State, Australia, November 10-12, 2016 are presented.

Finally AEPCOS is seeking a new Editor of AEPCOS Newsletter.

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MARCH 31, 2016

#### Editorial Board

#### In this issue:

- \* Endometrial Cancer in PCOS
- \* AEPCOS Update Meeting Program, Boston, MA, USA, March 31, 2016

Enrico Carmina, M.D., Palermo, Italy  
Ellen Connor, M.D., Madison, WI, USA  
Frank Gonzalez M.D., Indianapolis, IN, USA  
Helen Mason, Ph.D., London, United Kingdom  
Poli Mara Spritzer, M.D., Porto Alegre, Brazil

### FORTHCOMING AEPCOS MEETINGS

- AEPCOS Update Meeting, Boston, MA, USA, March 31, 2016
- Joint AEPCOS-ASRM Postgraduate Course, Salt Lake City, UT, USA, October 15, 2016
- 14th AEPCOS Annual Meeting, Lorne, Victoria, Australia, November 10-12, 2016

# 14th ANNUAL MEETING OF AEPCOS SOCIETY



The 14<sup>th</sup> Annual Meeting of AEPCOS Society will be held November 10-12, 2016 in Lorne, Victoria, Australia. The conference venue is the Mantra Lorne Resort, Mountjoy Parade, 3232 Lorne, Victoria, Australia

The Mantra Lorne Resort is located along the Great Ocean Road, one of the most famous attractions of Australia. The Melbourne airport is one hour away. It is the only

property in Lorne that has direct beach access and represents an ideal base for exploring the Twelve Apostles, a collection of limestone stacks off the shore, some wonderful beaches and Erskine Falls.



The Twelve Apostles



Melbourne



Lorne

For further information, please check our website or contact:

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# AEPCOS UPDATE MEETING

March 31, 2016 , 2:00 to 7:00 pm

THE JOSEPH B. MARTIN CONFERENCE CENTER at

HARVARD MEDICAL SCHOOL

77 Avenue Louis Pasteur, Boston, MA 02115, USA

2:30-2:40 pm	ANUJA DOKRAS, MD	PRESENTATION OF THE UPDATE MEETING
2:40-3:00 pm	HELENA TEEDE, MD	LIFESTYLE PROGRAMS IN WOMEN WITH PCOS: AN OVERVIEW
3:00-3:20 pm	POLI MARA SPRITZER, MD	NUTRITION PROGRAMS IN WOMEN WITH PCOS: QUALITY OF CARBOHYDRATE AND LIPID COMPONENTS
3:20-3:30 pm	ANGELA GRASSI, RD	UNIQUE CHALLENGES AND THE IMPORTANCE OF SPECIFIC FOOD SUPPLEMENTATION IN PCOS
3:30-3:40 pm	FELICE GERSH, MD	NURTURING THE GUT MICROBIOME IN WOMEN WITH PCOS
3:40-3:50 pm		<i>Short presentations</i>
3:50-4:15 pm	General discussion:	WHAT IS THE BEST DIET IN PCOS?
4:15-4:30 pm		<i>Coffee Break</i>
4:30-4:50 pm	NEILL EPPERSON, MD	FROM MENARCHE TO MENOPAUSE: AFFECTIVE AND COGNITIVE ISSUES AFFECTING WOMEN
4:50-5:10 pm	ELISABET STENER-VICTORIN, PhD	EXCESS TESTOSTERONE DURING PREGNANCY INCREASES ANXIETY IN OFFSPRING
5:10-5:30 pm	ANUJA DOKRAS, MD	MOOD AND BEHAVIORAL DISORDERS IN PCOS: AN AEPCOS STATEMENT
5:30-6:00 pm	<i>General discussion:</i>	MOOD AND BEHAVIORAL DISORDERS IN PCOS
6:00-7:00 pm		<i>Buffet Dinner</i>

## AEPCOS is seeking a new Editor for the AEPCOS Newsletter

Professor Enrico Carmina will be stepping down as Editor of the AEPCOS Newsletter and the Board is seeking candidates from among our membership to fill the position of Editor.

Qualified candidates should have a:

- Doctoral degree in a biomedical field
- A broad understanding of reproductive sciences
- Outstanding verbal and written communication skills

If you are interested in applying for this position, please send a short bio and cover letter via email to Anuja Dokras, President of AEPCOS Society:

[ADokras@obgyn.upenn.edu](mailto:ADokras@obgyn.upenn.edu)

## OTHER FUTURE MEETINGS

- ENDOCRINE SOCIETY, BOSTON, MA, USA, APRIL 1-4, 2016
- EUROPEAN SOCIETY OF ENDOCRINOLOGY, MUNICH, GERMANY, MAY 28-31, 2016
- JOINT INDIA PCOS SOCIETY AND AEPCOS SOCIETY CONFERENCE, MUMBAI, INDIA, JUNE 17-19, 2016
- ESHRE, HELSINKI, FINLAND, JULY 3-6, 2016
- ASRM, SALT LAKE CITY, UT, USA, OCTOBER 15-19, 2016

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William Atiomo, M.D.

## **UP-REGULATION OF GENES INVOLVED IN THE INSULIN SIGNALING PATHWAY MAY BE THE MOLECULAR BASIS FOR INCREASED RISK OF ENDOMETRIAL CANCER IN WOMEN WITH PCOS**

Enrico Carmina interviewed William Atiomo about the study he recently published in *Molecular and Cellular Endocrinology*. The study reports that some genes involved in the insulin signaling pathway are upregulated in women with PCOS and endometrial cancer. Dr. Atiomo is Clinical Associate Professor and Consultant Gynaecologist, Faculty of Medicine & Health Sciences at the University of Nottingham, UK.

*Paper Shafiee MN, Seedhouse C, Mongan N, Chapman C, Deen S, Abu J, Atiomo W. Up-regulation of genes involved in the insulin signaling pathway (IGF1, PTEN and IGFBP1) in the endometrium may link polycystic ovarian syndrome and endometrial cancer. Mol Cell Endocrinol. 2016 Mar 15;424:94-101.*

### **1. William, what were the main questions that motivated this study?**

Women with polycystic ovary syndrome (PCOS) have at least a three-fold increase in endometrial cancer (EC) risk compared to women without PCOS, the precise molecular mechanisms which link between PCOS and EC remain unclear. It had been suggested that insulin resistance may contribute to the increased risk of EC in PCOS.

The specific expression of genes related to the insulin-signaling pathway including the IGF system in the endometrium of women with PCOS had however never been measured and compared to that in women with EC without PCOS and control women without EC or PCOS.

The aim of this study was to test the hypothesis that insulin signaling played a key role in the development of endometrial cancer (EC) in women with PCOS.

The expression of three key genes involved in the insulin signaling pathway (**IGF1, PTEN and IGFBP1**) was measured and compared in endometrial tissue obtained from three groups of women (n=34 in each group): PCOS without EC, women with EC without PCOS and non-PCOS women without EC (controls).

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## **2. What did your study find?**

**IGF1, IGFBP1** and **PTEN** gene expression were significantly up-regulated in the endometrium of PCOS and EC women compared to controls. However there was no significant difference in the expression of these genes in PCOS compared to EC endometrium.

The body mass index (BMI) of women with PCOS and controls, were not significantly different (29.28 ( $\pm$ 2.91) vs 28.58 ( $\pm$ 2.62) kg/m<sup>2</sup>) respectively, women with EC however had a higher mean BMI (32.22 ( $\pm$ 5.70) kg/m<sup>2</sup>). PCOS women were younger (31.8 ( $\pm$ 5.97) years) than women with EC (63.44 ( $\pm$ 10.07) years) and controls (43.68 ( $\pm$ 13.12) years).

The changes in gene expression were independent of BMI, waist hip ratio, estradiol and androgen levels. Protein validation test in the serum samples in the three groups were consistent with the gene findings.

## **3. Why are these findings novel?**

This was the first study, as far as we know, that investigated the expression of genes involved in the insulin signaling pathway in the human PCOS endometrium compared to expression in endometrial biopsies from women with endometrial cancer (EC).

## **4. What are the implications of your findings?**

Up-regulation of genes involved in the insulin signaling pathway may be the molecular basis for the increased risk of EC in women with PCOS.

The potential translational implications of these findings include a firmer mechanistic basis for strategies aiming to reduce morbidity and mortality from EC. These include studies investigating drugs targeting endometrial expression of genes involved in the insulin signaling pathway in clinical trials to prevent EC in women with and without PCOS.

As the findings at the molecular level were not yet reflected in systemic measures of insulin resistance using the HOMA test, the findings also justify further studies aiming to identify clinically useful early biomarkers which might predict which women with and without PCOS will go on to develop EC.

We also proposed a gain of function mutation hypothesis, converting **PTEN** into a tumor promoter gene involving the **IGF1** pathway. This is a relatively novel hypothesis that requires further investigation in women with PCOS.