Author's response to reviews

Title: Comparative actions of progesterone, medroxyprogesterone acetate, drospirenone and nestorone on breast cancer cell migration and invasion

Authors:

Fu Xiao-Dong (fuxiaodong27@hotmail.com)
Maria Silvia Giretti (mariasilviagiretti@virgilio.it)
Lorenzo Goglia (lorenzo@obgyn.med.unipi.it)
Marina Ines Flamini (flaminimarinaines@hotmail.com)
Angel Matias Sanchez (angelsanchez20001@hotmail.com)
Chiara Baldacci (drsaiejikil@hotmail.com)
Silvia Garibaldi (silvia.Garibaldi@obgyn.med.unipi.it)
Regine Sitruk Ware (regine@popcbr.rockefeller.edu)
Andrea R Genazzani (argenazzani@tiscali.it)
Tomasso Simoncini (t.simoncini@obgyn.med.unipi.it)

Version: 5 Date: 15 January 2008

Author's response to reviews: see over
To Melissa Norton, MD
Editor-in-Chief
BMC Cancer

Dear Dr. Norton,

I am pleased to submit to BMC Cancer the original manuscript:

“COMPARATIVE ACTIONS OF PROGESTERONE, MEDROXYPROGESTERONE ACETATE, DROSPIRENONE AND NESTORONE ON BREAST CANCER CELL MIGRATION AND INVASION”.

Our experimental work describes the actions of different progestins on breast cancer cell migration and invasion. As a general outline, our MS shows that four commonly used progestins (progesterone, MPA, drospirenone and nestorone), all enhance the movement and invasion of PR+ breast cancer cells, which is relevant for the ongoing debate on the effects of progestins on breast cancer in post-menopausal women.

In particular, we here show that the administration of these progestins to T47-D breast cancer cells results in rapid morphological changes of the cells, due to a remodelling of the actin cytoskeleton. These actions are triggered within 5 to 15 minutes and are linked to the extra-nuclear activation of rapid kinase cascades by the progestins.

We also identify the signaling intermediates in these pathways, showing that a signaling to the actin-regulatory protein, moesin is required for these events to be enacted. The paper further contains studies that identify differences in potency and to some extent in intracellular pathways recruited by the different progestins.

In conclusion, our study suggests that progestins may have an impact on the progression of PR+ breast cancer by altering the ability of cancer cells to interact with the extracellular environment and to eventually move or invade the surrounding environment. These biological effects are to some extent linked to partially discrepant recruitment of extra-nuclear signaling pathways by PR in the presence of each progestin. All together, these findings provide evidence that PR activation might play a role in the progression of ER+/PR+ breast cancers, and that the various available progestins might differ in this setting.

For all these reasons we feel that the findings reported in our manuscript are innovative and important, as well as of sufficient general interest to be worth of being possibly published on the BMC Cancer.
If this can be of help, I wish to suggest a few possible individuals who may be particularly suitable for serving as expert reviewers:

Jean Michel Foidart (jmfoidart@ulg.ac.be)
Hôpital de la Citadelle, Liège, Belgium

Alfred O Mueck (endo.meno@med.uni-tuebingen.de)
University Women’s Hospital of Tuebingen, Tuebingen, Germany

Bo Von Schoultz (b.vonschoultz@karolinska.se)
Department of Obstetrics and Gynecology, Karolinska University Hospital, SE-171 76 Stockholm, Sweden.

Piero Sismondi (psismondi@mauriziano.it)
Cattedra di Ginecologia Oncologica, Istituto per la Ricerca e la Cura del Cancro, Università Degli Studi di Torino, Candiolo, Italy

Ferdinando Auricchio (ferdinando.auricchio@unina2.it)
Dipartimento di Patologia Generale, II Università di Napoli, Via L. De Crecchio 7, 80138 Napoli, Italy

Please, be assured that the manuscript has not been published nor is being considered for publication elsewhere in whole or in part, in any language.

Yours Sincerely,

Tommaso Simoncini, MD, PhD,
(on behalf of the authors)

Molecular and Cellular Gynecological Endocrinology Laboratory
Department of Reproductive Medicine and Child Development
Division of Obstetrics and Gynecology
University of Pisa

Via Roma, 67, 56100
PISA, ITALY

Tel: +39.050.992690
Fax: +39.050.553410
E-mail: t.simoncini@obgyn.med.unipi.it
Web: http://www.med.unipi.it/MCGEL