Endocrinol Metab Syndr 2016, 5:5(Suppl)
http://dx.doi.org/10.4172/2161-1017.C1.015

Criteria, prevalence and phenotypes of polycystic ovary syndrome

Daria Lizneva
Augusta University, USA

Polycystic ovary syndrome (PCOS) is a highly prevalent disorder effecting reproductive-aged women worldwide. This presentation addresses the evolution of the criteria used to diagnosis PCOS; reviews recent advances in the phenotypic approach, specifically in the context of the extended Rotterdam criteria; discusses limitations of the current criteria used to diagnosis, particularly when studying adolescents and women in the peri- and postmenopause; and describes significant strides made in understanding the epidemiology of PCOS. We would discuss that although there is a high prevalence of PCOS, there is increased variability when using Rotterdam 2003 criteria, owing to limitations in population sampling and approaches used to define PCOS phenotypes. Last, we discuss the distribution of PCOS phenotypes, their morbidity, and the role that referral bias plays in the epidemiology of this syndrome.

dlizneva@augusta.edu

Immature myeloid cells in reproductive system-versus tumor angiogenesis

Ofer Fainaru
Rambam Medical Center, Israel

In close resemblance to other inflammatory states, gonadotropin stimulation is accompanied by influx of inflammatory cells such as neutrophils and monocyte-derived effector cells, into the ovarian stroma. Ovarian follicular development and corpora lutea formation are examples of the few physiologic events in which the formation of new blood vessels form existing ones, i.e. angiogenesis takes place. We have previously shown that bone marrow derived immature myeloid cells (IMCs) promote angiogenesis in both health (placentas) and disease (malignant tumors) and thus express similar proangiogenic genes. Nevertheless, the unique properties of IMCs populating these physiologic- versus malignant tissues have not been explored. We sought to determine whether ovarian stimulation and placental development leads to an influx of proangiogenic immature myeloid cells as observed in tumors. We used 4-5 week old C57Bl6J-*Cx3CR1GFP/+* transgenic mice, in which granulocytic (*Ly6G*+) and monocytic (Ly6C+) IMCs can be defined by flow cytometry. We analyzed placentas from timed pregnancies and tumor tissues from B16-melanomas that were implanted subcutaneously. For ovarian hyperstimulation, we treated mice with 20U pregnant mare serum gonadotropins (PMSG) for 2 days. On day 3, human chorionic gonadotropin (HCG) (5U) was injected to induce ovulation. Control unstimulated mice were treated with sham injections. Harvested tissues were weighed and enzymatically digested. Single cell suspensions were immune-stained using fluorescently labeled anti-CD11b, Gr-1, CD11c, major histocompatibility II (MHCII), CD45, *Ly6G* and Ly6C, and analyzed by flow cytometry. For global gene expression, IMCs were isolated by flow cytometry, RNA prepared and analyzed by affymetrix gene microarrays. Validation of single gene expression was performed by qPCR. Analysis of the subpopulations of IMCs revealed a significant enrichment (over 2-fold, $P<0.01$) of the *Ly6G*med/Ly6Chigh monocytic IMC fraction in tumor derived CD45+ hematopoietic cells compared to placenta, paralleled by a concomitant, more than 2-fold decrease ($P<0.01$) of the *Ly6G*high/Ly6Cmed granulocytic IMC subpopulation. In gonadotropin stimulated ovaries, we observed a ~2.5 fold increase in *Ly6G*high/Ly6Cmed granulocytic IMCs compared to unstimulated controls. Tumor derived- and gonadotropin- stimulated ovaries derived *Ly6G*med/Ly6Chigh IMCs expressed low levels of Cx3CR1 compared to the same cell population in placentas and unstimulated ovaries. Decreased expression of Cx3CR1 within IMCs has been shown to delineate a cellular population that actively contributes to tumor progression. We next assessed the global transcriptional signature of tumor derived IMCs (T-IMCs) compared to placental IMCs (P-IMCs). Analysis of the top overexpressed genes in T-IMCs revealed several key players in tumor angiogenesis including Sema3a, and matrix metalloproteinases such as Mmp2, Mmp3, Mmp13 and Mmp14, as well as genes that are involved in cancer progression and cell proliferation. Of note, various genes that were up-regulated in P-IMCs were shown to play a role in reproductive tissue angiogenesis, including *Serpine1, Arg1*, and *Flt1*. In conclusion - IMC subpopulations diverge in tumor versus reproductive tissues, favoring monocytic IMCs in the former and granulocytic IMCs in the latter. This divergence is associated with unique expression of proangiogenic genes. Selective targeting of these genes may thus be further investigated as selective angiogenic therapies for cancer, placental disease, and ovarian-hyperstimulation.

O_Fainaru@rambam.health.gov.il