larger than tumors from CD-fed mice, suggesting obesity promotes tumor growth. To investigate how obesity promotes tumor aggression, we dissociated the tumors from CD- and HFD-fed mice and plated isolated tumor cells in tumorsphere and invasion assays to test for cells with cancer stem-like cell (CSC) properties. Tumor cells from HFD-fed mice demonstrated increased tumorsphere formation and increased capacity for invasion compared to tumor cells from CD-fed mice, suggesting that obesity selects for tumor cells with CSC properties. Next, to address how obesity impacts the tumor microenvironment, we evaluated tumor necrosis and blood vessel formation through CD31 staining. Tumors from HFD-fed mice had significantly less necrosis and greater CD31 staining than those from CD-fed mice, suggesting that obesity promotes tumor angiogenesis. Since obesity promotes chronic, macrophage-driven inflammation within adipose tissue of the mammary gland, we stained tumors for the macrophage marker, F4/80. As with obese mammary glands, tumors from HFD-fed mice had significantly greater macrophage recruitment than tumors from CD-fed mice, together suggesting that obesity alters the tumor microenvironment. To determine how obesity stimulates tumor angiogenesis, we performed an *in vitro* assay by culturing dissociated tumor cells from HFD or CD-fed mice alone or with macrophages. Conditioned media (CM) isolated from tumor cells from HFD-fed mice cultured with macrophages enhanced the ability of endothelial cells to form networks *in vitro*. In contrast, CM from HFD tumor cells alone, macrophages alone, or those from CD-fed mice did not promote network formation. Together, these results suggest that cooperation between macrophages and tumor cells from HFD-fed mice promotes angiogenesis. Next, to investigate how macrophages and tumor cells interacting in obesity, we depleted macrophages using anti-F4/80 antibodies in CD-fed and HFD-fed tumor-bearing mice. In HFD-fed mice, macrophage depletion significantly reduced tumor volume and CD31 staining while increasing tumor necrosis compared to controls. Obesity promotes interactions between tumor cells and macrophages to enhance tumor angiogenesis and progression.

Thyroid

THYROID NEOPLASIA AND CANCER

Should Isthmic Thyroid Nodule Be Included in ACR TI-RADS Points in Predicting Thyroid Cancer?

Sina Jasim, MD[1], Thomas J. Baranski, MD,PHD[1], Sharlene Teefey, MD[2], William Middleton, MD[2].
[1]Washington University in St Louis, Saint Louis, MO, USA, [2]Mallinckrodt Institute of Radiology, Washington University in St Louis, Saint Louis, MO, USA.

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Should isthmic thyroid nodule be included in ACR-TIRADS points in predicting thyroid cancer?
Background: Thyroid nodules are routinely evaluated with ultrasound. Isthmic nodules carry higher risk of malignancy (in press). Surgical studies suggest higher risk of metastasis from thyroid cancer located in isthmus region. In this study, we evaluate how adding an extra point for isthmic location to current ACR-TIRADS will affect the sensitivity and specificity to predict thyroid cancer.
Methods: We performed a subanalysis of isthmic nodules contained in a retrospectively created database of 3313 adult patients from six referral centers with confirmed benign or malignant nodules. Sensitivity and specificity were calculated using the current ACR TI-RADS scoring system and compared to a system that would add an extra point based on nodule location in the isthmus.
Results: There were 195 nodules in the isthmus (34 malignant). If a recommendation for FNA was considered a positive test result, the sensitivity and specificity would be 50% (17/34) and 61% (99/161) respectively using current ACR TI-RADS scoring. If an additional point was added the sensitivity and specificity would be 62% (21/34) and 36% (58/161) respectively. Adding the additional point would lead to detection of 4 additional malignant nodules at the cost of biopsying 41 additional benign nodules. If a recommendation for *either* FNA *or* follow-up ultrasound for 5 years was considered a positive test result, the sensitivity and specificity would be 82% (28/34) and 35% (56/161) respectively using current ACR TI-RADS scoring. If an additional point was added the sensitivity and specificity would be 94% (32/34) and 15% (24/161) respectively. Adding the additional point would lead to detection of 4 additional malignant nodules at the cost of either biopsying or following 32 additional benign nodules.
Conclusions: Isthmic nodules are more likely to be malignant than nodules in other locations. When using the ACR TI-RADS, adding a point for isthmic nodules improves detection of cancer with a moderate increase in the rate of FNA and follow-up of benign nodules. Given the higher risk of extra thyroidal extension and nodal metastases for isthmic cancers, this tradeoff between sensitivity and specificity may be acceptable and should be considered when dealing with nodules in the isthmus.
Keywords: thyroid nodule, ACR TI-RADS, location, isthmus, thyroid cancer

Reproductive Endocrinology

CLINICAL STUDIES IN FEMALE REPRODUCTION I

Non-Classic POR Deficiency as a Cause of Menstrual Disorders & Infertility

Georgios E. Papadakis, MD[1], Agathe Dumont, MD[2], Jerome Bouligand, PhD[3], Fanny Chasseloup, MD[3], Anna Raggi, MD[4], Sophie Catteau-Jonard, MD, PhD[2], Odile Boute-Benejean, MD[5], Nelly Pitteloud, MD[1], Jacques Young, MD, PhD[6], Didier R. Dewailly, MD[2].
[1]Service of Endocrinology, Diabetes and Metabolism, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland, [2]Department of Reproductive Medicine, Univ. Lille, CHU Lille, Lille, France, [3]Service of Molecular Genetics, Pharmacogenetics and Hormonology, Assistance Publique-Hôpitaux de Paris, Bicetre Hospital, Le Kremlin-Bicêtre, France, [4]Fertisuisse, Olten and Basel, Switzerland, [5]Department of Clinical Genetics, Univ. Lille, CHU Lille, Lille, France, [6]Department of Reproductive Medicine, Assistance Publique-Hôpitaux de Paris, Bicetre Hospital, Le Kremlin Bicetre, France.

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P450 oxidoreductase deficiency (PORD) is an autosomal recessive disease caused by bi-allelic mutations of the *POR*