examination. The sensitivity, specificity, positive and negative predictive values and accuracy of TVS for predicting non-ovarian endometriosis were assessed.

RESULTS: Ovarian and non-ovarian endometriosis were found by laparoscopy and confirmed by histology in 12% of women with subfertility and 26.4% of women with chronic pelvic pain. The overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of TVS in diagnosis of ovarian and non-ovarian endometriosis were 96.5 and 77.2%, 99.6 and 94.1%, 96.6 and 88.2%, 99.5 and 92.1%, 99.2 and 89.6%, respectively. The diagnostic accuracy of TVS for diagnosis of endometriotic involvement of the USL, RVS and bladder were 86.3%, 93.9% and 80.3%, respectively. The overall positive and negative likelihood ratios for diagnosis of non-ovarian endometriosis were 12.92(95% CI, 7.18-23.26) and 0.24 (95%CI, 0.15-0.37), respectively.

CONCLUSIONS: In women with subfertility or chronic pelvic pain, TVS is a tool with high sensitivity and specificity for the diagnosis of ovarian endometriosis. TVS is a test with high specificity that can accurately exclude most cases with non-ovarian-endometriosis. The implementation of TVS prior to laparoscopy, for this group of patients, may minimize the need for diagnostic laparoscopy.

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TRANSCRIPTOMIC ANALYSIS REVEALS BLUNTED ACTIVATION OF THE PKA PATHWAY IN HUMAN ENDOMETRIAL STROMAL FIBROBLASTS (HESF) FROM WOMEN WITH VS. WITHOUT ENDOMETRIOSIS. L. Aghajanova, J. A. Horcajadas, J. L. Weeks, F. J. Esteban, C. Nezhat, L. C. Giudice. Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, San Francicso, CA; Department of Experimental Biology, University of Jaén, Jaén, Spain; Center for Special Minimally Invasive Surgery, Stanford university, Stanford, CA.

OBJECTIVE: To determine transcriptomic differences between hESF from women with vs. without endometriosis after cAMP treatment.

DESIGN: Laboratory-based study with full IRB approval and consents.

MATERIALS AND METHODS: hESF from n=5 women with and n=5 without (mild) endometriosis were isolated from endometrial biopsies and treated +/- 0.5mM 8-Br-cAMP for 96 hrs. Purified total RNA was subjected to microarray analysis using the whole genome Gene 1.0 ST Affymetrix platform. Validation of several genes and functional analyses were performed.

RESULTS: 733 genes were regulated in cAMP-treated hESF from women without vs.172 genes in hESF from women with endometriosis, suggesting a blunted response to cAMP/PKA pathway activation in women with disease. In the absence of disease, 8-Br-cAMP down-regulated progression through the cell-cycle due to a decrease in Cyclin D1, cyclin-dependent kinase 6 and cell division cycle 2, and an increase in cyclin-dependent kinase inhibitor 1A. However, cell cycle components in hESF from women with endometriosis were not responsive to cAMP, resulting in persistence of a proliferative phenotype. BrdU incorporation demonstrated a significant decrease in proliferation of hESF from women without endometriosis upon decidualization with cAMP that was not evident in hESF from women with disease, and changes in phosphodiesterases were not different among experimental groups.

CONCLUSIONS: Eutopic endometrial stromal fibroblasts with increased proliferative potential may seed the pelvic cavity with retrograde menstruation and promote endometriotic lesions. Resistance to cAMP in hESF is not dependent on hydrolysis and is likely due to an inherent abnormality in the PKA pathway in the presence of disease.

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EFFECT OF HISTONE DEACETYLASE INHIBITOR ON THE DEVELOPMENT OF ENDOMETRIOSIS AND NUCLEAR FACTOR-KAPPA B ACTIVATION OF ENDOMETRIOTIC LESIONS IN AN IN VIVO EXPERIMENTAL MODEL. E. Park, C.-H. Kim, H.-A. Lee, H.-Y. Nah, Y.-J. Lee, B.-M. Kang. Obstetrics and Gynecology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; Obstetrics and Gynecology, Kangwon National University Hospital, Chuncheon-City, Kangwon-Do, Republic of Korea.

OBJECTIVE: To investigate whether histone deacetylase inhibitor (HDACI), trichostatin A (TSA) could suppress the development of endometriotic lesions and the transcription factor nuclear factor-kappa B (NF-kB) is involved in this process in vivo

DESIGN: Prospective experimental study

MATERIALS AND METHODS: The endometrial fragments obtained from 6-8 weeks old green fluorescent protein (GFP)-expressing mice were injected into the peritoneal cavity of recipient nude mice that ovaries were removed and estradiol was supplemented for induction of endometriosis. We divided recipient mice into 3 groups: group 1 was treated with TSA 2mg/kg, group 2 was treated with dimethyl sulfoxide (DMSO) and group 3 was treated with saline only by intraperitoneal injection for 21days. After scheduled treatment, the amount of GFP-expressing endometriotic lesions to body weight and NF-kB activation evaluated by counting RelA-positive and –negative nuclei of all epithelial and stromal cells were compared among three groups

RESULTS: The ratio of endometriotic lesions to body weight was significantly smaller in group 1, with 0.000978 ± 0.0001462 compared with 0.002295 ± 0.0005130 and 0.002539 ± 0.0002196 in group 2 and 3, retrospectively ($P<0.01$). NF-kB activation of endometriotic lesions was significantly reduced in TSA-treated mice among three groups ($P<0.01$).

CONCLUSIONS: Endometriosis model using GFP-expressing mice was useful for expeditious identification and quantitative evaluation of endometriotic lesions. HDACIs could inhibit NF-kB activation in endometriotic lesions, and thereby suppress the development of endometriosis.

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INHIBITION OF O-LINKED GLYCOSYLATION OF CD-44 DECREASES ENDOMETRIAL CELLS ATTACHMENT TO PERITONEAL MESOTHELIAL CELLS. A. K. Rodgers, P. A. Binkley, R. R. Tekmal, R. S. Schenken. Obstetrics and Gynecology, University of Texas Health Science Center San Antonio, San Antonio, TX.

OBJECTIVE: CD44, the major glycoprotein ligand for hyaluronan (HA), has multiple N- and O-linked glycosylation sites. We previously demonstrated that abrogation of peritoneal mesothelial cell (PMC) -associated HA inhibits endometrial cell (EC) attachment to PMCs [1] and inhibition of N-linked CD44 glycosylation inhibited EC attachment to PMCs [2]. Here, we assessed the effect of O-linked glycosylation inhibition on EC attachment to PMCs.

DESIGN: *In-vitro* study

MATERIALS AND METHODS: EM-42 cells, an endometrial epithelial cell line (EEC), and HES cells, an immortalized endometrial stromal cell line (ESC), were grown to subconfluence. Cells were treated with B-GalnAC (BGn), an O-linked glycosylation inhibitor, at 0.25 mM, 0.5 mM, and 0.75 mM for 24 hours. The binding of the fluorescence-conjugated lectin, Artocarpus integrifolia (Jacalin), was used to assess the degree of glycosylation inhibition. Attachment of EECs and ESCs to the PMC line LP9 was compared to controls after one hour of co-culture using an established *in vitro* assay. Cell viability was assessed using CellTiter-Glo® Luminescent Cell Viability Assay. CD44 expression was assessed by flow cytometry using a CD44 monoclonal antibody.

RESULTS: BGn decrease in O-linked glycosylation in EEC and ESC with a maximal inhibition of 37% and 40%, respectively, at 0.5 nM. BGn inhibited EECs attachment to PMCs by 21%, 31%, and 25% at the 0.25, 0.5, and 0.75mM doses, respectively, and ESCs attachment to PMCs by 16%, 21%, and 34% at the 0.25, 0.5, and 0.75mM doses, respectively. BGn had no effect on cell proliferation or CD44 expression at any dose.

CONCLUSIONS: This study demonstrates that BGn decreases O-linked glycosylation without affecting cell viability or CD44 expression. Inhibition of O-linked glycosylation with BGn significantly inhibits EEC and ESC attachment to PMCs. These findings suggest a role for CD44 O-linked glycosylation in the development of the early endometriotic lesions. 1. F&S 84:16-21, 2005 2. F&S 86:S33, 2006

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P-81 Tuesday, October 20, 2009

PETAL STUDY: SAFETY, TOLERABILITY AND EFFECTIVENESS OF ELAGOLIX, AN ORAL GNRH ANTAGONIST FOR ENDOMETRIOSIS. R. Imani, D. Thai-Cuarto, R. Jimenez, J. Burke, R. Kroll, C. O'Brien. Clinical Development, Neurocrine Biosciences, Inc., San Diego, CA; Gynecology, Women's Clinical Research Center, Seattle, WA.

OBJECTIVE: Estradiol (E2) suppression reduces signs and symptoms of endometriosis. A dose-related partial suppression of E2 and reduction of pain

associated with endometriosis have been achieved in 3-month studies with an oral, non-peptide GnRH antagonist, elagolix (NBI-56418). The Petal study assessed treatment impact on bone mineral density, secondary endpoints assessed tolerability, safety and effectiveness of elagolix during 6-month's treatment and 6-month's follow up.

DESIGN: Randomized, double-blind and active-control study. Endometriosis subjects were randomized to 6 months of treatment with elagolix dose regimens 150 mg qd or 75 mg bid or DepoProvera SC104 every 3 months; n=84 each.

MATERIALS AND METHODS: Monthly assessments were collected with the Composite Pelvic Signs Symptom Scale and the Endometriosis Health Profile. Pain was assessed daily using a Visual Analog Scale. Mean change from baseline at each study visit was tested for significance using a mixed-effects repeated measures analysis of covariance model (Intent-to-Treat population).

RESULTS: 252 subjects randomized, 168 completed treatment. Total CPSSS, peak VAS, mean VAS and EHP-5 pain dimension were improved by first visit; scores were improved at Week 24 compared to baseline for elagolix on these measures ($p<0.0001$). Symptoms remained improved in the majority of the subjects 6 months after last dose. Elagolix was well tolerated; the most common adverse events were headache and nausea. Mean daily hot flash frequency was comparable during screening, treatment and post treatment. Median E2 concentrations were 45 pg/ml (150 mg qd) and 29 pg/ml (75 mg bid) at Week 24. The favorable BMD data are reported separately.

CONCLUSIONS: Rapid and sustained improvement of endometriosis signs and symptoms occurred with elagolix and the mean scores did not return to baseline severity after discontinuation of study drug. These findings may reflect disease modification, an observation requiring additional study. Elagolix was well tolerated.

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P-82 Tuesday, October 20, 2009

THE RELATIONSHIP BETWEEN SERUM TUMOR NECROSIS FACTOR-ALPHA (TNF-α) AND INTERLEUKIN-6 (IL-6) WITH PELVIC PAIN SYMPTOMS IN WOMEN WITH ENDOMETRIOSIS. S. Senapati, D. Clauw, S. As-Sanie. Obstetrics and Gynecology, University of Michigan Health System, Ann Arbor, MI; Rheumatology, University of Michigan Health System, Ann Arbor, MI.

OBJECTIVE: Il-6 and TNF-α have been implicated in the initiation and maintenance of endometriosis implants; however, their role in the development of pelvic pain remains unclear. This study seeks to evaluate the relationship of these cytokines to pain perception in women with endometriosis and chronic pelvic pain (CPP).

DESIGN: This is a cross-sectional study to assess serum IL-6 and TNF-α levels and pelvic pain symptoms in women with endometriosis and CPP, endometriosis without CPP, and pain-free controls.

MATERIALS AND METHODS: 38 women with surgically-confirmed endometriosis and 39 controls underwent medical interviews, physical exams, and validated questionnaires to assess pain severity. CPP was defined as $\geq$6 months of pelvic pain, occurring for >7 days per month. Serum IL-6 and TNF-α levels were measured via standard enzyme-linked immunosorbent assay (ELISA). The relationship between serum cytokine levels and pain severity was evaluated with the Kruskall-wallis test and Spearman's correlation coefficient, as appropriate, using STATA 10.0.

RESULTS: There was a trend towards serum TNF-α elevation in women with endometriosis both with and without CPP.

TABLE. Serum cytokine levels in women with endometriosis and pain-free controls

	Endometriosis with CPP (n=18)	Endometriosis without CPP (n=14)	Pain-free controls (n=39)	K-wallis p-value
TNF-α	8.6 (4.9, 14.2)	7.8 (5.1, 12.5)	5.2 (4.6, 7.0)	0.07
IL-6	2.2 (0, 2.9)	2.7 (1.8, 3.0)	2.2 (0, 2.5)	0.28

Values expressed as median (95% CI)

However, neither TNF-α nor IL-6 correlated with overall pain intensity, or with severity of dysmenorrhea, dypareunia, dyschezia, or dysuria.

CONCLUSIONS: Although it appears as though serum TNF-α (but not IL-6) is elevated in women with endometriosis, it was elevated in women with and without CPP, and neither of these measures appear related to severity of pain symptoms in this cohort.

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P-83 Tuesday, October 20, 2009

POSSIBLE INVOLVEMENT OF SURVIVIN IN RESISTANCE TO DRUG-INDUCED APOPTOSIS OF ENDOMETRIOTIC STROMAL CELLS. A. Watanabe, F. Taniguchi, M. Izawa, T. Harada, N. Terakawa. Ob & Gyn, Tottori University Faculty of Medicine, Yonago, Tottori, Japan; Biosignaling, Tottori University Faculty of Medicine, Yonago, Tottori, Japan.

OBJECTIVE: Endometriosis is defined as the presence of endometrial tissues outside uterus. Despite decades of clinical experiences and experimental researches, endometriosis remains an enigma and its pathogenesis is still controversial. Altered apoptosis in endometriotic tissues is a notion that illuminates some aspect of the pathogenesis of endometriosis. We sought to investigate the role of survivin in the pathophysiology of endometriosis and to determine the action of ectopic and eutopic endometrial stromal cells (ESCs) in resistance to apoptosis.

DESIGN: Prospective study.

MATERIALS AND METHODS: Stromal cells were prepared from endometrial and endometriotic tissues. Ectopic ESCs were obtained from ovarian chocolate cysts in patients who underwent the laparoscopic surgery (n=22). Eutopic ESCs were collected from uteri of premenopausal women who underwent hysterectomy for fibroids (n=22). Number of surviving cells and activation of caspases were assessed by WST-8 assay and immunoblotting. Using cDNA array and real-time RT-PCR, gene expression was analyzed. Effects of gene silencing were examined by WST-8-assay, Annexin-V staining and immunoblotting.

RESULTS: After staurosporine (SS), an apoptosis-inducing agent, treatment, 55 % of eutopic ESCs survived compared with 70 % of ectopic ESCs. Active procaspase -3 or -7 in eutopic ESCs was more intensely presented by SS treatment than in ectopic ESCs. Analysis using the cDNA array exhibited that the IAP-family genes, such as cIAP-1, XIAP and survivin, were highly expressed in ectopic ESCs before SS treatment. The degree of survivin expression before and after SS treatment was different between ectopic and eutopic ESCs (2.8+-0.27 vs. 0.69+-0.07), whereas that of cIAP-1, cIAP-2, and XIAP expression was not changed. Survivin silencing in SS-treated ectopic ESCs led to an increase of apoptotic cells, and markedly potentiated the cleavage of caspase -3 and -7.

CONCLUSIONS: Aberrant survivin expression in ectopic ESCs may sustain their abnormal survival in unfavorable environment.

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THE GRADUATED EMBRYO SCORE (GES) AND TOTAL GRADUATED EMBRYO SCORE (TGES) WERE NOT ASSOCIATED TO ENDOMETRIOSIS. V. Genro, C. Souza, L. Guedes da Luz, D. Silva, C. Andreoli, J. Cunha-Filho. Programa de Pós-Graduação em Ciências Médicas, UFRGS, Porto Alegre, RS, Brazil; Centro de Reprodução Humana, Insemine, Porto Alegre, RS, Brazil; Serviço de Ginecologia e Obstetrícia, HCPA, Porto Alegre, RS, Brazil.

OBJECTIVE: Our objective was to determine the GES and TGES in infertile patients with endometriosis (EDT) submitted for the first time to In Vitro Fertilization (IVF), compared with infertile patients without EDT.

DESIGN: We did a cross-sectional study.

MATERIALS AND METHODS: We compared 170 embryos (63 from 20 infertile patients without EDT and 107 from 30 infertile patients with EDT). All patients were submitted to IVF using the oestradiol-antagonist-recombinant FSH protocol described elsewhere. GES was performed evaluating all embryos four times (16-18h, 25-27h, 40-43h and 64-67h, post IVF by the same embryologist).The GES described: cytoplasm, pronuclear morphology, fragmentation, nucleolar alignment, polar body apposition, blastomere number/morphology and symmetry. TGES was performed by the sum of GES from all transferred embryos. We considered statistic significance when $P < 0.05$ using t test student or qui-square tests.

RESULTS: The groups were comparable in terms of age (32±0.9 and 32±0.6) and body mass index (22.5±0.8 and 22.7±0.5) for the control and study groups respectively. Moreover, infertility characteristics, number of MII oocytes and fertilization rates were also similar. The number of transferred embryos in infertile patients without EDT (1.6±0.2) was not different