Selección de Resúmenes de Menopausia

Semana del 24 al 30 de enero de 2018

Juan Enrique Blümel. Departamento Medicina Sur. Universidad de Chile

Nat Commun. 2018 Jan 26;9(1):387. doi: 10.1038/s41467-017-02697-5.

GWAS of epigenetic aging rates in blood reveals a critical role for TERT.

Lu AT, Xue L, Salfati EL, Chen BH, Ferrucci L, Levy D, Joehanes R, Murabito JM, Kiel DP, et al.

DNA methylation age is an accurate biomarker of chronological age and predicts lifespan, but its underlying molecular mechanisms are unknown. In this genome-wide association study of 9907 individuals, we find gene variants mapping to five loci associated with intrinsic epigenetic age acceleration (IEAA) and gene variants in three loci associated with extrinsic epigenetic age acceleration (EEAA). Mendelian randomization analysis suggests causal influences of menarche and menopause on IEAA and lipoproteins on IEAA and EEAA. Variants associated with longer leukocyte telomere length (LTL) in the telomerase reverse transcriptase gene (TERT) paradoxically confer higher IEAA ($P < 2.7 \times 10\text{-}11$). Causal modeling indicates TERT-specific and independent effects on LTL and IEAA. Experimental hTERT-expression in primary human fibroblasts engenders a linear increase in DNA methylation age with cell population doubling number. Together, these findings indicate a critical role for hTERT in regulating the epigenetic clock, in addition to its established role of compensating for cell replication-dependent telomere shortening.

Eur J Obstet Gynecol Reprod Biol. 2018 Jan 9;222:75-79. [Epub ahead of print]

Does vaginal estriol make urodynamic changes in women with overactive bladder syndrome and genitourinary syndrome of menopause?

Matarazzo MG, Caruso S, Giunta G, Valenti G, Sarpietro G, Cianci A.

OBJECTIVES: OAB is a common finding in postmenopausal women. Hypoestrogenism is the root cause of many signs and symptoms of Genitourinary Syndrome of Menopause (vaginal dryness, atrophy, dyspareunia, urinary disorders, etc.). As such the aim of this study was to evaluate the urodynamic effects of ultralowdose estriol vaginal gel formulation to treat women with Genitourinary Syndrome of Menopause and Overactive Bladder Syndrome. STUDY DESIGN: This open-labeled, single center, prospective study involved 37 women with OAB recruited in our Urogynecological Unit between January and July 2016. They received estriol 50 mcg/g vaginal gel, one applicator-dose per day for 3 weeks followed by one dose twice a week for 12 weeks. Objective and subjective parameters were evaluated before and after treatment through the urodynamic examination, Overactive Bladder symptom score and Short Form Health Survey-36 questionnaires. RESULTS: Vaginal atrophy symptoms and signs as well as the overactive bladder subjective symptom parameter improved significantly. Urodynamic evaluation showed significant improvement in first desire to void and maximum cystometric capacity after estriol usage. Patients who had detrusor overactivity did not show any improvement for this parameter after treatment. The voiding function parameters did not significantly change. Short form-36 showed a better quality of life after treatment especially for the emotional role, as well as mental and general health. CONCLUSIONS: A local ultra-low dose concentration of estriol could be effective in women with vaginal atrophy and Overactive Bladder Syndrome for improving both subjective symptoms and urodynamic parameters of storage function not affecting voiding function.

Rheumatol Int. 2018 Jan 23. doi: 10.1007/s00296-018-3929-0. [Epub ahead of print]

Variability of Denosumab densitometric response in postmenopausal osteoporosis.

Laroche M, Baradat C, Ruyssen-Witrand A, Degboe Y.

The objective of our prospective study is to specify the variability of densitometric response to Denosumab, given in the second line, and to try to understand the reasons. All menopausal patients with primary osteoporosis, treated by Denosumab in our centre from 2014 to 2015, were included in this open prospective work. At T0, the patient's age, type of fracture, and previous treatments were collated. At T0 and T1, after 1 year of treatment by Dmab, a DXA of the spine and the hip and a determination of CTX were performed. Sixty-three patients aged 68.8 ± 8.3 years were included. The median number of treatments prescribed for osteoporosis before switch to Denosumab was 2.4. The median duration of these treatments was 7.2 years. At T1, CTX was less than 33 pg/ml (minimum threshold for our

assay kit) in all patients. The median BMD in the spine increased by + 5.44% compared to T0. 14 patients in the upper quartile had a median BMD gain in the spine of + 11.07%. Fourteen patients in the lower quartile had a median BMD gain in the spine of + 0.6%. Only the duration of previous treatments, which was greater in the non-responder group, differed between these two groups. In the total cohort, the spinal densitometric gain was negatively correlated with the age of the patient at baseline (p = 0.04), the duration of previous treatment (p = 0.02), and positively with the CTX level (p = 0.05). The Dmab densitometric response is highly variable, partly explained by the duration of previous treatments and the level of bone resorption at initiation of treatment.

Eur J Clin Nutr. 2018 Jan 23. doi: 10.1038/s41430-017-0081-y. [Epub ahead of print]

Bone turnover, calcium homeostasis, and vitamin D status in Danish vegans.

Hansen TH, Madsen MTB, Jørgensen NR, Cohen AS, Hansen T, Vestergaard H, Pedersen O, Allin KH.

BACKGROUND/OBJECTIVES: A vegan diet has been associated with increased bone fracture risk, but the physiology linking nutritional exposure to bone metabolism has only been partially elucidated. This study investigated whether a vegan diet is associated with increased bone turnover and altered calcium homeostasis due to insufficient intake of calcium and vitamin D. SUBJECTS/METHODS: Fractionated and total 25-hydroxyvitamin D (25(OH)-D), parathyroid hormone (PTH), calcium, and four bone turnover markers (osteocalcin, N-terminal propeptide of type I procollagen (PINP), bone-specific alkaline phosphatase (BAP), and C-terminal telopeptide of type I collagen (CTX)) were measured in serum from 78 vegans and 77 omnivores. RESULTS: When adjusting for seasonality and constitutional covariates (age, sex, and body fat percentage) vegans had higher concentrations of PINP (32 [95% CI: 7, 64]%, P = 0.01) and BAP (58 [95% CI: 27, 97]%, P < 0.001) compared to omnivores, whereas CTX (30 [95% CI: -1, 72]%, P = 0.06) and osteocalcin (21.8 [95% CI: -9.3, 63.7]%, P = 0.2) concentrations did not differ between the two groups. Vegans had higher serum PTH concentration (38 [95% CI: 19, 60]%; P < 0.001) and lower 25(OH)-D serum concentration (-33 [95% CI: -45, -19]%; P < 0.001), but similar serum calcium concentration (-1 [95% CI: -3, 1]%, P = 0.18 compared to omnivores. CONCLUSIONS: Vegans have higher levels of circulating bone turnover markers compared to omnivores, which may in the long-term lead to poorer bone health. Differences in dietary habits including intake of vitamin D and calcium may, at least partly, explain the observed differences.

Br J Cancer. 2018 Jan 23. doi: 10.1038/bjc.2017.435. [Epub ahead of print]

Postmenopausal breast cancer and oestrogen associations with the IgA-coated and IgA-noncoated faecal microbiota.

Goedert JJ, Hua X, Bielecka A, Okayasu I, Milne GL, Jones GS, Fujiwara M, Sinha R, Wan Y, Xu X, Ravel J, et al.

BACKGROUND: The diversity and composition of the gut microbiota may affect breast cancer risk by modulating systemic levels of oestrogens and inflammation. The current investigation tested this hypothesis in postmenopausal women by identifying breast cancer associations with an inflammation marker, oestrogen levels, and faecal microbes that were or were not coated with mucosal immunoglobulin A (IgA). METHODS: In this population-based study, we compared 48 postmenopausal breast cancer cases (75% stage 0-1, 88% oestrogen-receptor positive) to 48 contemporaneous, postmenopausal, normal-mammogram, age-matched controls. Microbiota metrics employed 16S rRNA gene amplicon sequencing from IgA-coated and -noncoated faecal microbes. High-performance liquid chromatography/mass spectrometry (HPLC/MS) and radioimmunoassay were used to quantify urine prostaglandin E metabolite (PGE-M), a possible marker of inflammation; urine oestrogens and oestrogen metabolites were quantified by HPLC/MS-MS. RESULTS: Women with pre-treatment breast cancer had non-significantly elevated oestrogen levels; controls' (but not cases') oestrogens were directly correlated with their IgA-negative microbiota alpha diversity (P=0.012). Prostaglandin E metabolite levels were not associated with case status, oestrogen levels, or alpha diversity. Adjusted for oestrogens and other variables, cases had significantly reduced alpha diversity and altered composition of both their IgA-positive and IgA-negative faecal microbiota. Cases' faecal microbial IgA-positive imputed Immune System Diseases metabolic pathway genes were increased; also, cases' IgA-positive and IgA-negative imputed Genetic Information Processing pathway genes were decreased (P⩽0.01). CONCLUSIONS: Compared to controls, breast cancer cases had significant oestrogen-independent associations with the IgA-positive and IgA-negative gut microbiota. These suggest that the gut microbiota may influence breast cancer risk by altered metabolism, oestrogen recycling, and immune pressure.

Bone. 2018 Jan 20;110:1-10. doi: 10.1016/j.bone.2018.01.019. [Epub ahead of print]

The effects of estrogen deficiency on cortical bone microporosity and mineralization.

Sharma D, Larriera A1, Palacio-Mancheno PE, Gatti V, Fritton JC, Bromage TG, Cardoso L, Doty SB, Fritton SP.
Recent studies have demonstrated matrix-mineral alterations in bone tissue surrounding osteocytes in estrogen-deficient animals. While cortical bone porosity has been shown to be a contributor to the mechanical properties of bone tissue, little analysis has been done to investigate the effects of estrogen deficiency on bone's microporosities, including the vascular and osteocyte lacunar porosities. In this study we examined alterations in cortical bone microporosity, mineralization, and cancellous bone architecture due to estrogen deficiency in the ovariectomized rat model of postmenopausal osteoporosis. Twenty-week-old female Sprague-Dawley rats were subjected to either ovariectomy or sham surgery. Six weeks post-surgery tibiae were analyzed using high-resolution micro-CT, backscattered electron imaging, nanoindentation, and dynamic histomorphometry. Estrogen deficiency caused an increase in cortical bone vascular porosity, with enlarged vascular pores and little change in tissue mineral density in the proximal tibial metaphysis. Measurements of cancellous architecture corresponded to previous studies reporting a decrease in bone volume fraction, an increase in trabecular separation, and a decrease in trabecular number in the proximal tibia due to estrogen deficiency. Nanoindentation results showed no differences in matrix stiffness in osteocyte-rich areas of the proximal tibia of estrogen-deficient rats, and bone labeling and backscattered electron imaging showed no significant changes in mineralization around the vascular pores. The findings demonstrate local surface alterations of vascular pores due to estrogen deficiency. An increase in cortical vascular porosity may diminish bone strength as well as alter bone mechanotransduction via interstitial fluid flow, both of which could contribute to bone fragility during postmenopausal osteoporosis.

WMJ. 2017 Dec;116(5):200-204.

Muscle Cramps Do Not Improve With Correction of Vitamin D Insufficiency.

Weiker MK, Nielsen B, Waclawik AJ, Staples AC, Hansen KE.
BACKGROUND: Minimal treatment options exist for idiopathic muscle cramps. OBJECTIVE: We evaluated whether correction of vitamin D insufficiency relieved muscle cramps in postmenopausal women. METHODS: We conducted a post hoc analysis of a randomized, double-blind, placebo-controlled trial at a single academic medical center in the Midwest to evaluate the benefits of treating vitamin D insufficiency. Two hundred thirty postmenopausal women participated. Eligible women were ≤75 years old, 5 years past menopause or oophorectomy, or ≥60 years if they had previously undergone hysterectomy without oophorectomy. Women had vitamin D insufficiency at baseline (25-hydroxyvitamin D 14-27 ng/mL). We excluded subjects with a glomerular filtration rate <45 mL/minute. INTERVENTIONS FOR CLINICAL TRIALS: Participants completed food diaries, laboratory studies, and functional tests including the Timed Up and Go test, Physical Activity Scale for the Elderly, Health Assessment Questionnaire (a measure of disability), and pain scores. Subjects recorded muscle cramp frequency and severity using a standardized form at 6 visits over 1 year. RESULTS: During the trial, over half of participants (n=121, 53%) reported muscle cramps. Despite unequivocal vitamin D repletion, vitamin D had no effect on muscle cramps. Pain levels, disability, and dietary potassium predicted presence of cramps. Serum albumin and physical activity were inversely associated with, and disability was positively associated with, severity of muscle cramps. CONCLUSIONS: Further studies are needed to evaluate the link between pain, disability, dietary potassium intake, and muscle cramps.