Selección de Resúmenes de Menopausia

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The skeletal cell-derived molecule sclerostin drives bone marrow adipogenesis.

Fairfield H, Falank C, Harris E, Demambro V, McDonald M, Pettitt JA, Mohanty ST, Croucher P, Kramer I, et al.

The bone marrow niche is a dynamic and complex microenvironment that can both regulate, and be regulated by the bone matrix. Within the bone marrow (BM), mesenchymal stromal cell (MSC) precursors reside in a multi-potent state and retain the capacity to differentiate down osteoblastic, adipogenic, or chondrogenic lineages in response to numerous biochemical cues. These signals can be altered in various pathological states including, but not limited to, osteoporotic-induced fracture, systemic adiposity, and the presence of bone-homing cancers. Herein we provide evidence that signals from the bone matrix (osteocytes) determine marrow adiposity by regulating adipogenesis in the bone marrow. Specifically, we found that physiologically relevant levels of Sclerostin (SOST), which is a Wnt-inhibitory molecule secreted from bone matrix-embedded osteocytes, can induce adipogenesis in 3T3-L1 cells, mouse ear- and BM-derived MSCs, and human BM-derived MSCs. We demonstrate that the mechanism of SOST induction of adipogenesis is through inhibition of Wnt signaling in pre-adipocytes. We also demonstrate that a decrease of sclerostin in vivo, via both genetic and pharmaceutical methods, significantly decreases bone marrow adipose tissue (BMAT) formation. Overall, this work demonstrates a direct role for SOST in regulating fate determination of BM-adipocyte progenitors. This provides a novel mechanism for which BMAT is governed by the local bone microenvironment, which may prove relevant in the pathogenesis of certain diseases involving marrow adipose. Importantly, with anti-sclerostin therapy at the forefront of osteoporosis treatment and a greater recognition of the role of BMAT in disease, these data are likely to have important clinical implications.

Int J Cancer. 2018 Jan 15;142(2):230-237. doi: 10.1002/ijc.31046. Epub 2017 Oct 16.

Red and processed meat intake and cancer risk: Results from the prospective NutriNet-Santé cohort study.

Diallo A, Deschasaux M, Latino-Martel P, Hercberg S, Galan P, Fassier P, Allès B, Guéraud F, Pierre FH, Touvier M.

The International Agency for Research on Cancer (WHO-IARC) classified red meat and processed meat as probably carcinogenic and carcinogenic for humans, respectively. These conclusions were mainly based on studies concerning colorectal cancer, but scientific evidence is still limited for other cancer locations. In this study, we investigated the prospective associations between red and processed meat intakes and overall, breast, and prostate cancer risk. This prospective study included 61,476 men and women of the French NutriNet-Santé cohort (2009-2015) aged ≥35 y and who completed at least three 24 hrs dietary records during the first year of follow-up. The risk of developing cancer was compared across sex-specific quintiles of red and processed meat intakes by multivariable Cox models. 1,609 first primary incident cancer cases were diagnosed during follow-up, among which 544 breast cancers and 222 prostate cancers. Red meat intake was associated with increased risk of overall cancers [HRQ5vs.Q1 =1.31 (1.10-1.55), ptrend = 0.01) and breast cancer (HRQ5vs.Q1 = 1.83 (1.33-2.51), ptrend = 0.002]. The latter association was observed in both premenopausal [HRQ5vs.Q1 =2.04 (1.03-4.06)] and postmenopausal women [HRQ5vs.Q1 =1.79 (1.26-2.55)]. No association was observed between red meat intake and prostate cancer risk. Processed meat intake was relatively low in this study (cut-offs for the 5th quintile = 46 g/d in men and 29 g/d in women) and was not associated with overall, breast or prostate cancer risk. This large cohort study suggested that red meat may be involved carcinogenesis at several cancer locations (other than colon-rectum), in particular breast cancer. These results are consistent with mechanistic evidence from experimental studies.

Bone. 2017 Dec 16. pii: S8756-3282(17)30472-6. doi: 10.1016/j.bone.2017.12.016. [Epub ahead of print]

Perimenopausal bone histomorphometry before and after menopause.

Recker RR, Lappe JM, Davies M, Kimmel D.

Investigators and clinicians have had few normal bone histomorphometry data available to compare with those found in diseased patients, or in the results of treatments. The Goals and Objectives of this work are two-fold: 1. to present static and dynamic bone histomorphometry data from transilial bone biopsies performed on 76 healthy, premenopausal women. 2. To present paired static and dynamic bone histomorphometry data from bone biopsies on a subset (N=51 pairs) of these same healthy women whose biopsies were repeated 12months after their last menses. Statistical comparisons between the pre- and postmenopausal data are presented. These data will shrink this important gap, both for clinicians and investigators. We enrolled 76 healthy, premenopausal women over age 46, performed transilial bone biopsies after tetracycline labeling, and during a period of 9.5years, we re-biopsied 51 of them who passed through menopause and remained healthy the entire time. We also obtained serum biochemical measurements, and serial DXA exams during the period of observation. The dynamic bone histomorphometry demonstrated a doubling of bone remodeling, and increases in serum bone markers at the time of the second biopsy. Lumbar spine bone density also declined, and there were significant correlations between serum markers and histomorphometry variables. The data demonstrate that healthy menopause results in an important increase in bone remodeling, and a loss of bone density. We do not fully understand the mechanisms of these transmenopausal changes, but the data provide some clues that are helpful.

J Steroid Biochem Mol Biol. 2017 Dec 16. pii: S0960-0760(17)30381-3. [Epub ahead of print]

Calcium and Vitamin D in Human Health: Hype or Real?

Wimalawansa SJ, Razzaque DMS, Al-Daghri NM.

The incidence and the prevalence of vitamin D deficiency are increasing worldwide. It is estimated that over 50% of population in the world have low in vitamin D (i.e., hypovitaminosis D; levels below 30 ng/mL). 80% of our vitamin D requirement comes from the ultraviolet rays from sunlight, and for the remainder, we rely from the diet and supplements. The latter become important when one is exposing to less than optimal amounts of sunlight, inability of the skin to generate vitamin D efficiently, and/or having secondary causes that leads to increase catabolism of vitamin D. The normal serum vitamin D level is thought to be about 30 ng/mL (75 nmol/L); a range between 30 and 60 ng/mL (75 and 150 nmol/L). The Institute of Medicine (IOM) report of 2011 suggests, 600 IU is adequate for people below the age 71 who are not exposed to sunshine. Although IOM amount might be of relevance to the ambulatory healthy individuals, in disease conditions, very few patients would manage to reach serum vitamin D level above 30 ng/mL, which most scientists consider the minimum adequate level for optimal health. While the natural way to obtain vitamin D is through safe sunlight exposure, an additional daily intake of 1,000 IU of vitamin D is needed for people with lighter-skin color. With suboptimal sun exposure in those with dark-skinned and older adults need an additional 2,000 IU/day or more, vitamin D to maintain serum 25-hydroxyvitamin D levels over 30 ng/mL; the safe upper limit of oral daily supplementation is considered as 5,000 IU. However, vulnerable groups including those who are disabled, obese, and those with gastrointestinal abnormalities and/or malabsorption syndromes, institutionalized people (e.g., nursing homes and in prisons), and during pregnancy and lactation, needs approximately 4,000 IU per day for optimal physiological activities. Vitamin D is critical for enhancing gastrointestinal calcium absorption and mineralization of the osteoid tissue. In is also important for other physiological functions, such as muscle strength and neuromuscular coordination, release of hormones, subduing autoimmunity, and curtailing the development of certain cancers.

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In-utero cigarette smoke exposure and the risk of earlier menopause.

Honorato TC, Haadsma ML, Land JA, et al.; Avon Longitudinal Study of Parents and Children (ALSPAC).

OBJECTIVE: Cigarette smoking is a risk factor for earlier menopause. Animal studies show that in-utero smoke exposure is toxic to developing ovaries. Our aim was to evaluate whether in-utero smoke exposed women reach menopause earlier compared with nonexposed women. METHODS: This is a cohort study within the Avon Longitudinal Study of Parents and Children. Participants included in this study were followed from 1991/1992 until 2010. Participant characteristics for the current analysis were obtained from obstetric records and from annual follow-up questionnaires. When not available, age at natural menopause was estimated by age at filling in the questionnaire minus 1 year. Cox proportional hazards modeling was used to estimate hazard ratios of menopause for in-utero exposed and nonexposed women. RESULTS: There were 695/2,852 postmenopausal women, of whom 466 had natural menopause, 117 had hormonal therapy, and 112 had surgical menopause. Age at natural menopause was 50.6±3.7 years. Of all participants, 20.2% (577/2,852) were exposed to smoke in-utero. Participants who were in-

utero exposed but were not smokers did not have higher hazards of menopause (adjusted hazard ratio [HR] 0.92, 95% CI 0.72-1.18), whereas participants who were ever smokers (current or previous) and were in-utero exposed (adjusted HR 1.41, 95% CI 1.01-1.95) or were ever smokers but not exposed (adjusted HR 1.24, 95% CI 1.00-1.53) did have higher hazards of earlier menopause. CONCLUSIONS: In-utero smoke exposure was not associated with earlier menopause, but the effect of in-utero smoke exposure was modified by the smoking habits of the participants themselves increasing the risk for smokers who were in-utero exposed.

Menopause. 2018 Jan;25(1):46-53. doi: 10.1097/GME.0000000000000954.

Hormone therapy use in the Canadian Longitudinal Study on Aging: a cross-sectional analysis.

Costanian C, Edgell H, Ardern CI, Tamim H.

OBJECTIVE: The aim of the study was to assess the prevalence and factors associated with hormone therapy (HT) use among Canadian women. METHODS: Baseline data from the Tracking cohort of the Canadian Longitudinal Study on Aging (CLSA) was used for this analysis. The main outcome was HT use among women aged 45-85 years, defined as current, past, and never users. Multinomial logistic regression models were used to examine the differences between current, past, and never HT users in terms of sociodemographic, health behavior, and health-related variables. RESULTS: Overall, 9.5% of the sample reported current use of HT, whereas 21.9% reported past use. The main factors associated with a lower likelihood of current HT use were older age (>80 y), nonwhite ethnic background, current employment, regular smoking, obesity, and breast cancer. By contrast, alcohol consumption, and the presence of allergies or mood disorders were positively associated with current HT use. CONCLUSIONS: These findings provide a recent national picture of HT use in Canada that may be used to inform opportunities for improved physician-patient communication regarding menopause management.

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FRAX-based intervention and assessment thresholds in seven Latin American countries.

Clark P, Denova-Gutiérrez E, Zerbini C, Sanchez A, Messina O8, Jaller JJ, Campusano C, Orces CH, Riera G, et al

INTRODUCTION: Intervention thresholds are proposed using the Fracture Risk Assessment (FRAX) tool. We recommended their use to calculate the ten-year probability of fragility fracture (FF) in both, men and women with or without the inclusion of bone mineral density (BMD). The purpose of this study is to compute FRAX-based intervention and BMD assessment thresholds for seven Latin American countries in men and women ≥ 40 years. METHODS: The intervention threshold (IT) was set at a 10-year probability of a major osteoporotic fracture (MOF) equivalent to a woman with a prior FF and a body mass index (BMI) equal to 25.0 kg/m2 without BMD or other clinical risk factors. The lower assessment threshold was set at a 10-year probability of a MOF in women with BMI equal to 25.0 kg/m2, no previous fracture and no clinical risk factors. The upper assessment threshold was set at 1.2 times the IT. RESULTS: For the seven LA countries, the age-specific IT varied from 1.5 to 27.5% in Argentina, 3.8 to 25.2% in Brazil, 1.6 up to 20.0% in Chile, 0.6 to 10.2% in Colombia, 0.9 up to 13.6% in Ecuador, 2.6 to 20.0% in Mexico, and 0.7 up to 22.0% in Venezuela at the age of 40 and 90 years, respectively. CONCLUSIONS: In the LA countries, FRAX-based IT offers a substantial advance for the detection of men and women at high fracture risk, particularly in the elderly. The heterogeneity of IT between the LA countries indicates that country-specific FRAX models are appropriate rather than a global LA model.