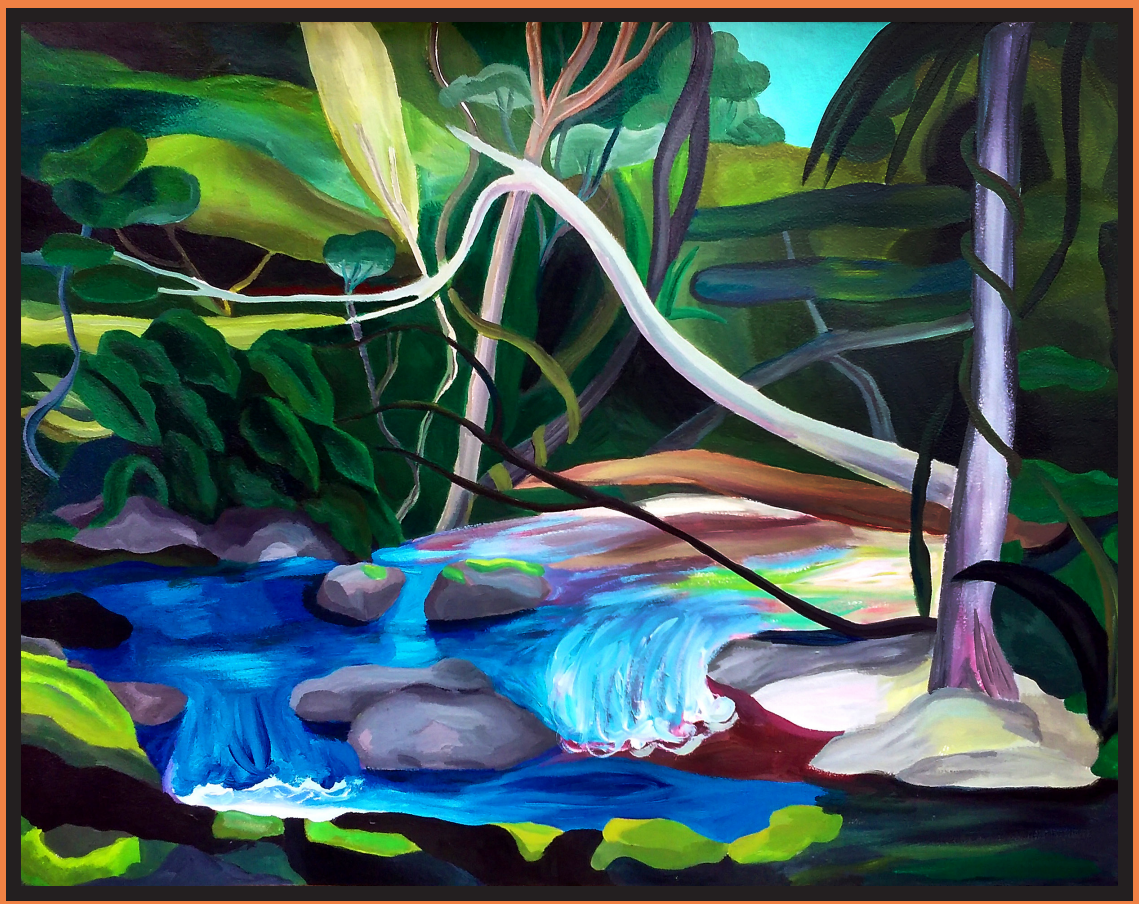
2023

medicina

BUENOS AIRES, VOL. 83 Supl. V - 2023



MEDICINA

Volumen 83, Supl. V, Págs. 1- 262

medicina

BUENOS AIRES, VOL. 83 Supl. V - 2023

La Tapa
Todo, 2016
Daniela Kantor

MEDICINA (Buenos Aires) - Revista bimestral – ISSN 1669-9106 (En línea)

Registro de la Propiedad Intelectual N° 02683675
Personería Jurídica N° C-7497
Publicación de la Fundación Revista Medicina (Buenos Aires) Propietario de la publicación: Fundación Revista Medicina
Queda hecho el depósito que establece la Ley 11723

Publicada con el apoyo del Ministerio de Ciencia, Tecnología e Innovación Productiva.
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Incluida en el Núcleo Básico de Revistas Científicas Argentinas del CONICET.

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e-mail: revmedbuenosaires@gmail.com – http//: www.medicinabuenosaires.com

Vol. 83, Supl. V, Noviembre 2023

Diagramación y Diseño: Andrés Esteban Zapata - aez.sgi@gmail.com

REUNIÓN CONJUNTA SAIC SAB AAFE AACYTAL 2023

LXVIII REUNIÓN ANUAL DE LA SOCIEDAD ARGENTINA DE INVESTIGACIÓN CLÍNICA (SAIC)

XXV JORNADAS ANUALES DE LA SOCIEDAD ARGENTINA DE BIOLOGÍA (SAB)

LV REUNIÓN ANUAL DE LA ASOCIACIÓN ARGENTINA DE FARMACOLOGÍA EXPERIMENTAL (AAFE)

VIII REUNIÓN CIENTÍFICA REGIONAL DE LA ASOCIACIÓN ARGENTINA DE CIENCIA Y TECNOLOGÍA DE ANIMALES DE LABORATORIO (AACYTAL)

15-17 de noviembre de 2023
Hotel 13 de Julio – Mar del Plata

EDITORES RESPONSABLES
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JOINT MEETING SAIC SAB AAFE AACYTAL 2023

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tissue involved.

92. 86. **EFFECT OF ESTROGEN ESTRONE ON UTERINE AND ADIPOSE TISSUE UNDER OBESITY**

María I. Valle, Sabrina B. Cepeda, Pablo H. Cutini, Marisa J. Sandoval, Virginia L. Massheimer
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Previously we reported that, estrone (E_1) counteracts uterine oxidative stress induced by an inflammatory environment. In this work, using an experimental model of obesity, the direct action of E_1 on uterus (Ut) and adipose tissue (AT) was evaluated. In order to rule out the influence of the hormonal impact during estrous cycle, animals were bilaterally ovariectomized (OVX). Rats were fed with high-fat diet (OVX-Ob) for 10 weeks. After isolation, Ut and retroperitoneal AT explants were in vitro expose to 10 nM E_1. Histological analysis of Ut explants (H&E staining) showed that in non-OVX rats exhibited a thicker endometrial layer with great amount of uterine glands compared to uterus sections from OVX rats, verifying the absence of estrous cycles in OVX group. The serum biochemical evaluation showed that, Ob rats exhibited higher levels of serum H_2O_2; TBARS, and leptin than non-obese (8; 65; 122% above non-Ob, respectively, $p< 0.05$), profile compatible with obesity. After E1 treatment (4h), Ut slices exhibited an enhancement in nitric oxide synthesis (33% above control $P<0.001$) and reduction in ROS production (30% below control, $P<0.01$). To assess whether the effect of E_1 on H_2O_2 generation depends on its ability to enhance NO synthesis, an irreversible NOS inhibitor (L-NAME) was employed. In the presence of L-NAME, the reduction on ROS production elicited by E1 was blocked, suggesting NO dependence. Indeed, in OVX-Ob rats the steroid treatment stimulates uterus angiogenesis. Concomitantly, on AT explants isolated from OVX-Ob rats, E_1 prompted an antioxidant action. E_1 reduced H_20_2 secretion (2375±263 vs 1978±241 nmol/g AT, C vs E1 $p<0.05$), and TBARS released (502±195 vs 353±30 nmol/g AT, C vs E_1 $p<0.05$). Indeed, a 14% reduction on leptin secretion was also detected ($p<0.05$). The results presented evidenced that adipose tissue is targeted of E_1 action, and that under obesity the hormone exerts a protective action on Ut and AT reducing oxidative stress.

93. 168. **OVARIECTOMY PREVENTS THE LOSS OF NUCLEAR MENIN EXPRESSION IN LACTOTROPHS PREVENTING PROLACTINOMA DEVELOPMENT**

Milagros Peña-Zanoni, Alejandra Abeledo-Machado, Dana Bornancini, Agustina Marcial-López, Susana Rulli, Graciela Díaz-Torga.
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Among its multiple functions, menin plays a key role in activins signalling in the pituitary. We previously showed the importance of activin inhibitory function on lactotrophs: decreased activin biological function is involved in prolactinoma development. Moreover, the loss of gonadal inhibins after a prepuberal ovariectomy (OVX) recovers the inhibitory function of pituitary activins preventing prolactinoma development. In this work, we analysed the effect induced by a prepuberal OVX on menin expression and cellular localization in lactotrophs, and its impact on menin targets as: *Inhbb* gene (which encodes activin subunit βb), $p27^{Kip1}$ and pAKT. We used a mouse model of prolactinoma: females overexpressing the β subunit of the human chorionic gonadotrophin (hCGβ+). Data was analysed by One-way ANOVA comparing groups: WT (normal pituitaries) vs hCGβ+ (prolactinomas) vs hCGβ+OVX (hCGβ+ with prepuberal OVX). We found nuclear and cytoplasmatic menin expression in lactotrophs from WT female mice (confocal microscopy). The nuclear expression of menin was lost in prolactinomas (hCGβ+ females). Accordingly, hCGβ+ prolactinomas presented lower levels of *Inhbb* (RTqPCR), reduced p27 expression in lactotrophs, with a concomitant sharp increase in the percentage of lactotrophs pAKT+ compared to WTs. Interestingly, after OVX, the nuclear localization of menin is recovered (hCGβ+OVX group). Accordingly, pituitary *Inhbb* levels sharply increases, the percentage of lactotrophs p27+ was recovered, with concomitant reduction in the percentage of lactotroph pAKT+ in hCGβ+OVX pituitaries. The present results demonstrate that a prepuberal OVX not only recovers activin inhibitory action but also prevents the loss of nuclear menin expression in lactotrophs, avoiding p27 dysregulation and pAKT increase, preventing prolactinoma development.

94. 197. **DEXAMETHASONE ACCELERATES WHITENING AFTER BROWNING OF WHITE ADIPOSE TISSUE IN MICE**

Alejandra Giordano[1], Patricia Castro[1], María Amanda Rey[1], María Guillermina Zubiría[1], Andrés Giovambattista[1]
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Browning is the emergence of thermogenic beige adipocytes in white adipose tissue (WAT), mainly in response to cold or B-adrenergic stimuli. Previously, we demonstrated that Dexamethasone (Dxm) inhibits browning in WAT depots from rats. However, it remains unexplored the Dxm effect in beige to white adipocyte transition (Whitening, wtng) and its relationship with mitophagy activation. Our aim was to study if Dxm affect this process in mouse inguinal AT (IAT), using in vivo and in vitro models. First, male mice were kept at 4°C during 7 days (CF) and then two groups were housed during 8h or 2 days at RT and treated daily with or without Dxm (Sc. injection: 0.03 mg/kg; experimental groups: DW8h, CW8h, DW2d and CW2d, respectively). IAT pads were dissected and processed for quantification (qPCR) of thermogenic (Ucp1) and mitophagy (Pink1 and Parkn2) marker expressions. We evaluated the effect of the variables Time (T) and Dxm (2-way ANOVA). First, we found that Dxm diminished Ucp-1 mRNA levels ($p<0.05$) at both times, supporting a stimulatory effect of Dxm in IAT wtng. On the other hand, Dxm caused differential effect in Pink1 and Parkn2 expressions: at 8h both markers were increased while at 2 days both were similar to control (Interaction TxDxm $p<0.05$), indicating an accelerate activation of mitophagy by Dxm. We also evaluated the in vitro Dxm effect in wtng process, using differentiated beige adipocytes. During the last 12h or 24h of culture T3 and rosiglitazone were withdrawn to allow wtng process occurs, and cells were incubated with or without Dxm 0,25 uM. We found that Dxm decreased Ucp1 and increased pink1 mRNA levels, in both times ($p<0.05$). While, Prkn2 and Resistin (white adipocyte marker) expressions were increased only at 24h, indicating a higher effect of Dxm at longer times (Interaction TxDxm $p<0.05$). Overall, here we described for the first time that Dxm accelerates the wtng of IAT, which could be due to an increase in mitophagy-related genes expression

95. 241. **SPEXIN PROMOTES WHITENING OF WHITE ADIPOSE TISSUE THROUGH MODULATION OF AUTOPHAGY**

Patricia Castro[1], Catalina Latina[1], Agustina Castro[1], Sabrina Gambaro[1,2], Andrés Giovambattista[1,2]
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[2]*Facultad de Ciencias Exactas, UNLP*

Spexin (SPX), a peptide adipokine, has been involved in many metabolic processes such as body weight regulation, food intake, energy balance and glucose and lipid metabolism. Recently, it was also related to disrupt the thermogenic profile of brown and white adipose tissue (AT), but no information was found about its role during white adipose tissue whitening. For this purpose, C57BL/6J male mice were exposed 7 days at 4°C and then returned to room temperature for 8h or 24h where spx was administered (ip. 29 μg/kg; 8SPXw and 24SPXw) or PBS (8CTRw and 24CTRw). Body weight and caloric intake were recorded daily. At the end of the experiment, plasma was collected for Triglycerides (TG) measurement and Epididymal AT (EAT) and Inguinal AT (IAT) was dissected and weighted. IAT was also processed for qPCR gene expression (Ucp1; thermogenic marker and Pink, Parkin, Atg12 and Atg7; autophagic markers) and for mitochondrial DNA (mitDNA) quantification. Two-way ANOVA was used to determine variable (SPX and Time) and interaction (SPX x Time) effects. No differences in total caloric intake were ob-