

resting metabolic rate and muscle strength were not confirmed by this study.

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## PS146

### **Titin phosphorylation by protein kinase G as a novel mechanism of diastolic adaptation to acute load**



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(R. Rocha).

**Aim:** To evaluate acute adaptations of myocardial stiffness to acute stretch and characterize the underlying mechanisms.

**Introduction:** Systolic adaptation to myocardial stretch/volume overload is known, but whether the heart is also able to modulate its stiffness following such challenges remains unknown.

**Methods:** Left ventricle (LV) of intact rat Langendorff hearts, rabbit papillary muscles and myocardial strips from cardiac surgery patients were acutely stretched. Skinned cardiomyocytes from Stretched and Non-stretched myocardium were studied. Stretch by increased venous return or volume loading was assessed by echocardiography in healthy volunteers; pressure-volume hemodynamics in cardiac surgery patients and in a rat model of LV hypertrophy. Myocardial cGMP, phosphorylated vasodilator-stimulated phosphoprotein (VASP) and titin phosphorylation were quantified. Pharmacological studies assessed the role of NO and natriuretic peptides (NP).

**Results:** After stretch, end-diastolic pressure (EDP) or passive tension (PT) decreased over 15 min in all preparations. Skinned cardiomyocytes from Stretched hearts showed decreased PT – abrogated by protein phosphatase incubation – those from Non-stretched hearts showed decreased PT after protein kinase (PKG) incubation. Stretched samples showed increased cGMP levels and phosphorylation of VASP. Titin phosphorylation was increased in Stretched samples – attenuated by PKG inhibition (PKG<sub>i</sub>). PT decay after stretch was blunted by PKG<sub>i</sub> or by joint NP antagonism, NO synthase inhibition and NO scavenging. Moreover, it was remarkably attenuated in hypertrophic rat hearts which showed reduced titin phosphorylation and no increase with stretch. Healthy volunteers and cardiac surgery patients showed E/E' and EDP decrease after sustained stretch maneuvers, respectively.

**Conclusion:** We describe a novel physiological mechanism whereby myocardial compliance is increased in response to

stretch/volume overload, by titin phosphorylation through cGMP-PKG signaling. The mechanism was translated to human physiology and may be abolished in the hypertrophic heart (potential role in the pathophysiology of heart failure with preserved ejection fraction).

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## PS172

### **Cannabis sativa tetrahydrocannabinol (THC) impact on placental endocrine function**



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(L. Midão).

**Aim:** The main goal of this work is to understand the impact of THC on placenta endocrine function.

**Introduction:** Cannabis sativa-based medicines have been used to help ease pain, nausea and loss of appetite in cancer and HIV patients. Endocannabinoid system plays an important role in the regulation of female fertility and pregnancy. This system is implicated in proliferation, differentiation and apoptosis of placental stem cells, the trophoblasts (1). These mediate critical steps such as hormone production, fetal immune protection and increase in maternal vascular blood flow. Previous studies have shown that cannabis consumption during pregnancy is associated with intrauterine growth restriction, preterm labor and low birth weight. Moreover, tetrahydrocannabinol (THC), the main psychoactive compound of cannabis, is able to cross the placental barrier. However its effect on trophoblasts turnover and hormone production are unknown.

**Methods:** Term placental explants were treated with THC [1–40 μM] for 24 h to 72 h. The relative mRNA levels of 3β-HSD, aromatase, leptin and PP13 were determined by qRT-PCR. The protein expression levels of 3β-HSD, aromatase and leptin were assessed by Western Blot. Progesterone, estradiol and β-human chorionic gonadotropin (β-hCG) levels were measured by ELFA.

**Results:** After 24 h, PP13 mRNA levels were significantly increased at 40 μM of THC, while for leptin this effect was observed at 10 μM. Moreover, after 72 h aromatase mRNA levels were increased, while there was no effect on 3β-HSD. No differences were observed regarding progesterone whilst, an increase in estradiol and β-hCG with 40 μM at 72 h was detected.

**Conclusion:** These findings suggest that THC may impair trophoblast turnover and endocrine function which may affect pregnancy outcome. Moreover these results may contribute to disclose the cellular effects of cannabis-derived drugs.

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## PS219

### Reactivity of the rat distal colon to autoantibodies targeting angiotensin type I receptors

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(R. Magalhães).

**Aim:** To describe the reactivity of the rat distal colon to AT1R-Abs and to compare it to that of Ang II.

**Introduction:** Agonistic IgG (IgG1 and IgG3 subclasses) autoantibodies against the angiotensin II type 1 receptor (AT1R-Abs) have been associated with hypertension, preeclampsia, placental ischemia, renal-allograft rejection and systemic sclerosis. It is thought that AT1R-Abs mimic the action of angiotensin II (Ang II) and contribute to the physiopathology of several diseases and the associated complications.

**Methods:** Male Wistar rats (9–12 weeks of age) were killed by decapitation and strips of the distal colon were mounted in organ baths along their longitudinal axis. Tissues were stretch to 1 g of resting force and isometric responses to AT1R-Abs (25, 50 and 100 mg/dl) obtained from sera of systemic sclerosis and renal-allograft rejection patients and to Ang II (10pM–1 μM) were recorded on a polygraph. The response of Ang II were expressed as % of the response to 125 mM potassium chloride (KCl).

**Results:** AT1R-Abs caused a long-lasting response. Very often, AT1R-Abs induced an increase in the frequency and amplitude of distal colon spontaneous contractions. Occasionally, AT1R-Abs caused a slight decrease in the resting tone and, more rarely, they caused colonic contraction. The effects of the AT1R-Abs seem to be attenuated by candesartan. The pattern of the response to Ang II was different; Ang II caused a fast developing contraction of the colon with an Emax of  $64.37 \pm 12.68$  (%KCl) and EC50 of  $1.22 \pm 0.20$  nM.

**Conclusion:** AT1R-Abs change the normal rhythm of spontaneous contractions of the rat distal colon but more studies are necessary to evaluate whether this reactivity is mediated by AT1 receptors. Moreover, Ang II cause a marked AT1 receptor-mediated contraction of the rat distal colon.

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Public Health & Medical Informatics Paralell Oral Session  
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## PS224

### Intestinal colonization by antibiotic-resistant Gram negatives in children



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(C.S. Cruz).

**Aim:** This study aims to further the knowledge of antibiotic-resistance in the commensal intestinal flora of children by studying the intestinal colonization by antibiotic-resistant Gram negative bacteria in portuguese children.

**Introduction:** Although it is known resistance to antibiotics is a growing problem worldwide, this scenario which constitutes a risk factor for infectious disease is an under-characterized reality in Portugal.

**Methods:** Faecal samples of 29 healthy children (4 months to 12 years-old) were collected from randomly selected localities of Portugal: Viana do Castelo ( $n=8$ ), Porto ( $n=6$ ), Braga ( $n=14$ ), Leiria ( $n=1$ ), from September 2016 to March 2017. Risk factors were assessed by questionnaire, namely antibiotic usage history and direct contact with dependent elders. Isolates were selected by spreading saline suspension (100 μL) on MacConkey agar and MacConkey agar with ampicillin (100 μg/mL), cefotaxime (2 μg/mL), and meropenem (1 μg/mL). Susceptibility profiles to β-lactam and non-β-lactam antibiotics were assessed by disk-diffusion methods according to the EUCAST. Presumptive identification of the isolates was performed with CHROMagar–Orientation culture media.

**Results:** In a total of 29 isolates (lactose fermenters ( $n=22$ ) and lactose non-fermenters ( $n=8$ )), 28 showed resistance to amoxicillin and 13 to amoxicillin with clavulanic acid. Of the 29 children analysed, 17 showed resistance to at least one of the antibiotics studied. Four children were colonized with bacteria resistant to cephalosporins ( $n=8$ ), two of which have daily contact with elders.

**Conclusion:** The results indicate that young children might be an important reservoir of commensals with clinically relevant resistance mechanisms. The clarification of this reality in Portugal could prove essential in the fight against silent dissemination of these threats and persistent infections.

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## PS187

### Is the oral mycobiome of young adults influenced by the delivery mode?



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(L. Costa).

**Aim:** To investigate whether the mode of delivery influences the oral yeast colonization in young adults.