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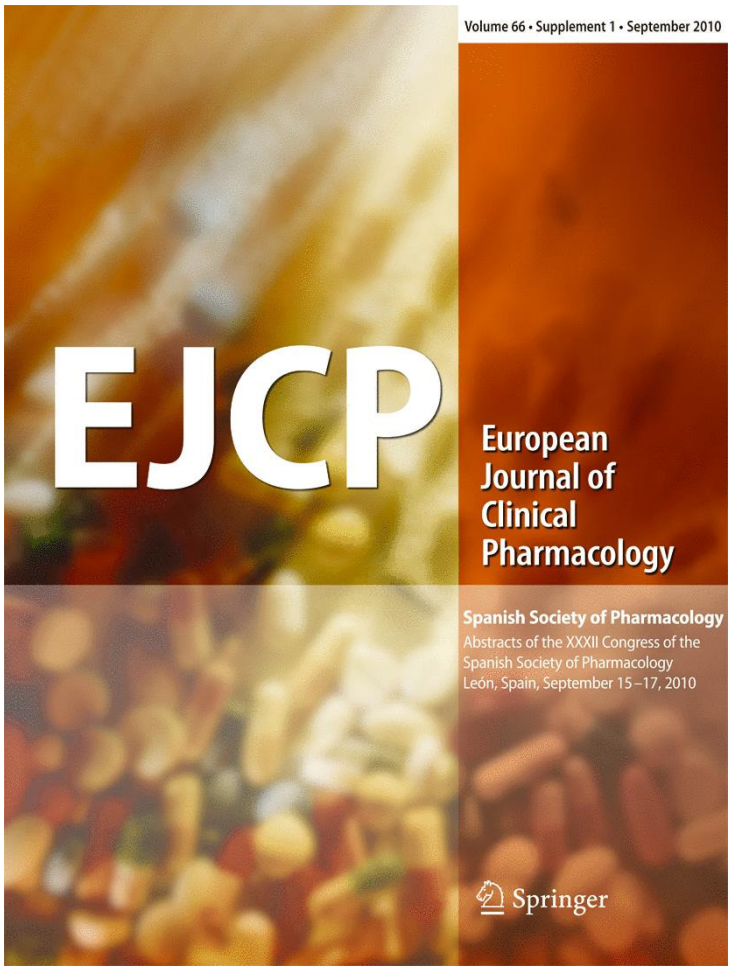

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O-6	**ROLE OF Ca^{2+}/CALCINEURIN/NFAT PATHWAY IN VASCULAR CONTRACTILITY**
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Introduction: Inflammation and hyperplasia play a key role in the developing of cardiovascular disorders. Ca^{2+}/Calcineurin/NFAT signalling pathway regulate the expression of inflammatory genes like COX-2, IL-2, TNF-α, INF-γ involved in the regulation of inflammation and hyperplasia of the myocardium and vascular smooth muscle cells. *Rcan1* is an endogenous inhibitor of Calcineurin, which expression is positively regulated by NFAT, thus *Rcan1* functions as a negative feedback regulator of Calcineurin/NFAT signalling. Angiotensin II (Ang II) participates in the control of vasomotor tone, cell growth and extracellular matrix deposition both in physiological and pathological conditions. It has been described that Calcineurin/NFAT signalling pathway is induced by Ang II.

Aim: To analyse the role of Ca^{2+}/Calcineurin/NFAT signalling pathway in vasoconstrictor response to phenylephrine. **Methods** *Rcan1* Knockout and wild type mice were used. Aortic vascular contraction was analysed by wire myography.

Results: Contractions induced by phenylephrine (1 nM-100 μM) was greater in aorta from *Rcan1* Knockout than from WT mice. The nitric oxide synthase inhibitor L-NAME (100 μM) increased the contraction to phenylephrine in aorta from WT but not in Rcan1 Knockout mice indicated a deficient NO modulation in this animals. The superoxide anion scavenger, tiron (1 mM) reduced vascular contraction to phenylephrine in aorta from both strain. Selective COX-2 inhibitor, etoricoxib (10 μM) reduced phenylephrine -induced contraction only in aorta from *Rcan1* Knockout mice, indicated the participation of COX-2-derived prostanoids in the increased vascular contraction to phenylephrine in this animals. Ang II (1 μM) potentiated contractile response to phenylephrine only in aorta from WT mice, and this potentiation was depended of Calcineurin/NFAT pathway and COX-2 since it was diminished by incubation of the arteries with cyclosporin A (CSA) (200 ngr/ml) or etoricoxib.

Conclusions: The activation of Calcineurin/NFAT signalling may be involved in the alteration of vascular function associated to cardiovascular pathologies

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O-7	**VASCULAR RESPONSES TO U-46619 OF SENESCENCE-ACCELERATED FEMALE MOUSE DURING AGEING**
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Aims: The present study is focused on the effects of ageing on vascular reactivity of aortas from female mice. We used the senescence-accelerated mouse (SAM) as one of the standard model of animal ageing. SAM strain is the result of selective inbreeding of mice showing a phenotype of severe exhaustion (SAM-prone) and a normal phenotype (SAM-resistant). We evaluated contractile responses to U-46619, a stable analog of thromboxane A2 at different ages.

Methods: Two different strains of mice, sensescent-resistant SAMR1 (n= 18) and senescent-accelerated SAMP8 (n= 18) were used at different ages: 3 months old (mo), 6 mo and 10 mo. Mice were sacrificed and thoracic aortas were collected. Vascular rings were mounted for isometric recording of tension and concentration-response curves for U46619 (10-9 - 10-7M) were performed in presence and absence of the nitric oxide (eNOS) inhibitor NG-nitro-L-arginine methyl ester (L-NAME, 10-4M). A segment of aorta from each mouse was immediately frozen for protein expression analysis.

Results: Contractile response to U-46619 (10-9 - 10-7M) of aortic segments from SAMR1 and SAMP8 were similar at 3 mo. At 6 mo, segments from SAMP8 evoked higher contractions than SAMR1 ($p<0.05$), differences that reached it maximal at 10 mo ($p<0.05$). The effect would point to an increased expression of thromboxane A2 receptor in SAMP8 arterial walls, which was confirmed by Western blot. SAMR1 aortic segments incubated with L-NAME showed an increase in the response evoked by 3x10-9M U-46119 at 3 mo ($p<0.05$), decreasing slightly at 6 mo and disappearing at 10 mo. In SAMP8 the differences at 3 mo ($p<0.05$) disappeared at 6 mo. These results suggest that senescence and not the strain increased contractile response in aorta from female mice. NO production in both strains is similar at 3 mo but decrease with ageing more in SAMP8 than in SAMR1.

Conclusions: Vascular response of senescent-accelerated female mice at 6 mo is similar to that obtained in standard mice aged at 12 mo. Results point to SAMP8 as a new experimental model for vascular research in female ageing allowing experimental work to be performed in no more than six months.

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