A005
AUGMENTATION DE LA RIGIDITÉ ARTÉRIELLE ASSOCIÉE AUX ANTICORPS ANTIPHOSPHOLIPIDES

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Le syndrome des anticorps antiphospholipides est une thrombophilie acquise, auto-immune. Les manifestations cliniques caractéristiques sont des thromboses veineuses ou artérielles et des manifestations obstétricales (fausses-couches précoces répétées ou liées à une pathologie vasculaire plaquetaire). Sur le plan biologique le syndrome est défini par la présence d’un anticorps antiphospholipide/antiprothrombine (anticoagulant circulant, anticorps anticalcidolipide ou anti-beta2-glycoprotéine I). Ce syndrome est associé dans 50% des cas à un lupus systémique. Une augmentation de la rigidité artérielle a pu être démontrée au cours du lupus systémique mais un rôle aggravant éventuel des anticorps antiphospholipides n’a pas été mis en évidence. Le but de notre étude était de montrer une augmentation de la rigidité artérielle chez les patients présentant des anticorps antiphospholipides. Nous avons inclus 33 patients et 109 témoins appariés pour l’âge et le sexe. La rigidité artérielle a été mesurée par la vitesse de l’onde de pouls carotido-fémorale par le dispositif Pulse-PenTM. Les valeurs moyennes de VOP étaient significativement augmentées chez les patients avec antiphospholipides par rapport aux témoins : 8,22 ± 0,50 vs 7,25 ± 0,20 respectivement.

Ces résultats montrent que la rigidité artérielle est augmentée de façon significative chez les patients qui ont des anticorps antiphospholipides. Des études complémentaires permettront d’identifier les facteurs qui contribuent à l’augmentation de la rigidité artérielle mais également la signification pronostique d’une rigidité augmentée chez les patients qui ont des anticorps antiphospholipides.

A006
INTERMITTENT HYPOXIA INDUCES INFLAMMATORY VASCULAR AND MYOCARDIAL REMODELING: ROLE OF THE ENDOTHELIN SYSTEM

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Introduction — Obstructive sleep apnea (OSA) syndrome, characterized by intermittent hypoxia (IH), is associated with an increased cardiovascular morbidity that can be partially corrected by continuous positive airway pressure (CPAP) therapy. We have shown previously that IH induces increased aortic intima-media thickness (IMT) and NFκB activation. OSA patients also exhibit increased IMT that correlates with inflammatory markers and nocturnal oxygen desaturation. Endothelin release is promoted by hypoxia and ET-1 is known to exert potent pro-inflammatory and pro-mitogenic effects on the cardiovascular system.

Objective — The aim of the present study was to investigate the involvement of the endothelin system in IH-induced inflammatory vascular and myocardial remodeling.

Methods and Results — 8 week-old C57Bl/6 mice (n=8 to 10 per group) were exposed 14 days to IH or normoxia (N). The role of the ET system was evaluated by treating the mice with the dual ET receptor antagonist, bosentan (b: 100mg/kg/day in food) throughout the period of exposure. Myocardial big ET-1 levels were significantly increased by IH (p<0.01). Bosentan treatment significantly inhibited the IH-induced NFκB activity in both aorta (p<0.05) and myocardium (p<0.01). This was associated with prevention of IH-induced increase of aortic IMT and systemic inflammation.

Conclusions — These results demonstrate that the endothelin system is involved in IH-induced inflammatory vascular remodeling. Therefore, endothelin receptor blockade could represent a new therapeutic approach, in addition to CPAP therapy, for OSA patients prone to develop cardiovascular alterations. Further studies will investigate the link between transcriptional activity, ET-1 system, and inflammatory response in our conditions of hypoxia.

A007
THE TRANSACTIVATING FUNCTION-1 OF ESTROGEN RECEPTOR ALPHA IS DISPENSABLE FOR THE VASCULOPROTECTIVE ACTIONS OF ESTRADIOL

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Full-length 66-kDa estrogen receptors (ERs) stimulates target gene transcription through two activation functions (AFs), AF-1 in the N-terminal domain and AF-2 in the ligand binding domain. Another physiologically expressed 46-kDa ERα isoform lacks the N-terminal A/B domains and is consequently devoid of AF-1. Previous studies in cultured endothelial cells showed that the N-terminal A/B domain might not be required for estradiol (E2)-elicited NO production. To evaluate the involvement of ERαAF-1 in the vasculoprotective actions of E2, we generated a targeted deletion of the ERαAF-1 isoform in LDLR-/- mice. In these ERαAF-1 zero mice, both basal endothelial NO production and reendothelialization process were increased by E2 administration to a similar extent than in control mice. Furthermore, exogenous E2 similarly decreased fatty streak deposits at the aortic root from both ovariectomized 18-week-old ERαAF-1+/+LDLR-/- (low-density lipoprotein receptor) and ERαAF-1 zero LDLR-/- mice fed with a hypercholesterolemic diet. In addition, quantification of lesion size on en face preparations of the ia tree of 8-month-old ovariectomized or intact female mice revealed that ERαAF-1 is dispensable for the atheroprotective action of endogenous estrogens. We conclude that ERαAF-1 is not required for three major vasculoprotective actions of E2, whereas it might not be required for estradiol (E2)-elicited NO production. To evaluate the involvement of ERαAF-1 in the vasculoprotective actions of E2, we generated a targeted deletion of the ERαAF-1 isoform in LDLR-/- mice. In these ERαAF-1 zero mice, both basal endothelial NO production and reendothelialization process were increased by E2 administration to a similar extent than in control mice. Furthermore, exogenous E2 similarly decreased fatty streak deposits at the aortic root from both ovariectomized 18-week-old ERαAF-1+/+LDLR-/- (low-density lipoprotein receptor) and ERαAF-1 zero LDLR-/- mice fed with a hypercholesterolemic diet. In addition, quantification of lesion size on en face preparations of the ia tree of 8-month-old ovariectomized or intact female mice revealed that ERαAF-1 is dispensable for the atheroprotective action of endogenous estrogens. We conclude that ERαAF-1 is not required for three major vasculoprotective actions of E2, whereas it might not be required for estradiol (E2)-elicited NO production. To evaluate the involvement of ERαAF-1 in the vasculoprotective actions of E2, we generated a targeted deletion of the ERαAF-1 isoform in LDLR-/- mice. In these ERαAF-1 zero mice, both basal endothelial NO production and reendothelialization process were increased by E2 administration to a similar extent than in control mice. Furthermore, exogenous E2 similarly decreased fatty streak deposits at the aortic root from both ovariectomized 18-week-old ERαAF-1+/+LDLR-/- (low-density lipoprotein receptor) and ERαAF-1 zero LDLR-/- mice fed with a hypercholesterolemic diet. In addition, quantification of lesion size on en face preparations of the ia tree of 8-month-old ovariectomized or intact female mice revealed that ERαAF-1 is dispensable for the atheroprotective action of endogenous estrogens. We conclude that ERαAF-1 is not required for three major vasculoprotective actions of E2, whereas it might not be required for estradiol (E2)-elicited NO production.