tridimensionnelle de type Matrigel®. Cette propriété dépend de la
dose de MPE, les faibles concentrations ayant un effet activateur
et les fortes concentrations un effet inhibiteur. Le blocage de ces
effets par des inhibiteurs de plasmine ou d’uPA, souligne le rôle
cclé de la plasmine générée par les MPE dans l’interface protéolyse-
angiogénèse.

Cette activité est détectée ex vivo sur les microparticules
circulantes humaines de patients atteints de pathologies associées
à une élévation des microparticules endothéliales (Drépanocytose,
Purpura Thrombotique, Thrombocytopénie).

En conclusion, nous avons démontré que les MPE agissent comme
des vecteurs participant au contrôle de la génération de plasmine.
Ce mécanisme constitue une nouvelle voie relevante chez l’homme
dans la régulation des activités protéolytiques de l’endothélium
avec des implications possibles dans l’inflammation, l’angiogénèse
et l’athérosclérose.

**Vendredi 3 avril 2009, de 11h00 à 12h30**

**F — HYPOXIE MYOCARDIQUE, REPERFUSION, ACCIDENT VASCULAIRE CEREBRAL**

**F001**

**PROMINENT ROLE FOR THE ENDOTHELIAL GAP JUNCTION PROTEIN CONNEXIN40 IN MYOCARDIAL ISCHEMIA-REPERFUSION INJURY IN MICE**

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Intercellular channels formed by connexins (Cx) have been shown
to play a critical role in cardiovascular disease. Indeed, connexin-
deficient mice showed modifications in cell signalling, that
appeared crucial in atherosclerosis and restenosis. In the heart,
Cx40 is expressed in atrial myocytes, the conduction system and
in endothelial cells. Here, we study the implication of endothelial
cx40 during ischemia and reperfusion in mice. For this purpose,
we used the Cre-loxP system to create a mouse line in which Cx40
is deleted from the endothelium only. Immunostainings on Tie2-
Cre+/- mice confirmed the absence of Cx40 in the
endothelium, whereas the protein was normally expressed in the
atria and cardiac conduction system. Moreover, mean arterial
pressure and heart rates were not different between controls (Tie2-Cre-Cx40f/fApoe-/- and Tie2-Cre+/-Apoe-/-) and Tie2-Cre-Cx40+/-Apoe-/- animals. Sixteen-week-old mice with or
without endothelial-specific deletion of Cx40 were subjected to in
vivo left coronary artery occlusion for 30 minutes and sacrificed
24-hours after reperfusion for analysis of infarct size. Myocardial
surfaces areas at risk and infarcted areas were measured from
computed images using NIH Image software. Areas at risk, normalized
to total left ventricle surfaces areas, were similar between the
computed images using NIH Image software. Areas at risk, normalized
to total left ventricle surfaces areas, were similar between the
controls and Tie2-Cre+/- mice as compared to controls
(20.67±4.74 % and 8.47±1.45 %, respectively, P<0.01). We conclude
that endothelial Cx40 is implicated in resistance of the heart to
ischemia-reperfusion injury. These findings underline once more
the importance of connexin-mediated intercellular communication
in cardiovascular inflammation, and may point towards novel
therapeutic strategies to limit the cardiac injury after coronary
interventions.

**F002**

**PREVENTION OF SKIN FLAP NECROSIS BY ESTRADIOL INVOLVES REPERFUSION OF A PROTECTED VASCULAR NETWORK**

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Whereas 17β-estradiol (E2) is protective in experimental models
of myocardial and brain ischemia, its effect on skin ischemia
remains unknown. Here, we assessed the protective effect of
E2 in a mouse model of skin ischemia, mimicking the surgery
of skin flaps. Whereas necrosis appeared in the half portion of the
skin flap within one week after surgery in ovariectomized mice,
it was reduced up to 10-fold when mice were pre-treated with
E2, at least 3 days before the surgery. The beneficial effect of
E2 appeared to be due to an increase in skin survival, revealed
by measuring viability of ex vivo explants and enhancement of the anti-apoptotic Bcl-2 protein expression in vivo. This
protective effect on the skin contributes to the protection of the
vascular network and facilitates reperfusion which is found to
be accelerated in ovariectomized E2-treated mice, while hemorrhages were observed in untreated mice. E2 also increased
expression of FGF-2 isofoms in the skin and circulating VEGF
in the serum. Finally, this protective effect of E2 was abolished
in estrogen receptor deficient mice (ERα/-) but maintained in
chimeric mice reconstituted with ERα-deficient bone marrow,
indicating dispensable action of E2 in bone-marrow derived cells.
This protective effect of E2 was mimicked by treatment with
tamoxifen, a selective estrogen receptor modulator (SERM).

In conclusion, we demonstrated for the first time that E2 exerts a
major preventive effect of skin flap necrosis through a prevention
of ischemic-induced skin lesions, including those of the
vascular network, which contributes to accelerate the reperfusion of the
skin flap.

**F003**

**LA DELÉTION DE MICROSOMAL PROSTAGLANDIN E2 SYNTHASE-1 (MPGES-1) DANS LES LEUCOCYTES DE LA MOELLE OSSEUSE ENTRAÎNE UN REMODELAGE VENTRICULAIRE GAUCHE DÉFAVORABLE EN POST INFARCTUS DU MYOCARDE**

N. DEGOUSEE 1, F. KONECNY 1, D. ANGOULVANT 1, S. FAZEL 1, E. STEFANSKI 1, X.-H. WANG 1, T.-F. LINDSAY 1, J. BUTANY 1, P.-J. JAKOBSSEN 1, A. KEATING 1, R.-K. LI 1, B. RUBBIN 1

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