Shear stress-induced endothelial cell migration involves integrin signaling via the fibronectin receptor subunits $\alpha_5$ and $\beta_1$.

Submission Type: Original Contribution
Re: Resubmission of manuscript MS 1836 : by Urbich et al

Dear Dr. Thyberg,

Please find enclosed the above mentioned manuscript entitled "Shear stress-induced endothelial cell migration involves integrin signaling via the fibronectin receptor subunit α5β1" for resubmission in “ATVB”.

All points raised by the 4 reviewers are fully addressed in the revised version of the manuscript. In detail, we performed additional experiments to confirm that indeed α5β1 is of particular importance for shear stress-induced endothelial cell migration (see new figures 1C/D). Furthermore, the role of the integrin-dependent down stream signaling has been more closely investigated. We now demonstrate that overexpression of dominant negative Shc prevents shear stress-induced cell migration (see new figure 4A).

The specific comments of the reviewers are addressed in the enclosed detailed point-by-point reply and the specific changes made are indicated in the revised version of the manuscript. Therefore, we hope that the manuscript is now suitable for acceptance at ATVB.

Finally, we would like to thank the reviewers and the editor for the helpful comments to improve our manuscript.

Yours sincerely

Stefanie Dimmeler, PhD
Professor of Experimental Medicine
University of Frankfurt

Date: 31 August 2001
Figure 1: MS 1836, Urbich et al.

Phospho-Akt

- + + + +
- + - - -
- - - + -
- - - - +

10% serum
LNMA (1 mM)
Ly294002 (10 μM)
PD98059 (10 μM)

Phospho-ERK1/2

- + + + +
- + - - -
- - - + -
- - - - +

10% serum
LNMA (1 mM)
Ly294002 (10 μM)
PD98059 (10 μM)

NO-staining with DAF-2DA

Shear stress
12 h

mean density (grey scale)

control | LNMA 2h | + LNMA
Attachment

Figure 2: MS 1836, Urbich et al.
Attachment

Figure 3: MS 1836, Urbich et al.

Integrin $\alpha_5$ expression in Huvec

Integrin $\beta_1$ expression in Huvec
Attachment

Figure 4: MS 1836, Urbich et al.

- Migration of HUVEC -

<table>
<thead>
<tr>
<th>Control</th>
<th>Shear Stress</th>
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<tbody>
<tr>
<td>0 min</td>
<td></td>
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<tr>
<td>5 min</td>
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