



Fluid Shear Stress: a modulator of the vasculo-protective effects of polyphenols?

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Fluid Shear Stress:

a modulator of the vasculo-protective
effects of polyphenols?

Laurent-Emmanuel Monfoulet

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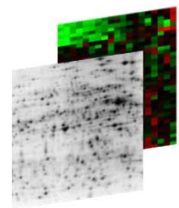
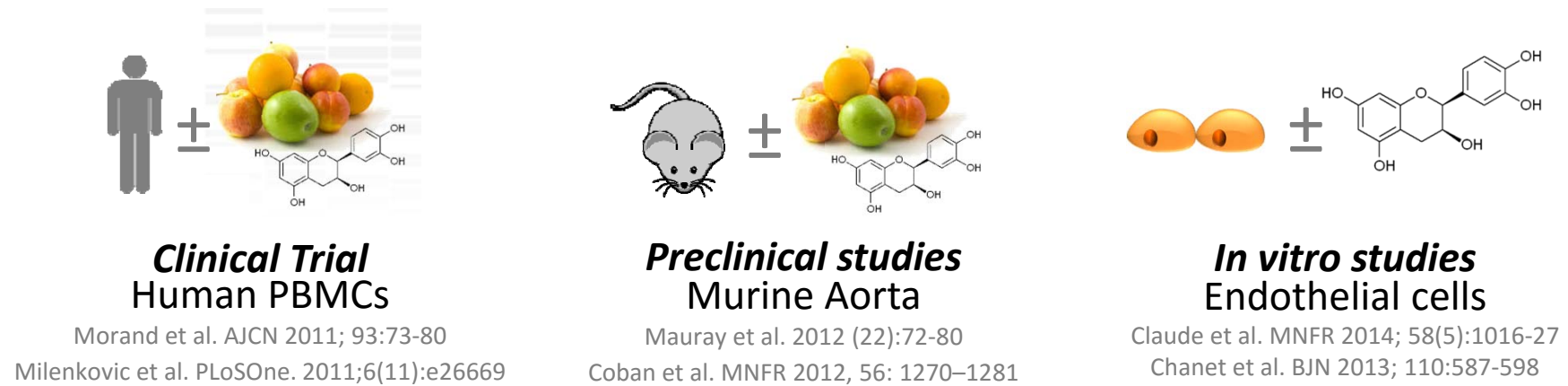
7th
ICPH

**International Conference
on Polyphenols and Health**



October, 27-30th 2015

Tours - France

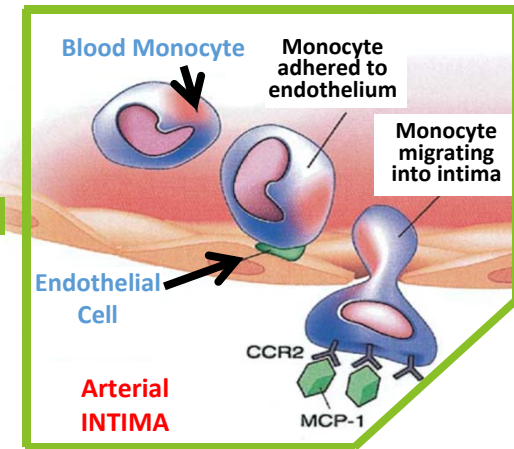


Nutrigenomic approaches:

- Transcriptomic
- Proteomic
- Epigenetic

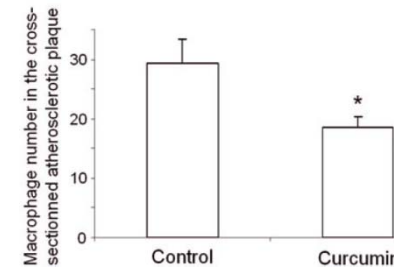
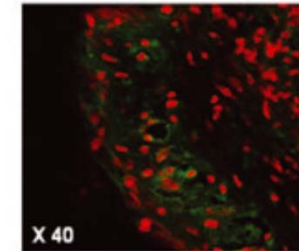
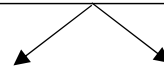
Hypothesis:

Polyphenols



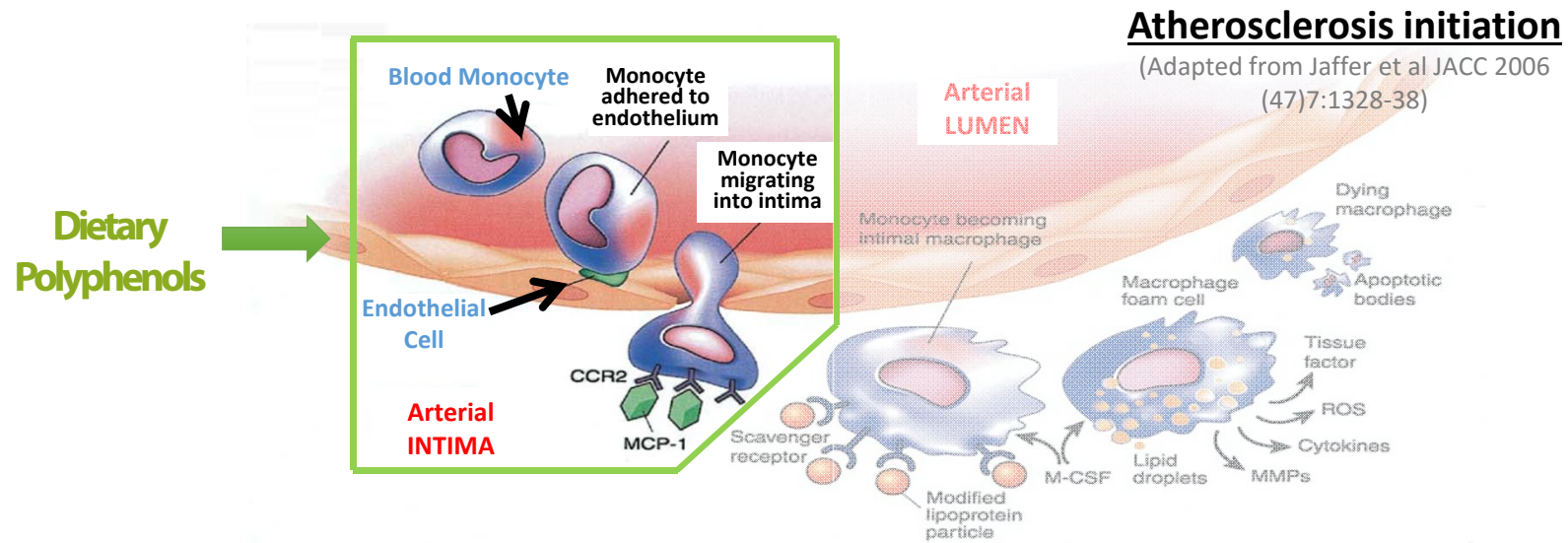
TransEndothelial Migration (TEM) as a common mode of action of polyphenols on vascular health

Coban et al. MNFR 2012,
56, 1270–1281



Curcumin intake reduces atherosclerotic lesion development and recruitment of immune cells

Underlying mechanisms of action in *in vitro* studies



Reproduce conditions as close as possible to the physiology

Polyphenols

- Circulating molecules
- Low plasma concentration (0.1 – 10 μ M)
- Time of exposure (= resident time in the plasma)

Milenkovic et al. FRBM 2013 (64):40-51

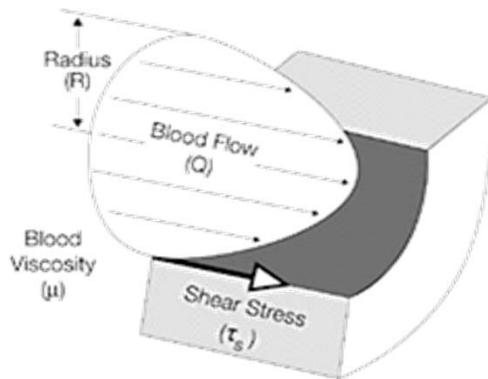
Endothelial cells :

- Hemodynamic conditions

Shear Stress: a vascular and physiological parameter

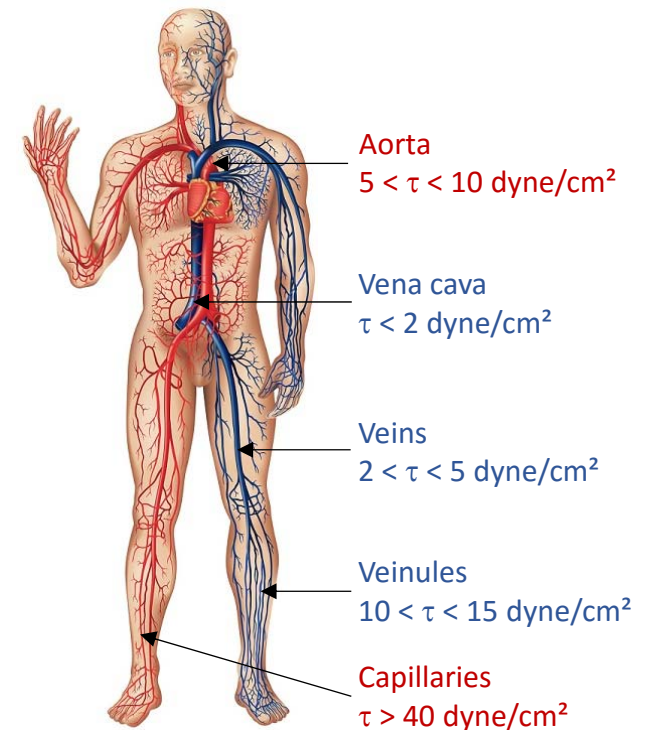
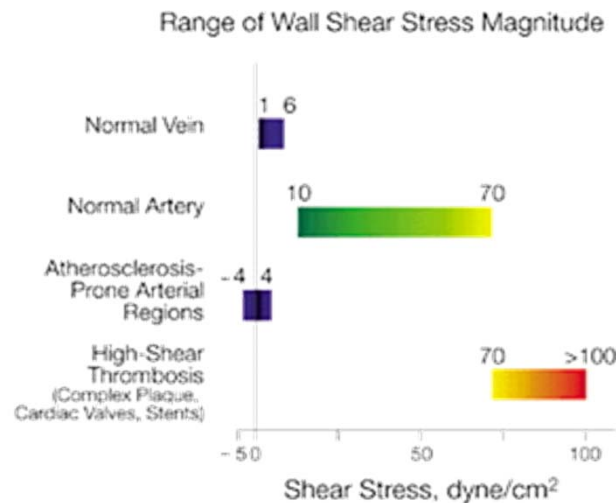
Shear Stress is:

- A force due to the blood flow
- Pulsatile (Heart beats)
- Continuous
- Laminar and unidirectional



Poiseuille's law

$$\tau = \frac{4Q\mu}{\pi R^3}$$



Malek et al. JAMA 1999. 282(21):2035-2042
Rocca et al. Cordiologie Conferences 2007. XII (8)

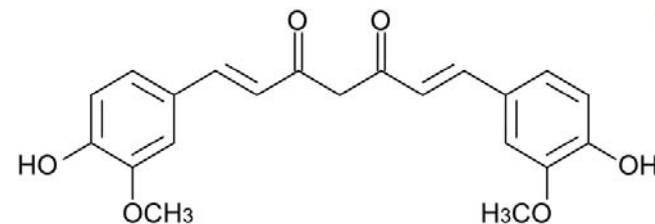
Aims

- To analyse the response of endothelial cells to physiological relevant concentrations of polyphenols under shear stress conditions
- To evaluate how shear stress modulates the response of endothelial cells to polyphenols regarding recruitment, adhesion and TEM of monocytes in comparison to static conditions

A proof of concept



Curcuma longa



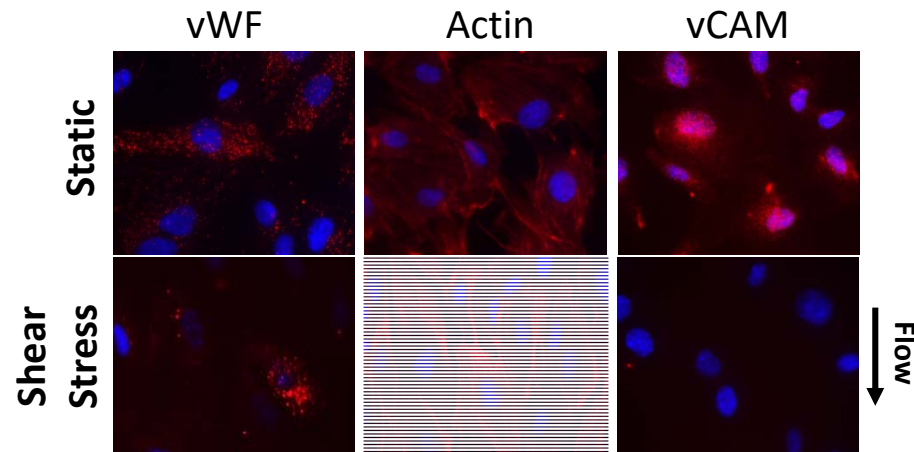
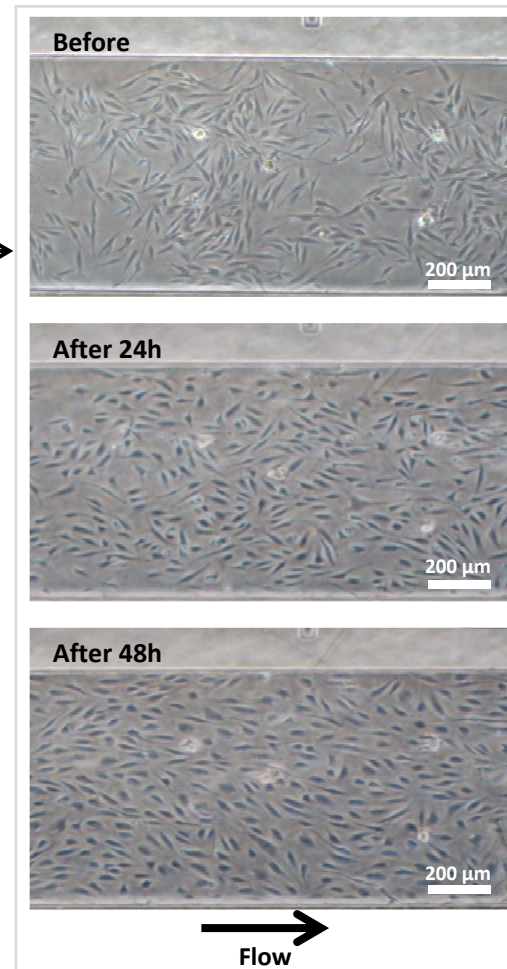
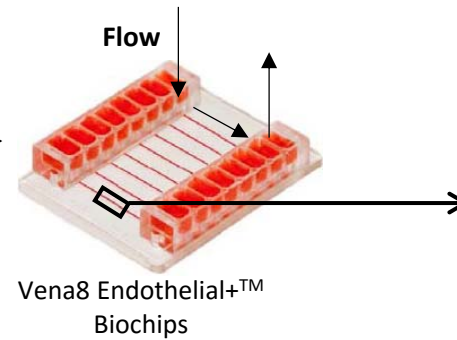
Curcumin

**Response of endothelial cells to physiological relevant concentrations
of CURCUMIN under shear stress conditions**

Imposed shear stress on cultured endothelial cells

Laminar Shear Stress characteristics:

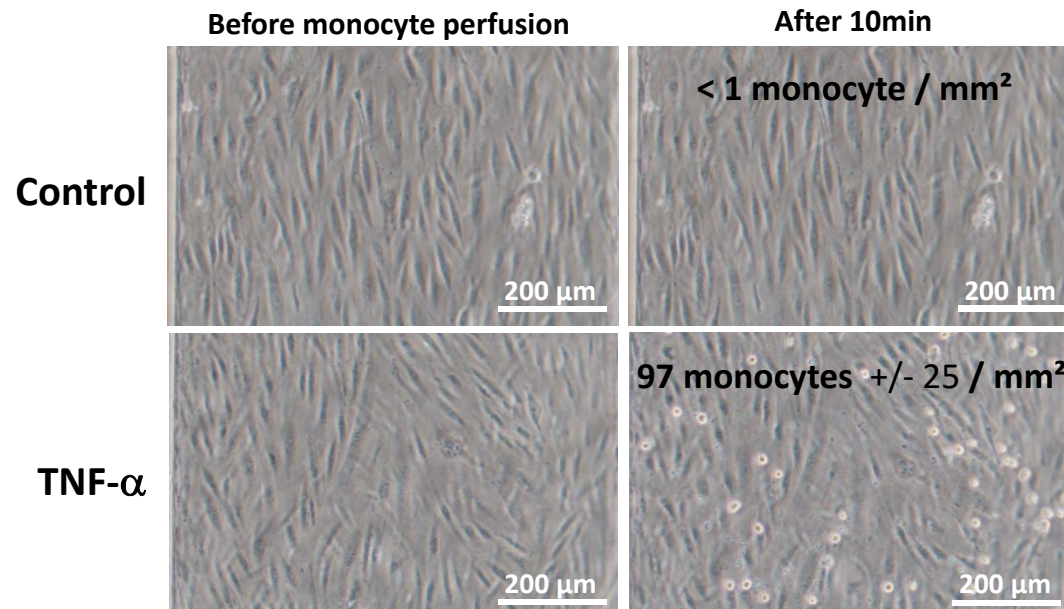
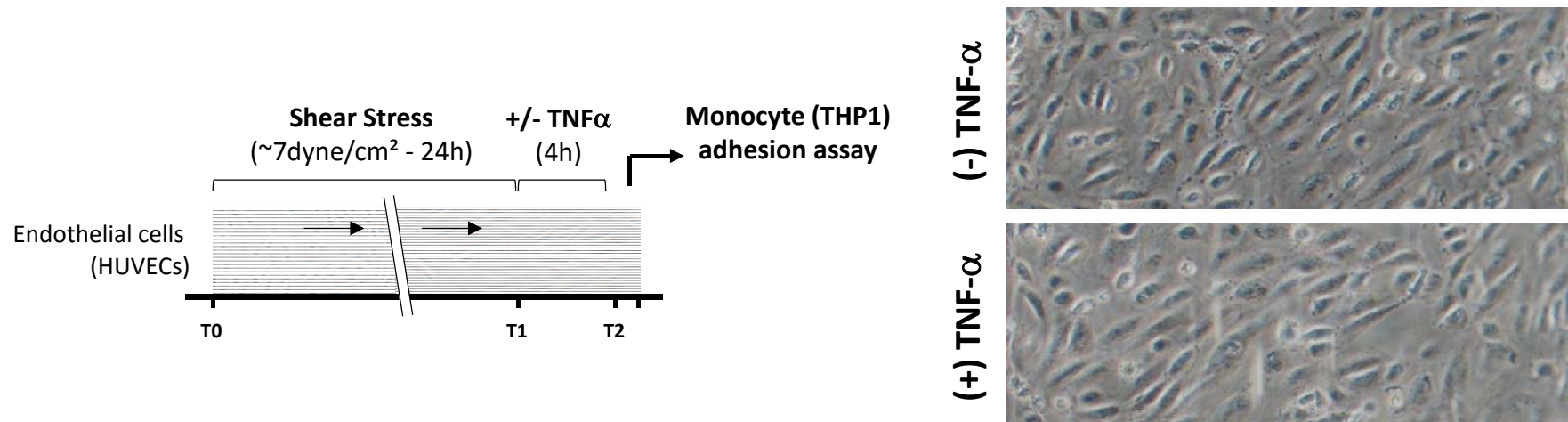
1 Hz pulsatile flow rate
Flow rate: 600 μ L/min
 τ : ~ 7 dyne/cm² (arterial)



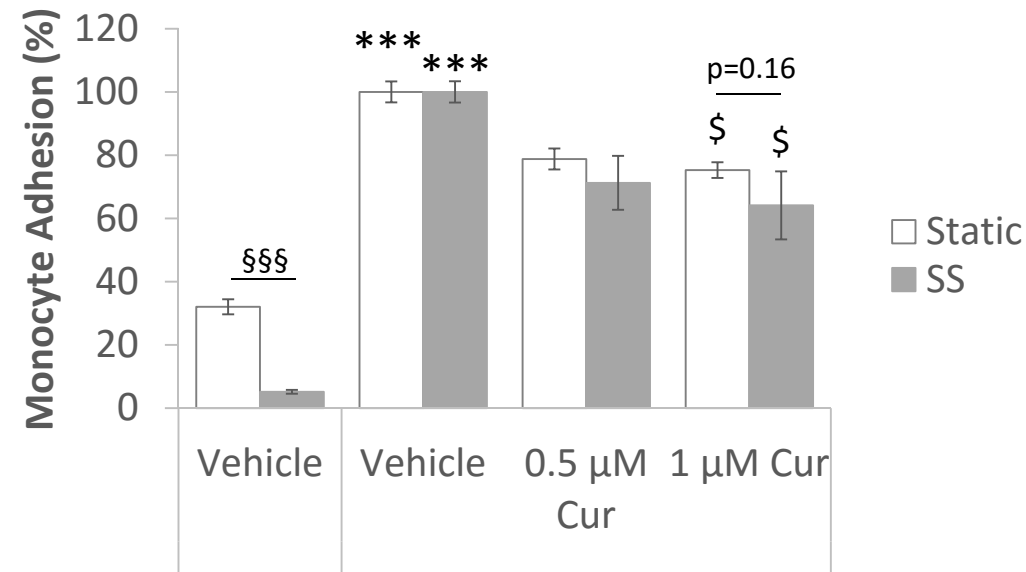
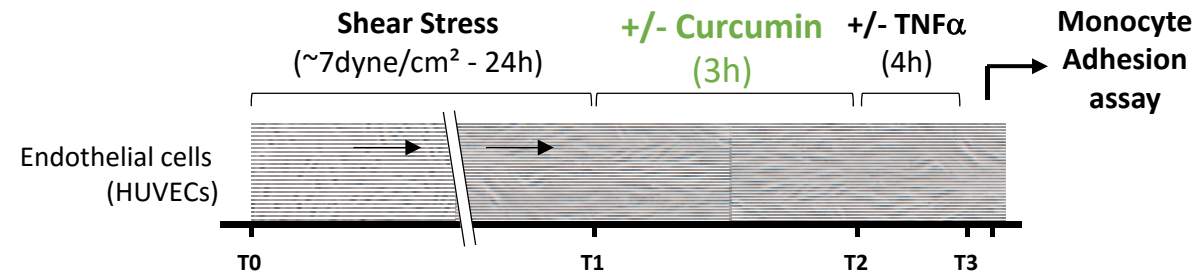
Under shear stress, endothelial cells:

- are firmly spread and aligned in the flow direction.
- have a physiological phenotype (anti-atherogenic).

Monocyte adhesion induced by inflammatory stress (TNF- α)



Impact of curcumin on monocyte adhesion

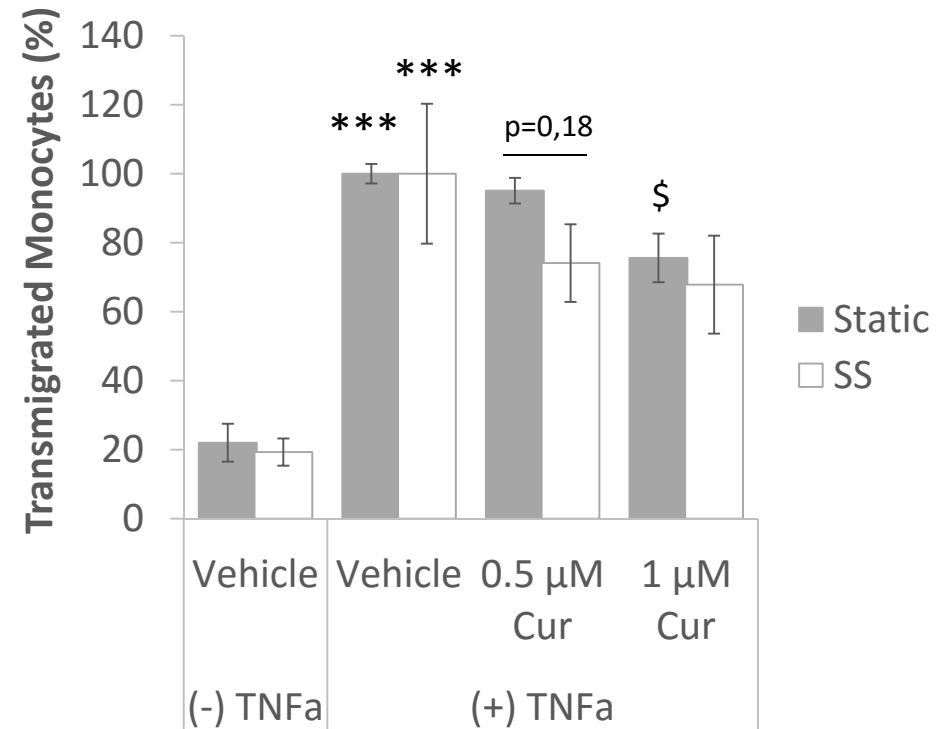
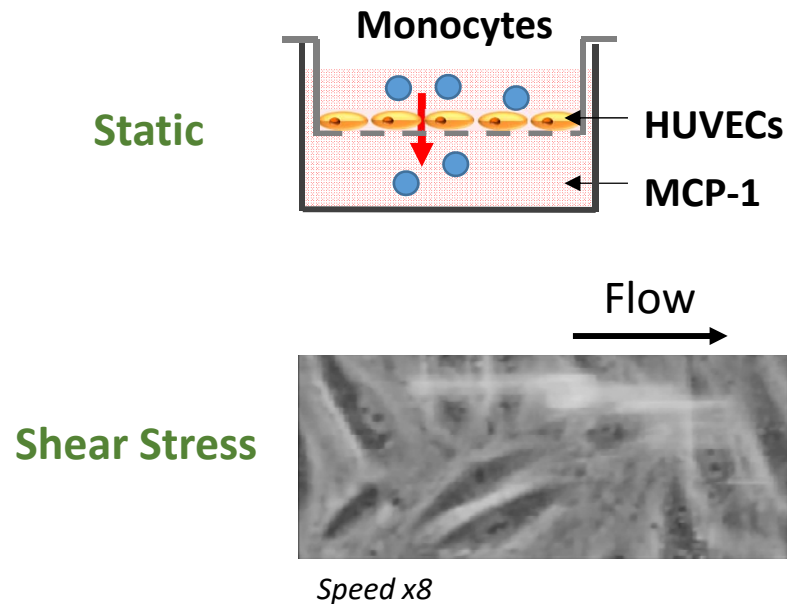


***p<0.001 compared to Vehicle (-) TNF- α
 \$ p<0.05 compared to Vehicle + TNF- α

The reduction of monocyte adhesion by curcumin is slightly enhanced in shear stress conditions

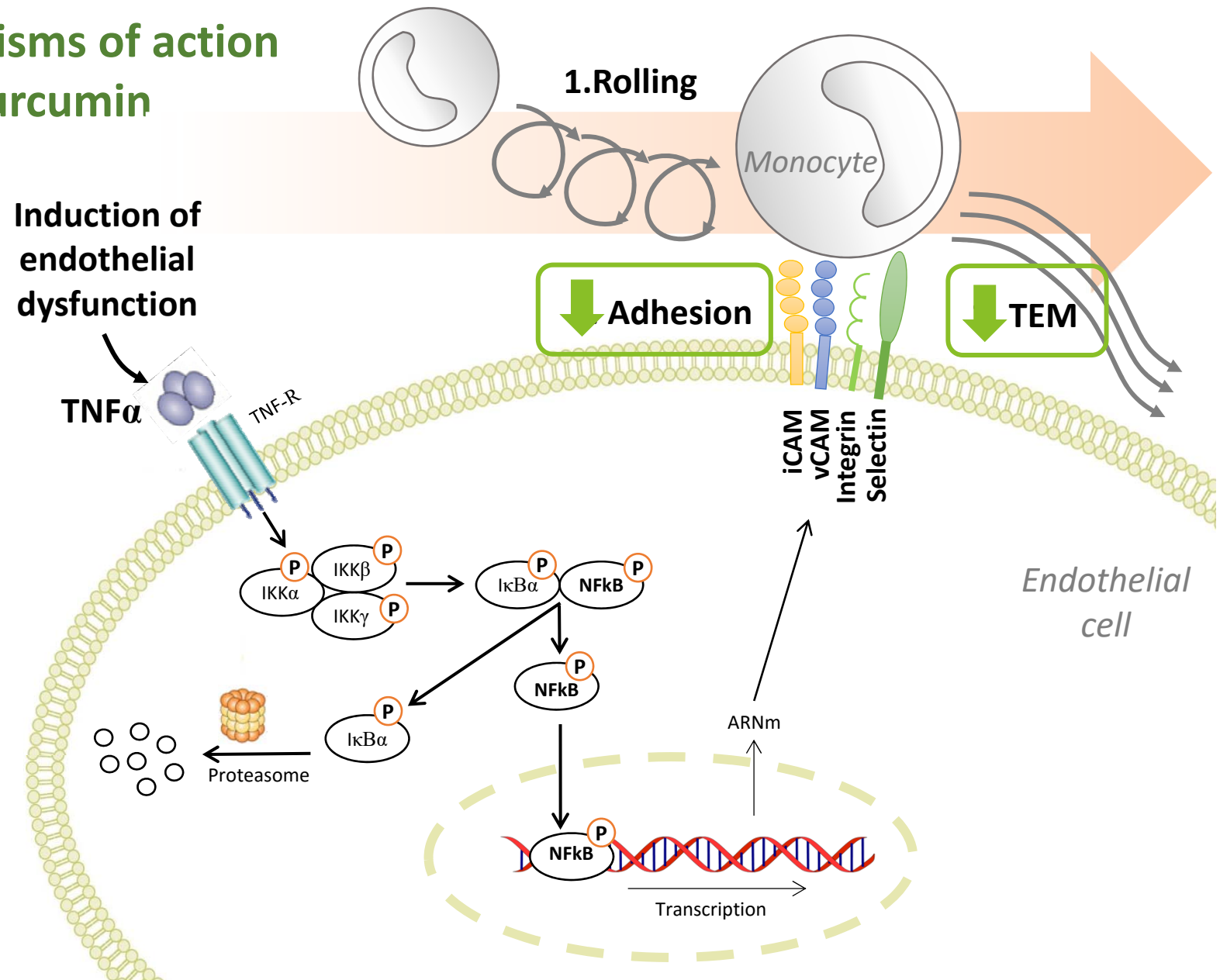
Impact of curcumin on monocyte TransEndothelial Migration

Preliminary results

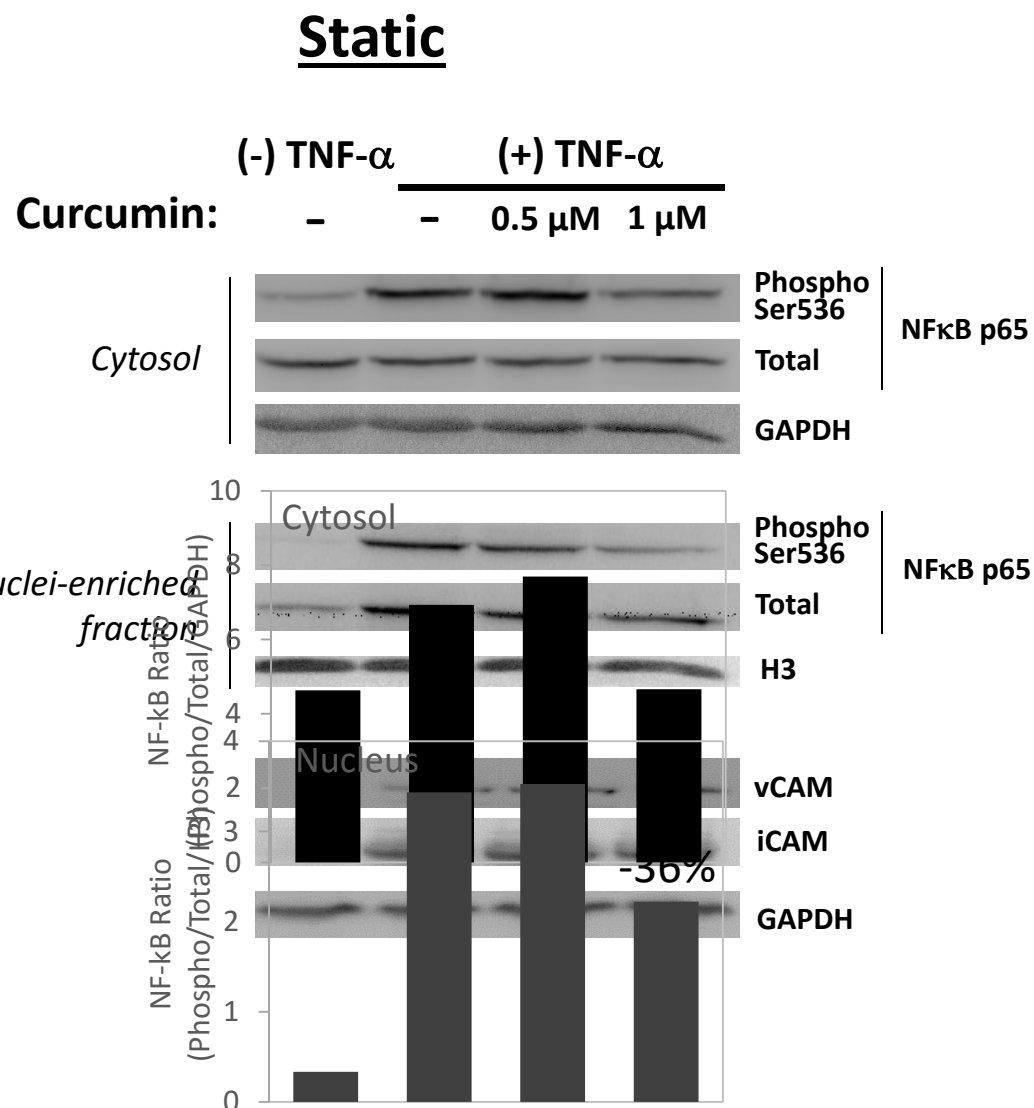
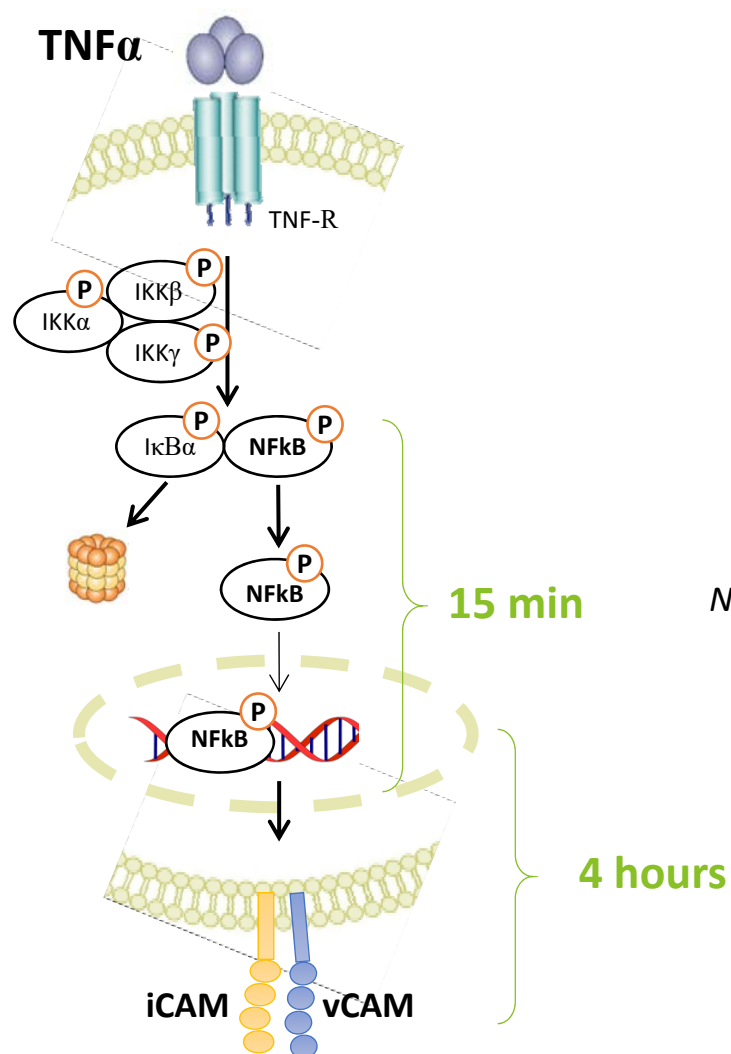


The reduction of TEM by curcumin is heightened in shear stress conditions

Mechanisms of action of the curcumin



Mechanisms of action of the curcumin



Conclusion

- We showed that a pre-exposition of endothelial cells to **curcumin significantly reduces the adhesion of monocytes to endothelial cells and their TEM.**
- The reduction of both adhesion and TEM by curcumin are **enhanced under physiological shear stress.**
- In static conditions, **curcumin modulates the TNF-R pathway** (NF- κ B phosphorylation and its nuclear translocation), but does not affect the expression of adhesion molecules.
- Other cellular process can be modulated by curcumin that could explain their inhibitory effect on monocyte infiltration (cytoskeleton & cell junction dynamic?)



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**Thomas
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**Dragan
Milenkovic**



**Christine
Morand**



**Cécile
Gladine**



**Claudine
Manach**



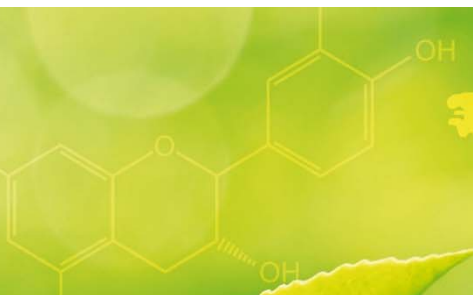
**Edmond
Rock**



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