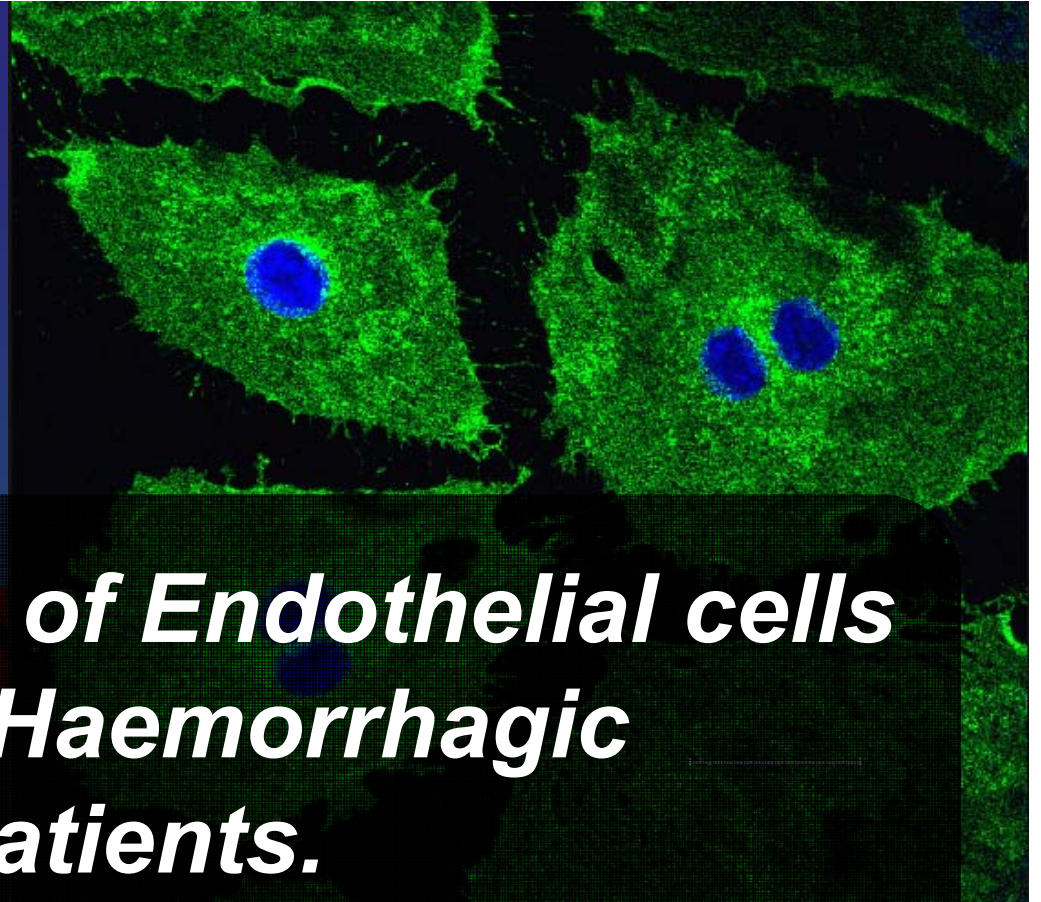
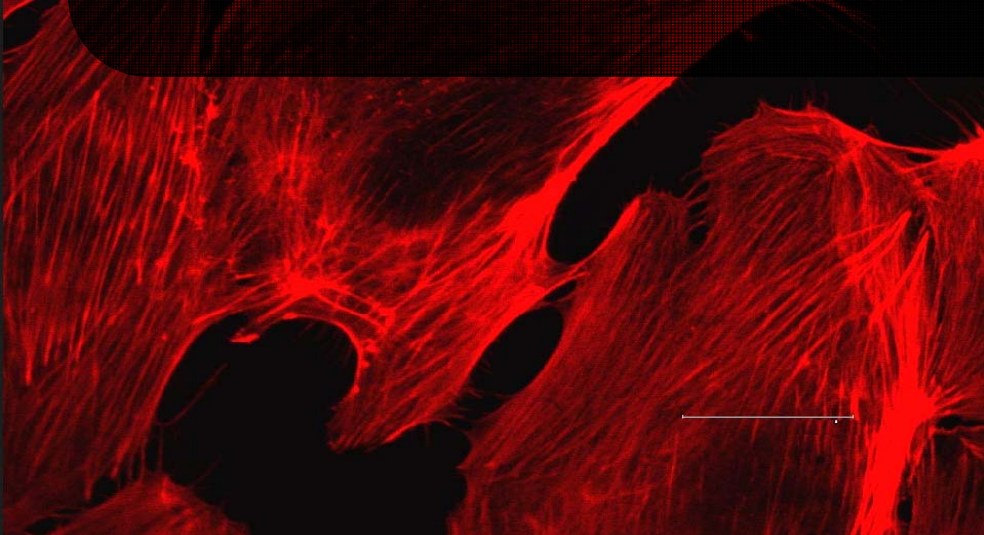


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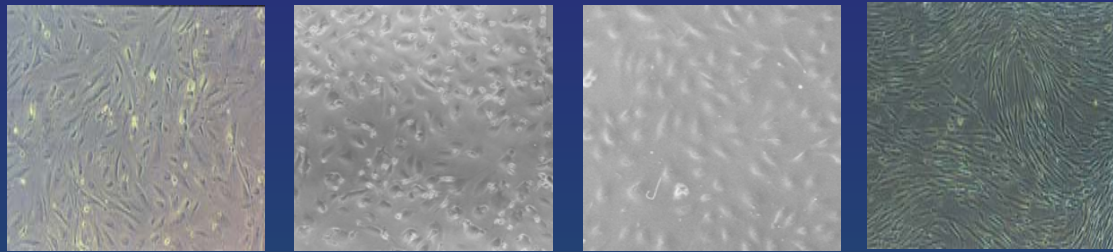
***Characterization of Endothelial cells
from Hereditary Haemorrhagic
Telangiectasia patients.***



Lab. Dr. Carmelo Bernabéu
Dr. Luisa M. Botella

Blood outgrowth endothelial cells characterization

Characterization



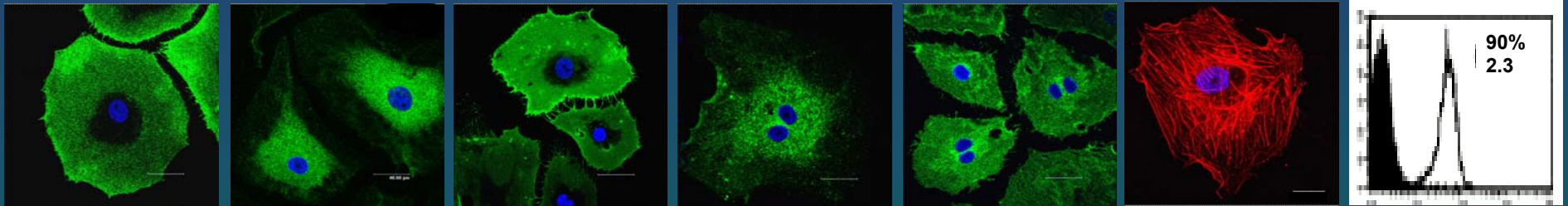
CONTROL

HHT1

HHT2 n

HHT2 m

- Controls
- HHT1
- HHT2 nonsense
- HHT2 missense



ENDOGLIN

ALK-1

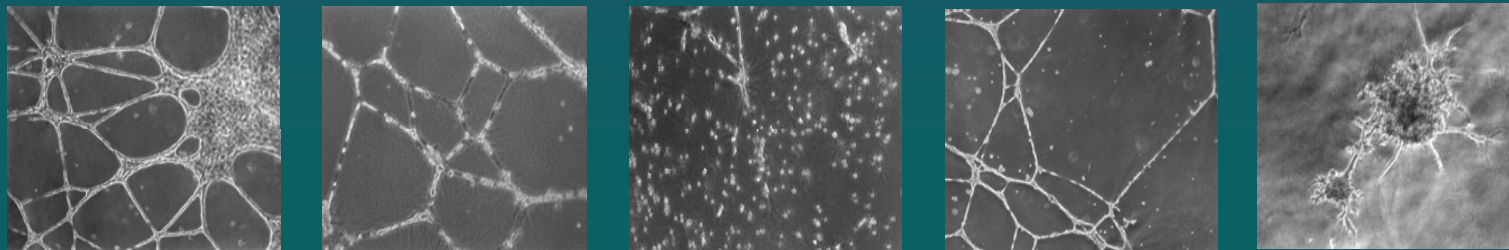
PECAM-1

vW-F

VE-Cad

F-Actin

FLK1



HUVEC

CONTROL

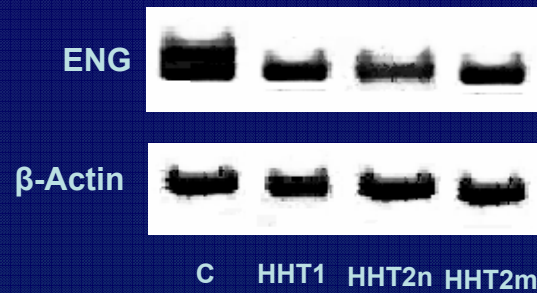
HHT1

HHT2 n

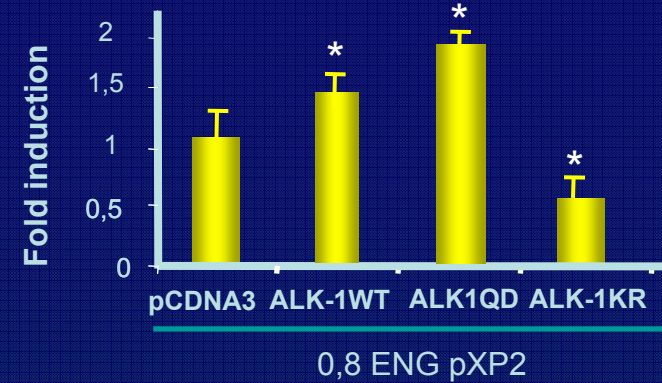
HHT2 m

Endoglin expression in BOECs

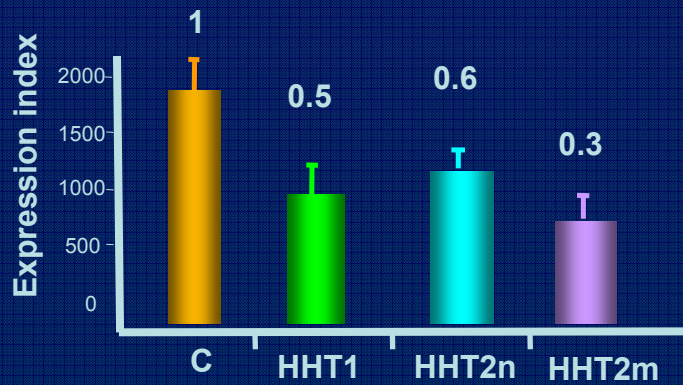
Endoglin expression



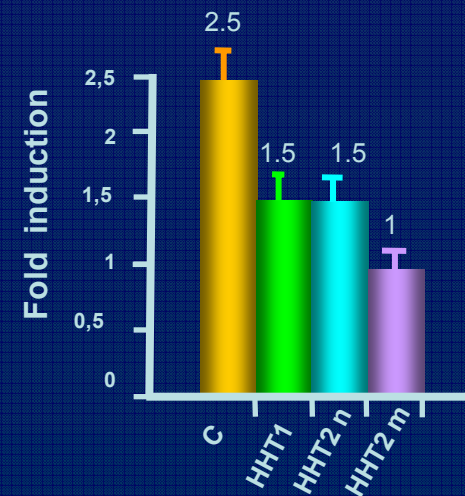
ALK1 acts over ENG promoter



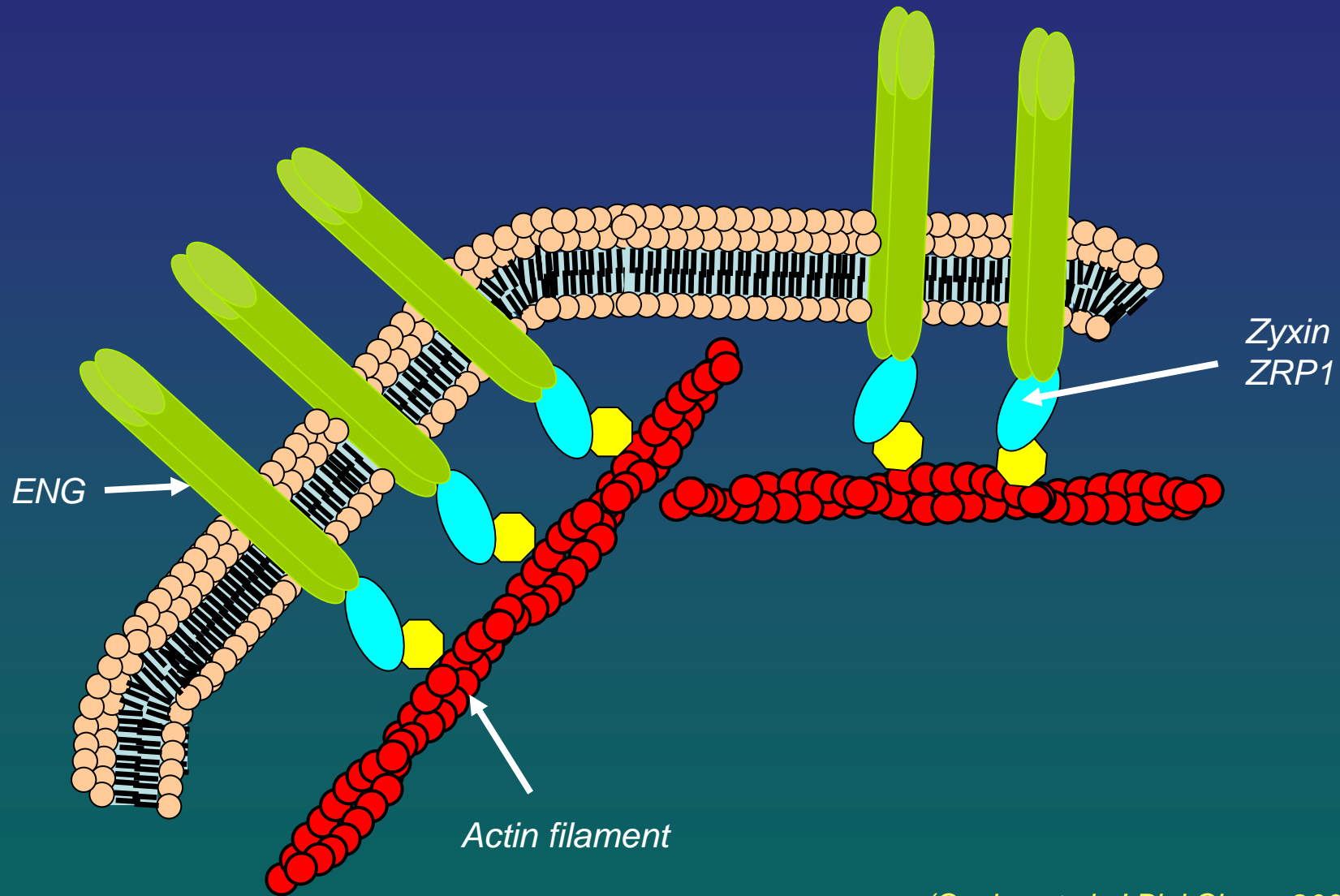
Endoglin expression by flow cytometry



ENG response upon TGF β treatment



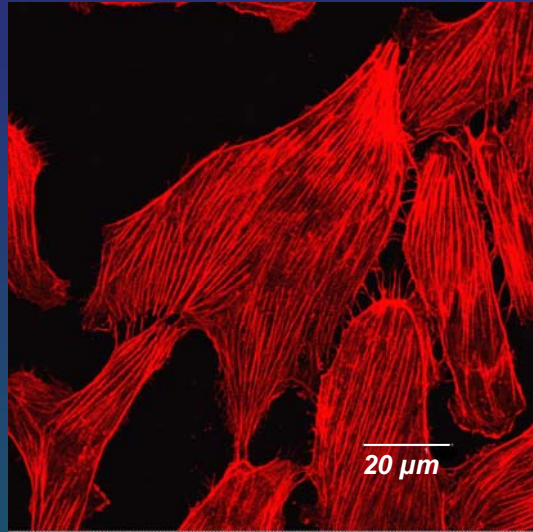
Endoglin-(ZRP-1/Zyxin)-Actin interaction



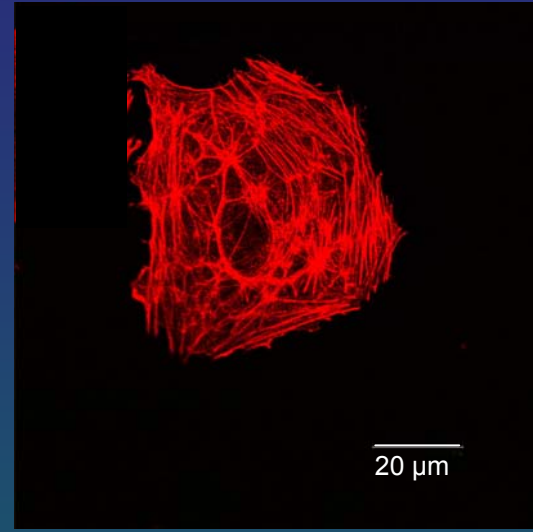
(Conley et al. *J Biol Chem.* 2004)
(Sanz-Rodriguez et al. *J Biol Chem.* 2004)

Disorganized cytoskeleton in BOECs

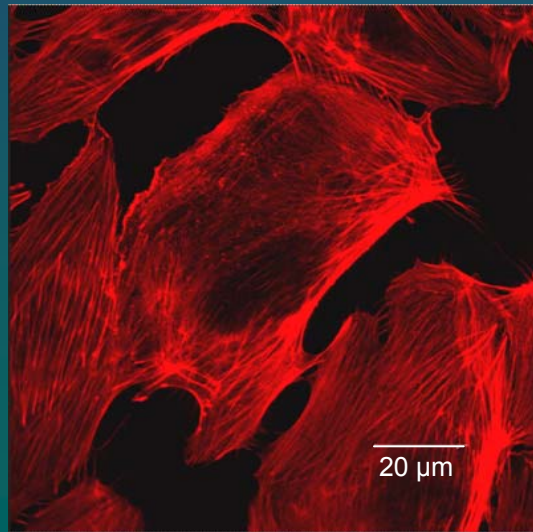
Control



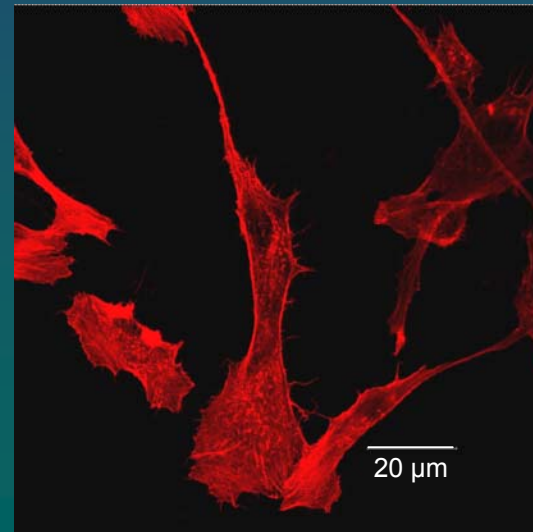
HHT1



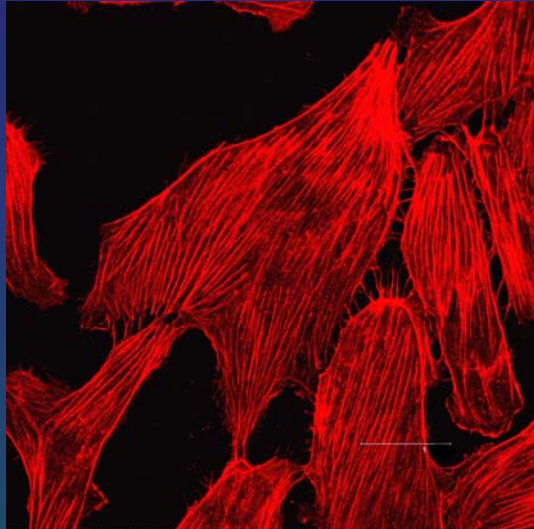
HHT2n



HHT2m

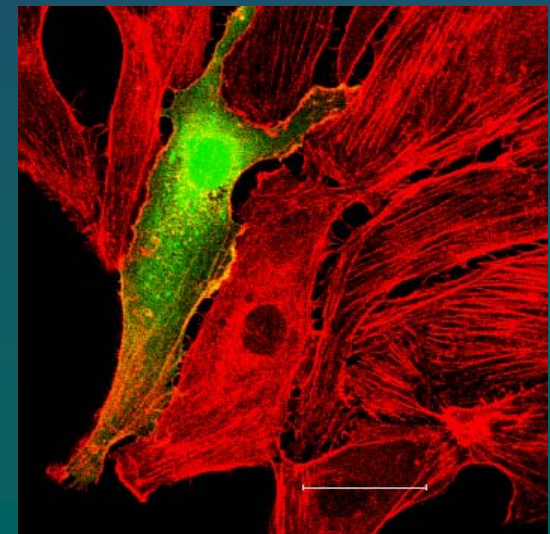
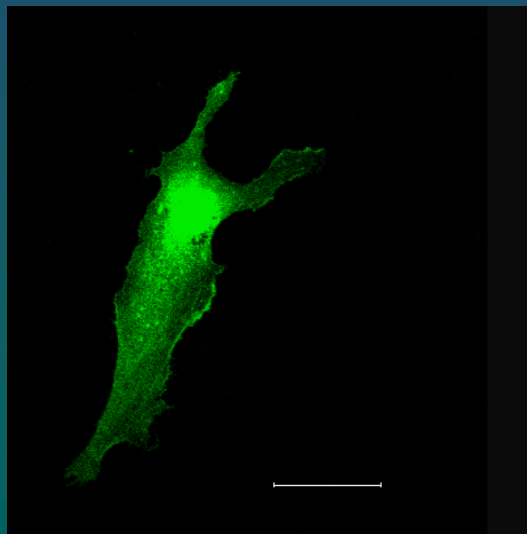
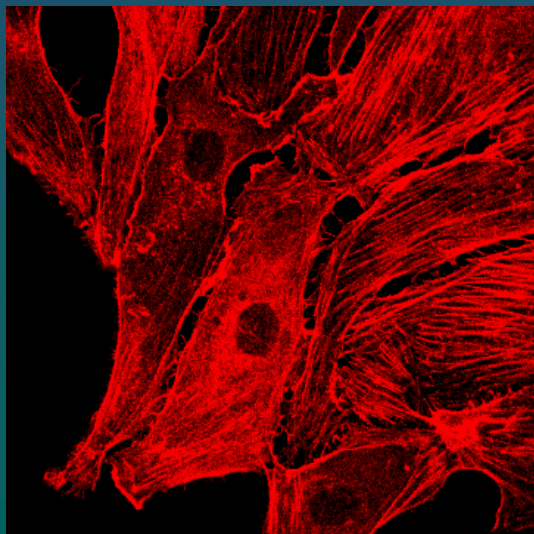


Cytoskeleton disruption by siRNA



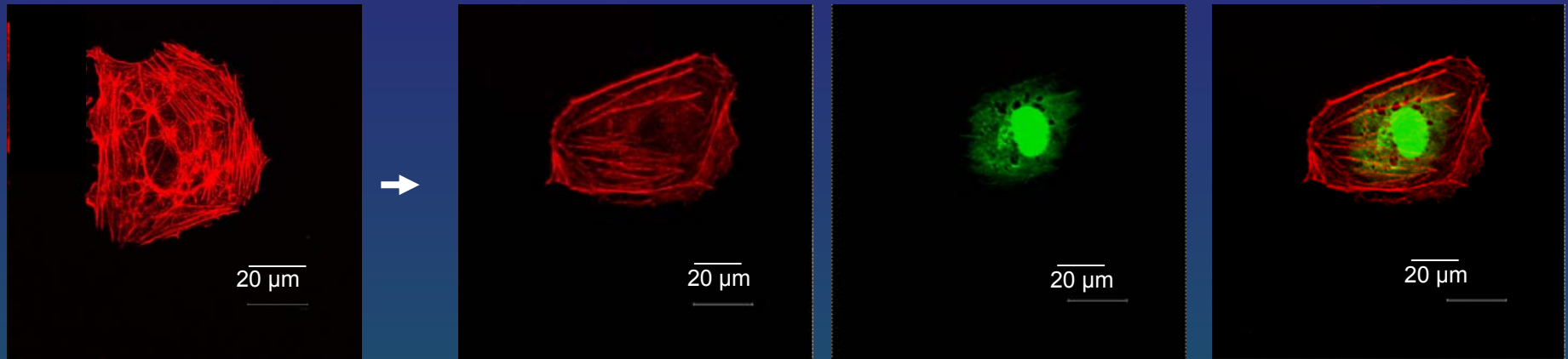
**Control
BOECs**

pSUPER-Endo-Ex4 + pEGFP



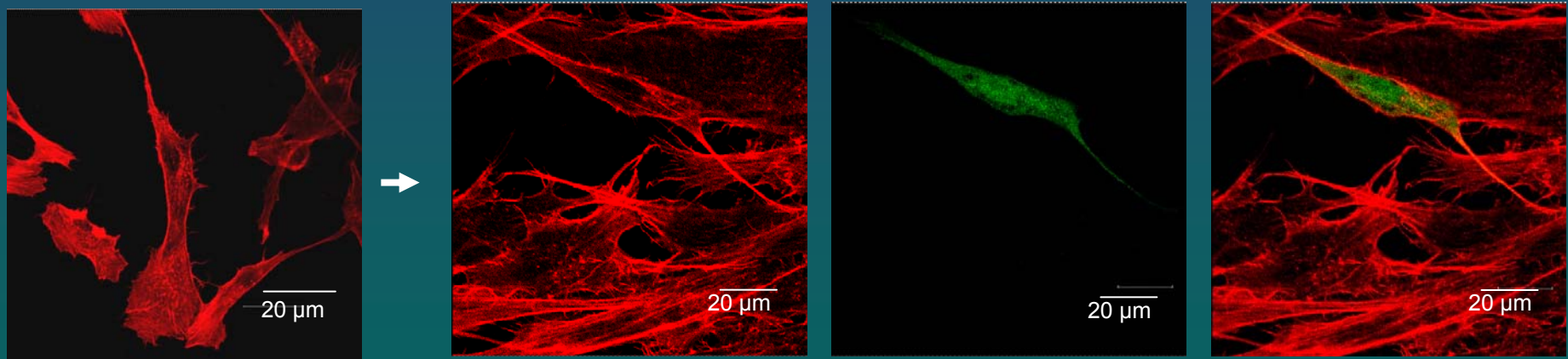
Cytoskeleton organization recovery

HHT1



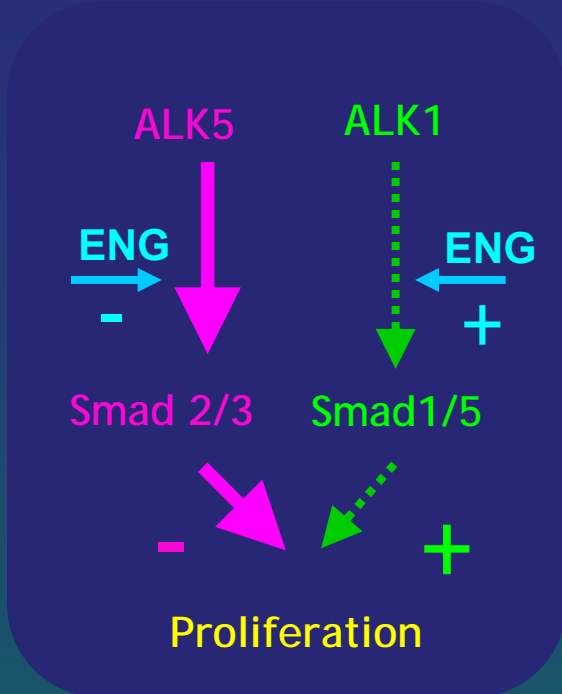
(Fernandez-L et al. Cardiovasc Res. 2005)

HHT2m

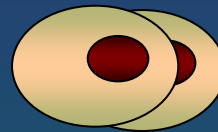


pCMV5-Endoglin + pEGFP

ALK1/ALK5 pathways equilibrium



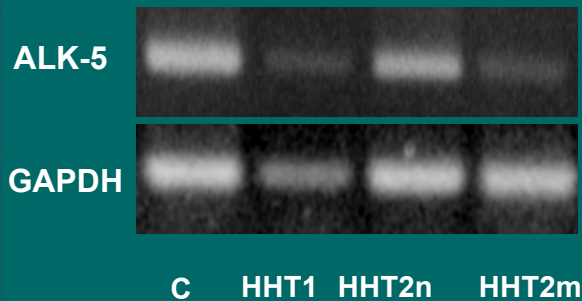
Mutated ALK1/ENG
 ↓
 Do cells stop proliferating?



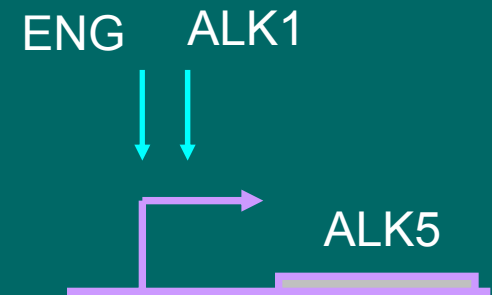
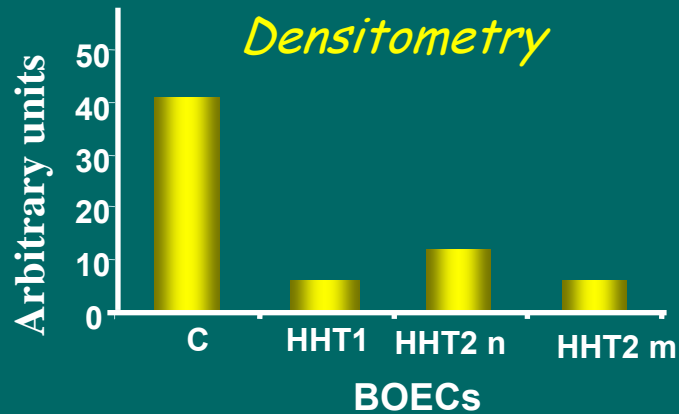
MEECs
 ENG +/-

↓ ALK5 (Lebrin et al., EMBO J., 2004)

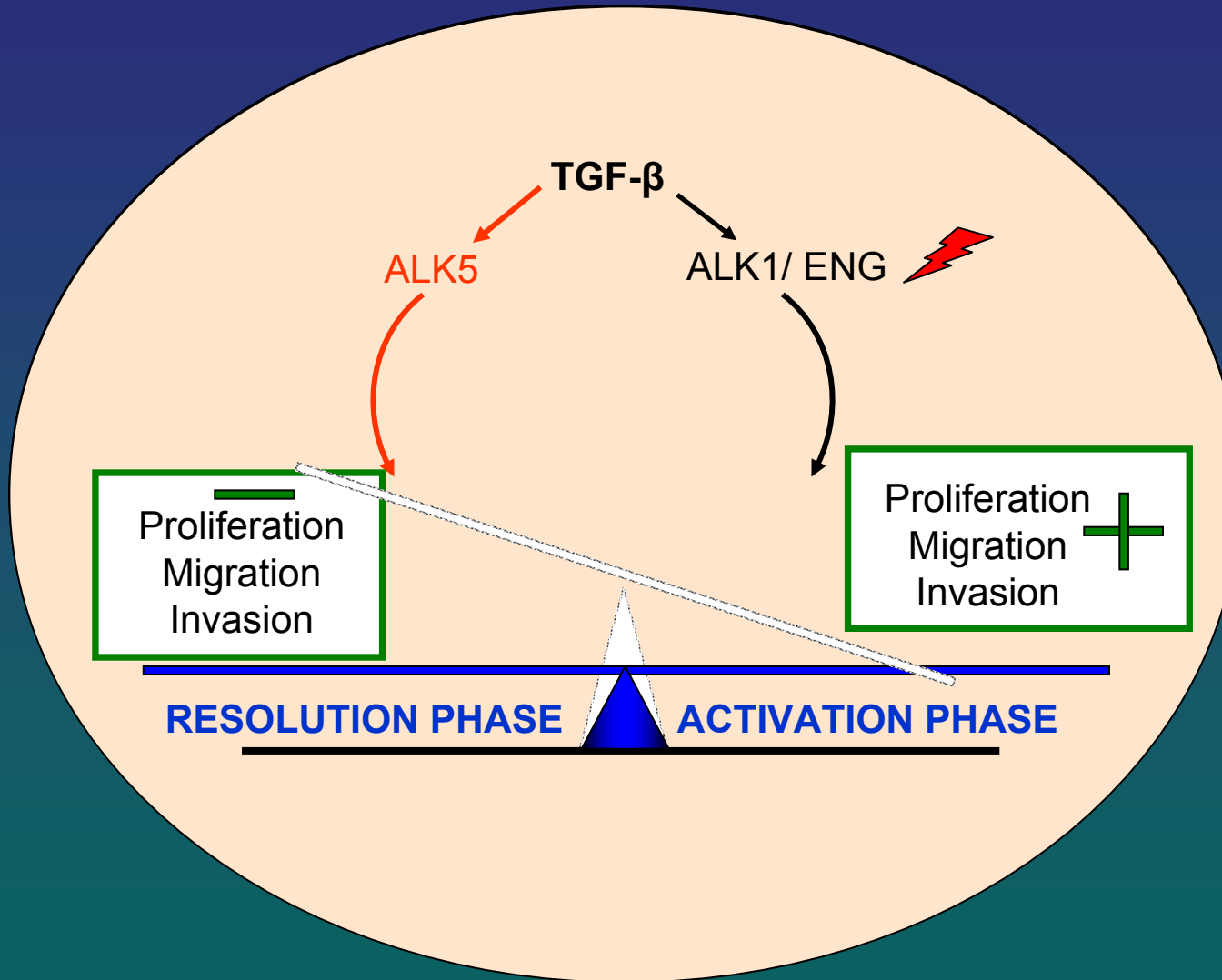
RT-PCR



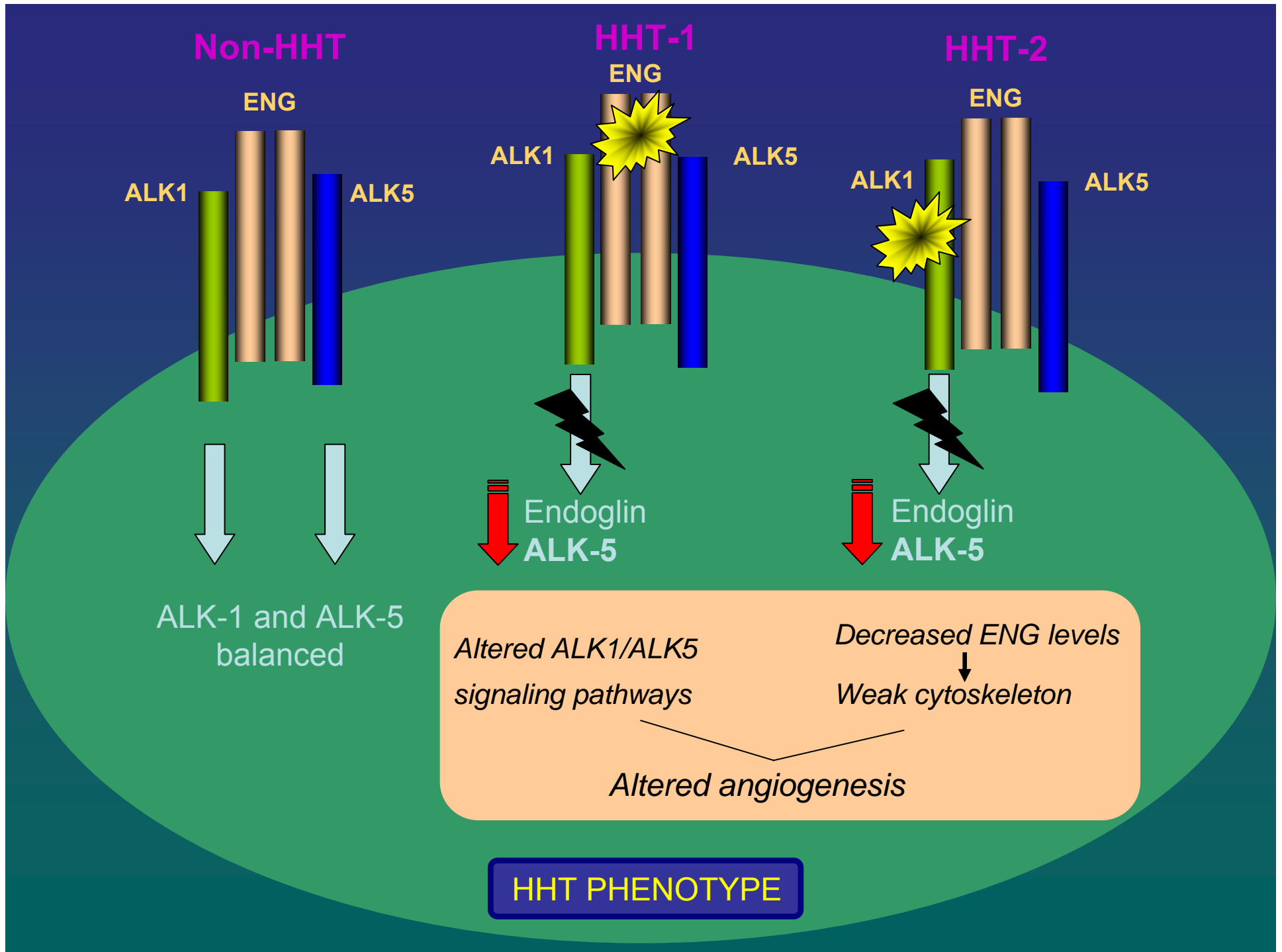
Densitometry



ALK1/ALK5 pathways equilibrium



Decreased ALK5 levels: New steady state



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África Fernández

Eva María Garrido

Carmen Langa



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HHT INTERNATIONAL FOUNDATION grant.*

