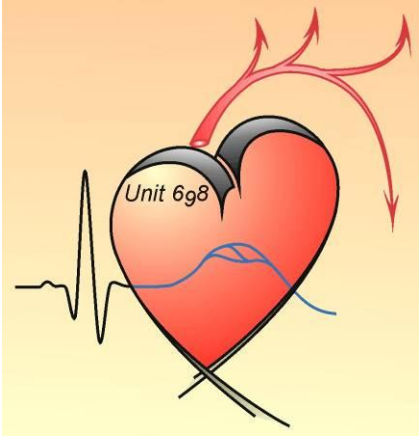
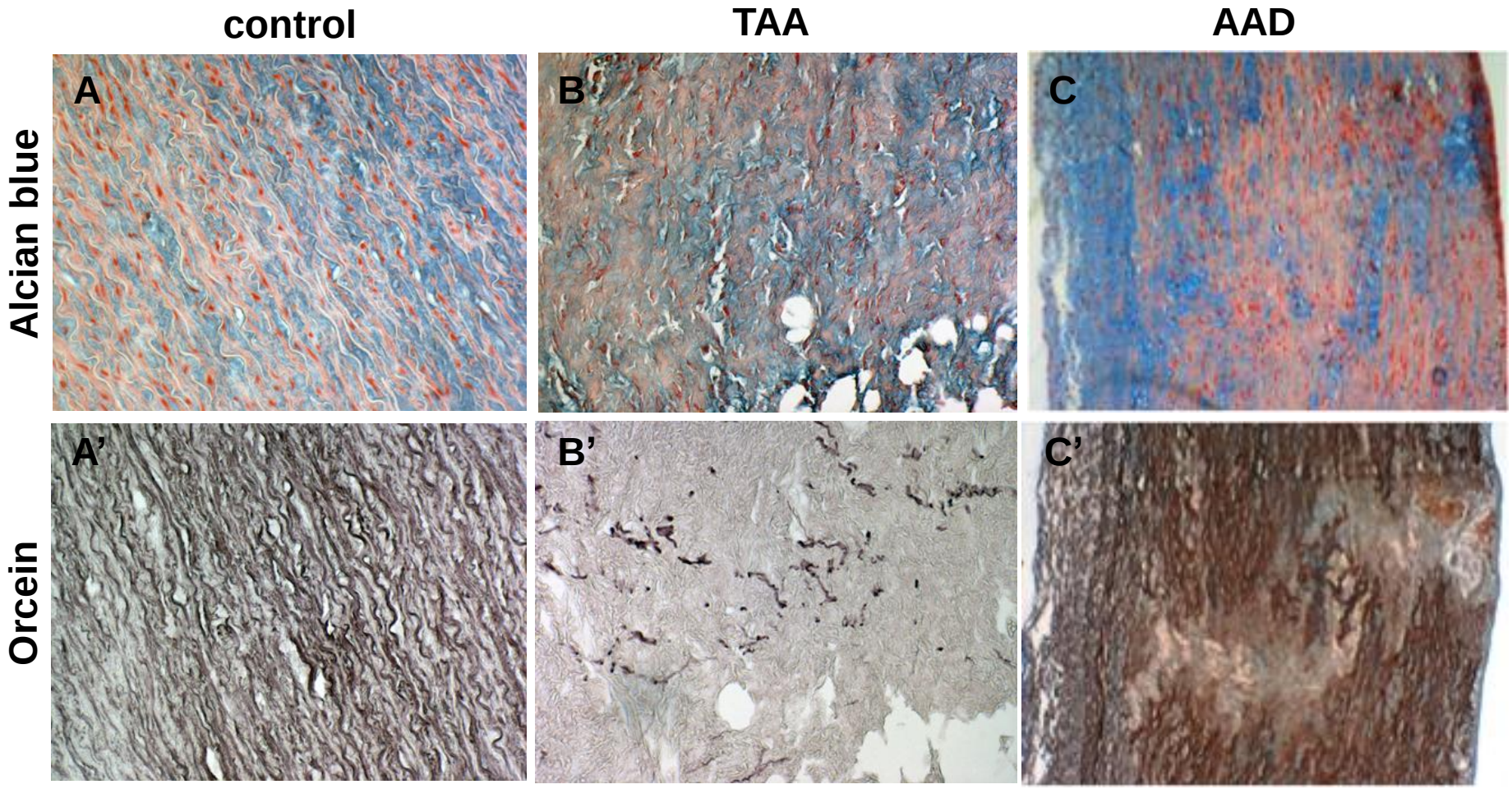



# Smad2-dependent PN-1 overexpression differentiates progressive aneurysms from acute dissections of human ascending aorta

**Inserm U698,**
**Xavier Bichat Hospital, Paris.**

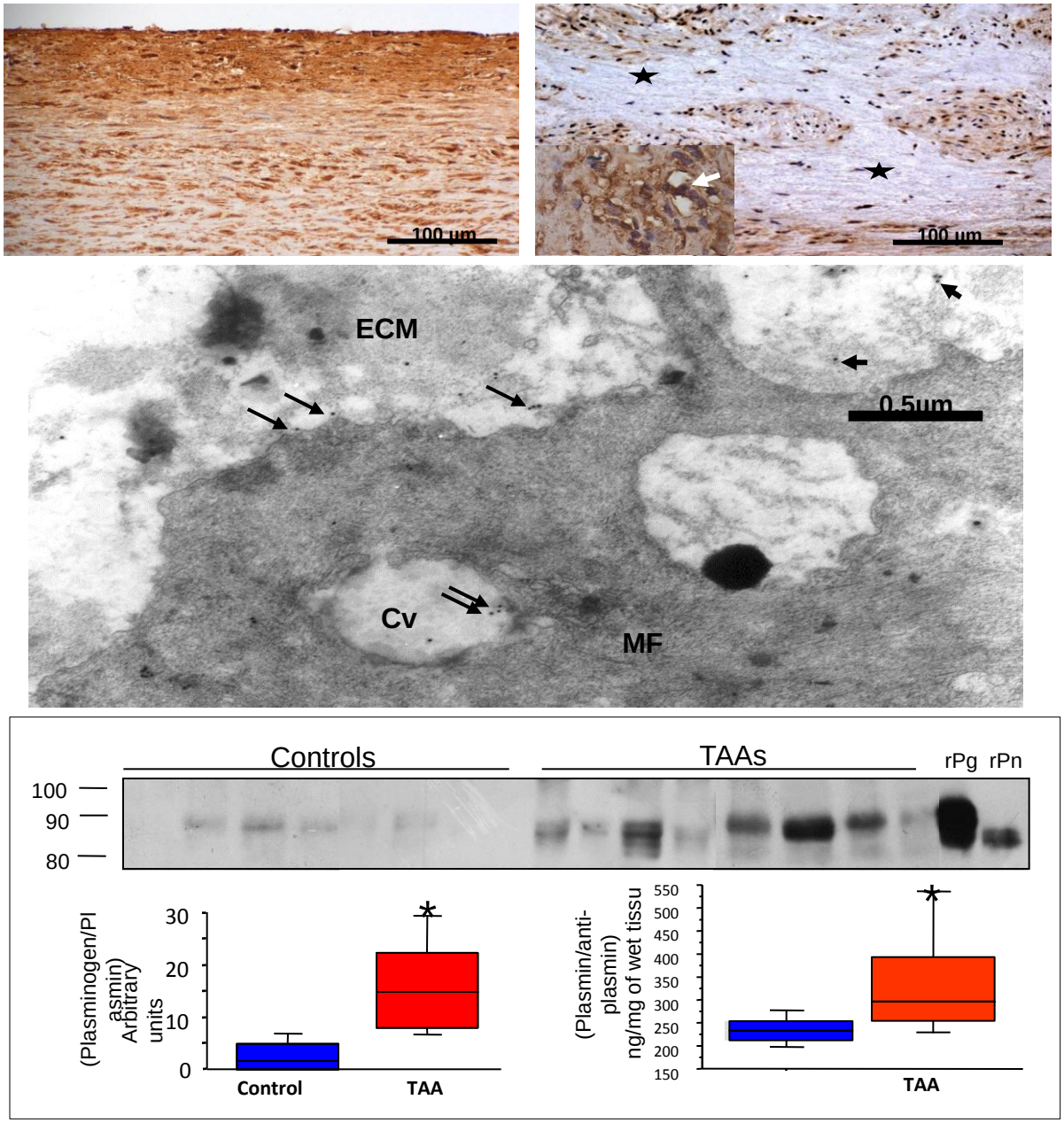
***Delphine Gomez &***
***Jean-Baptiste Michel***

Fighting
Aneurismal
Disease

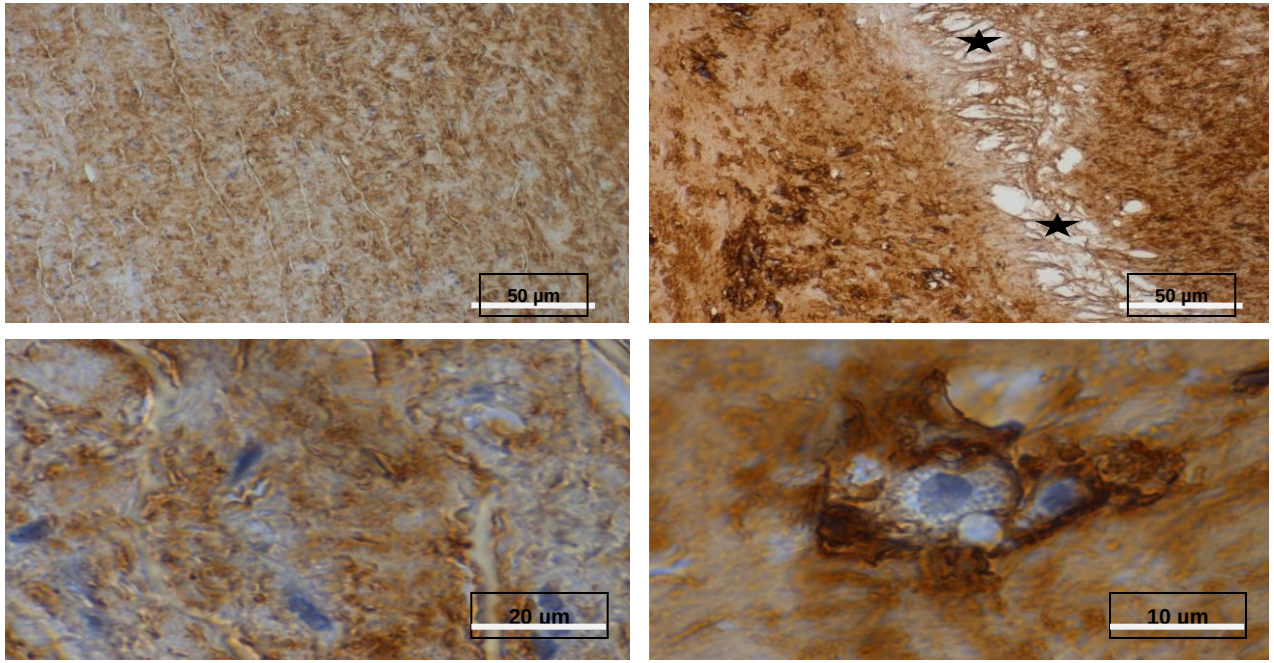


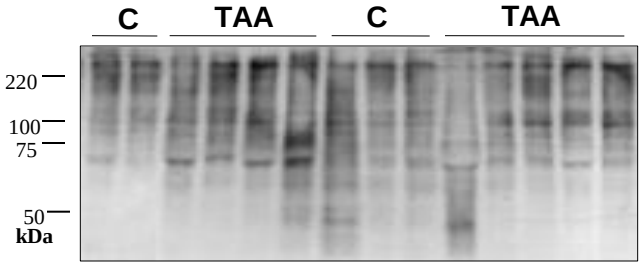

**Common pathology**

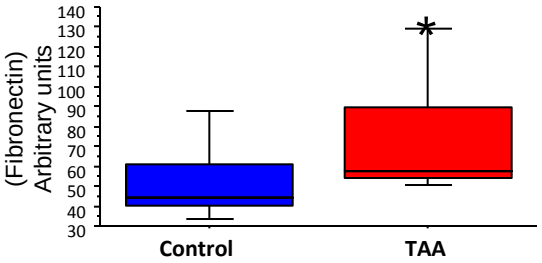
# Plasminogen convection and plasmine activation in TAA

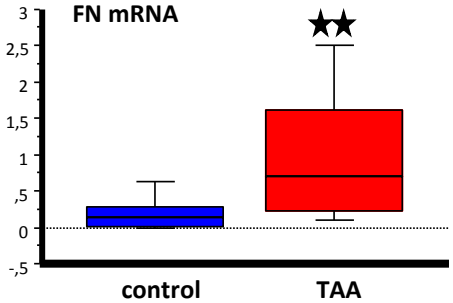


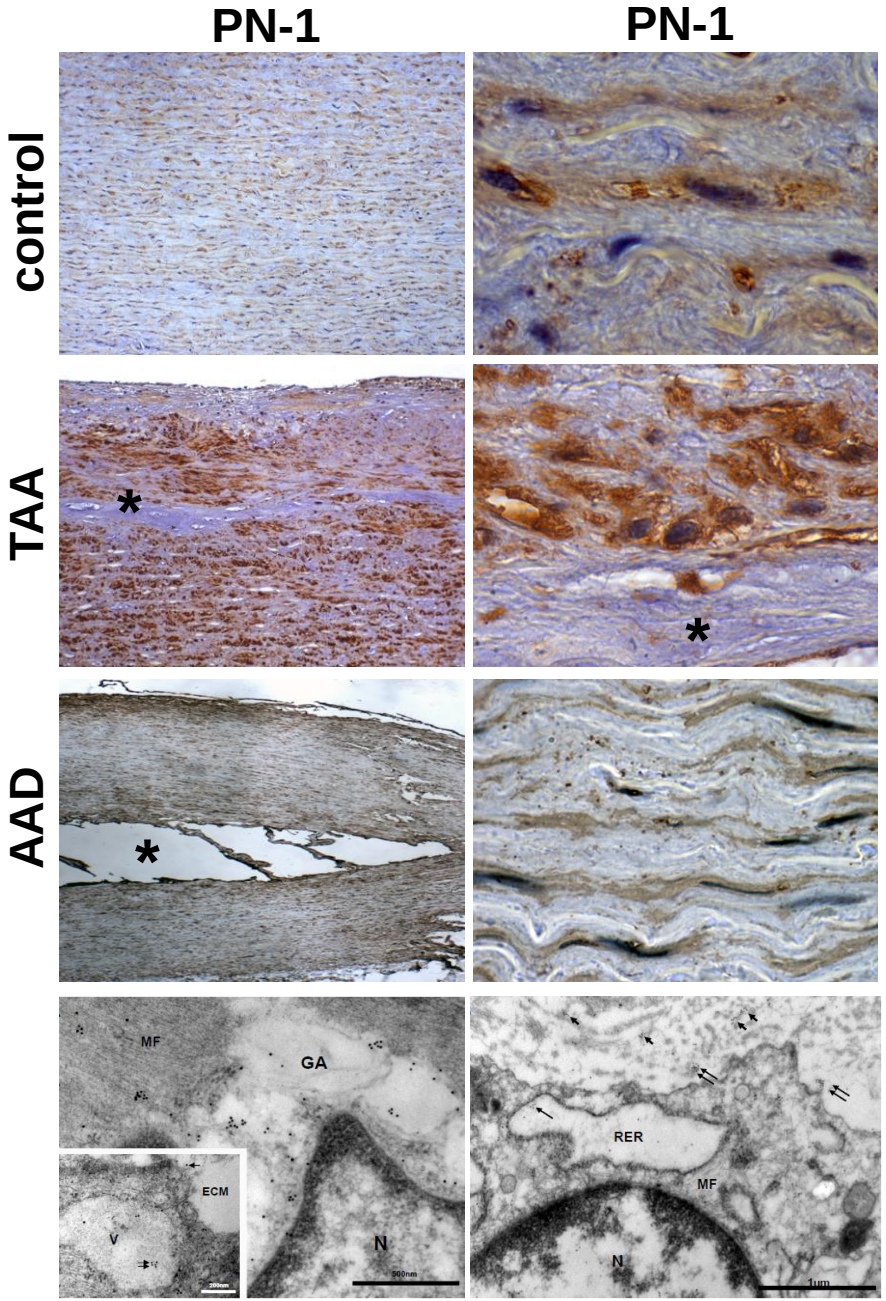
# Fibronectin turnover

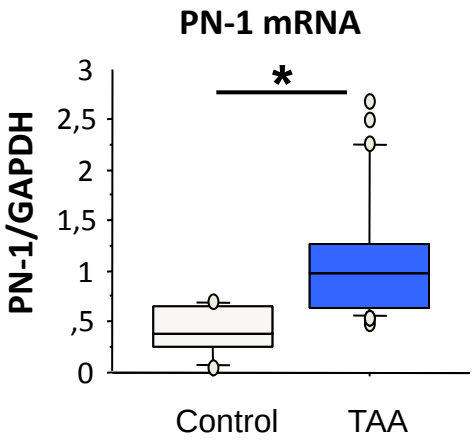


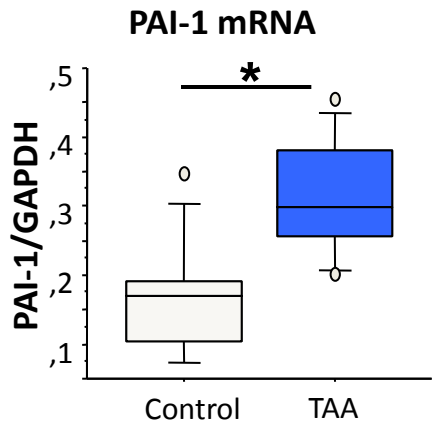



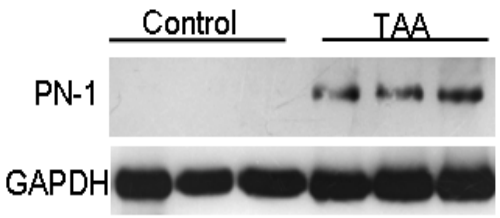



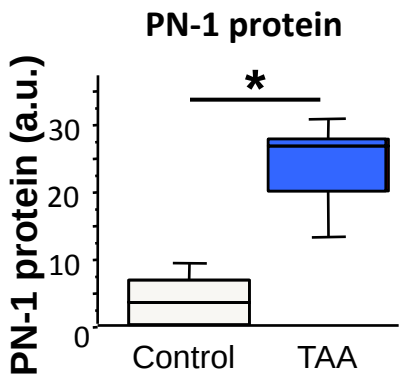



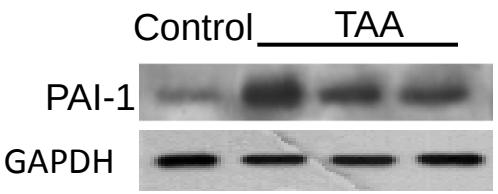


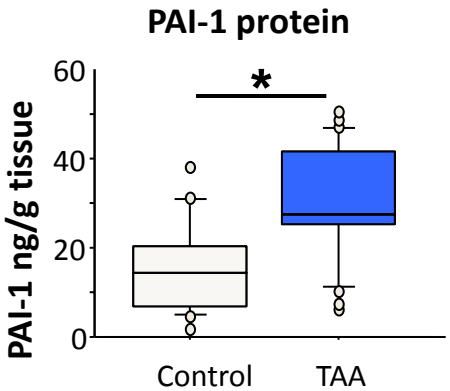



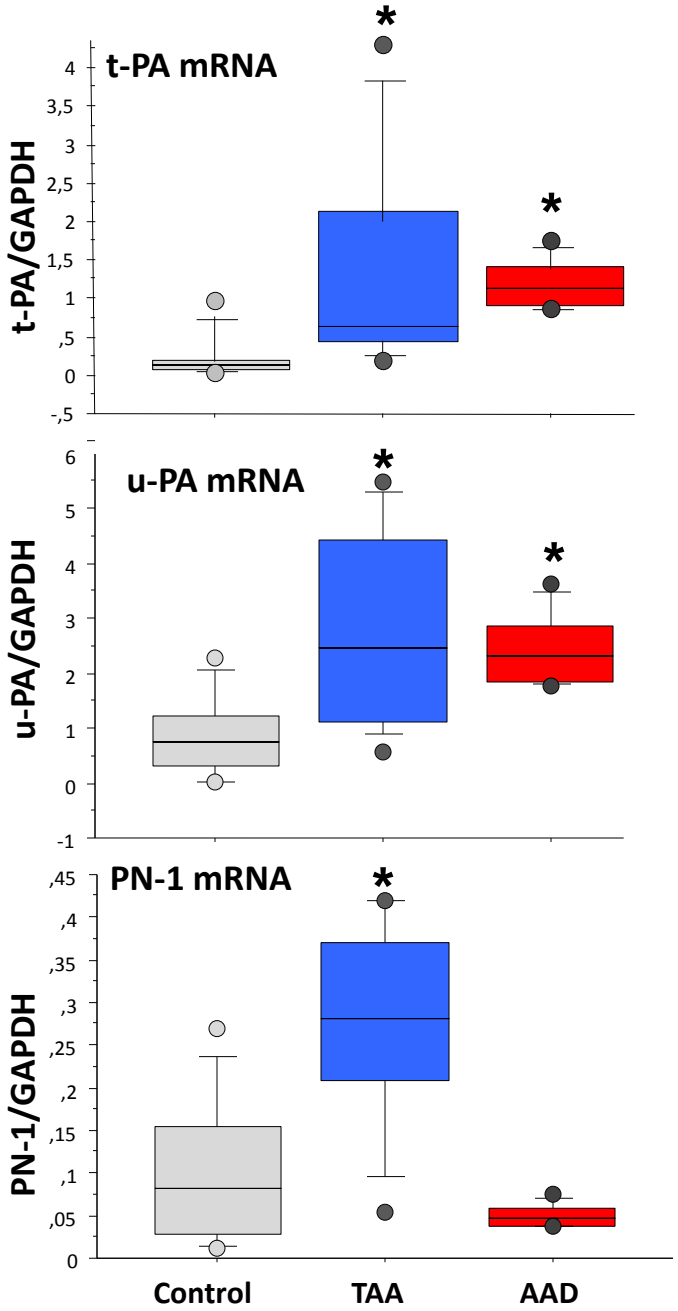



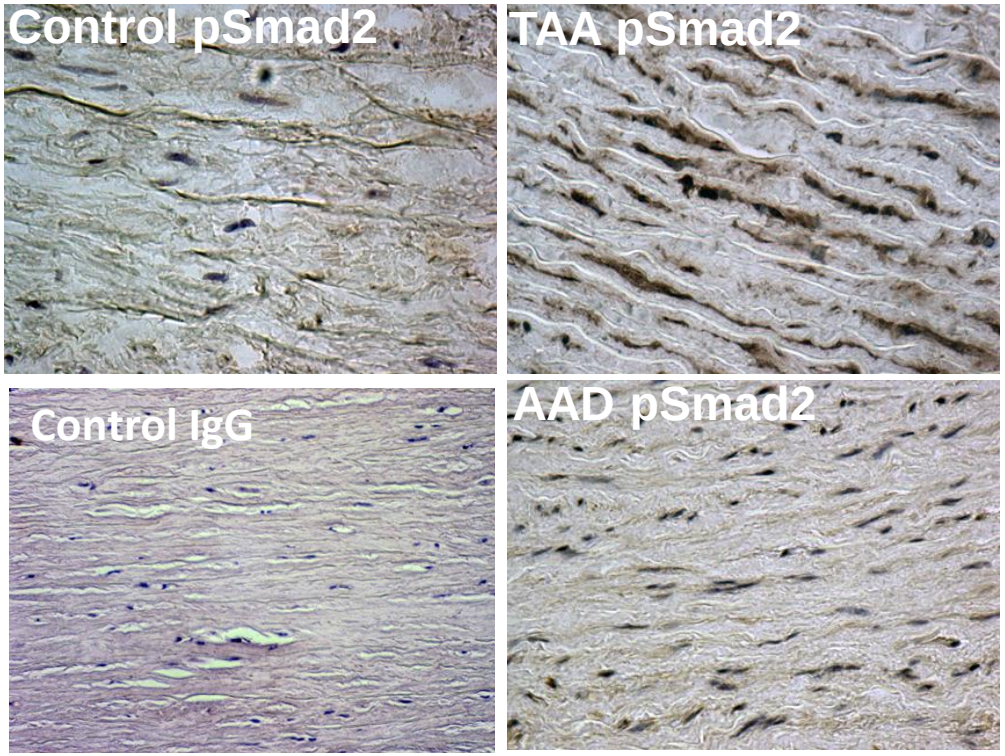



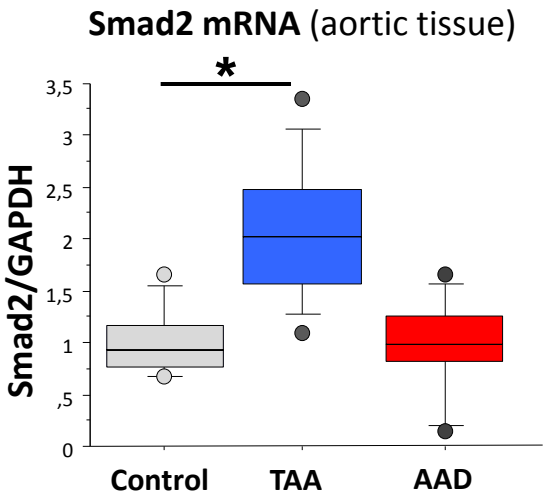



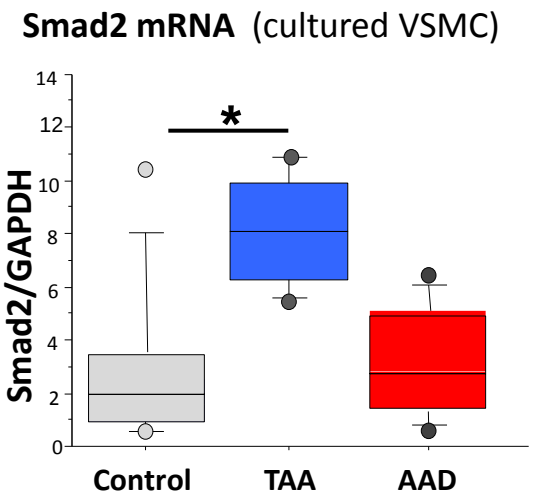

**Overexpression of antiproteases in TAA**

# Plasminogen activators and Smad2 expression

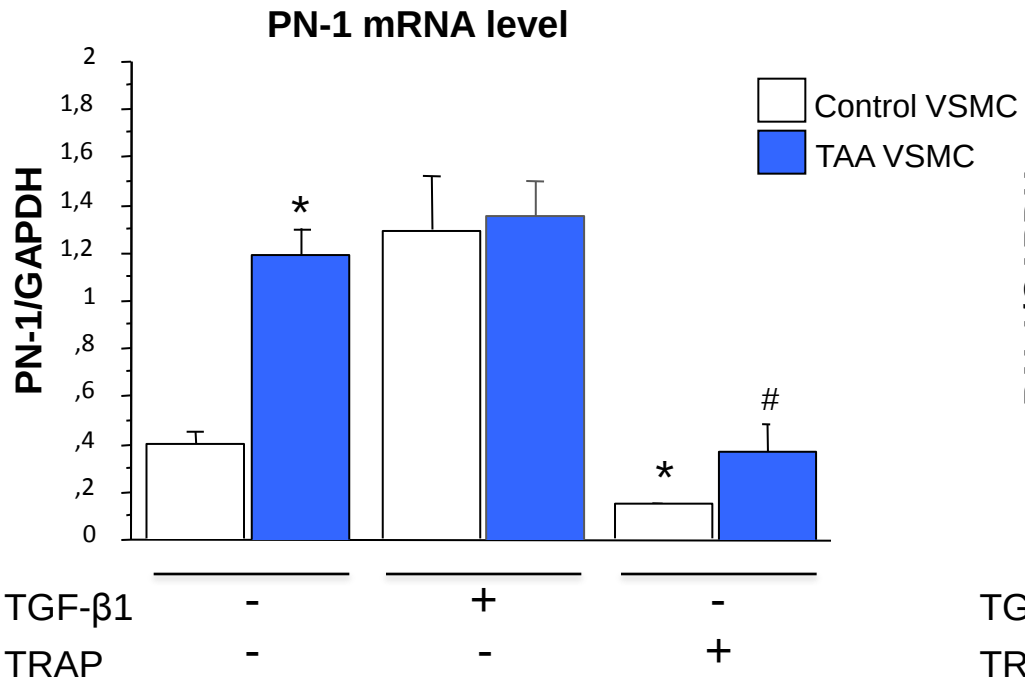


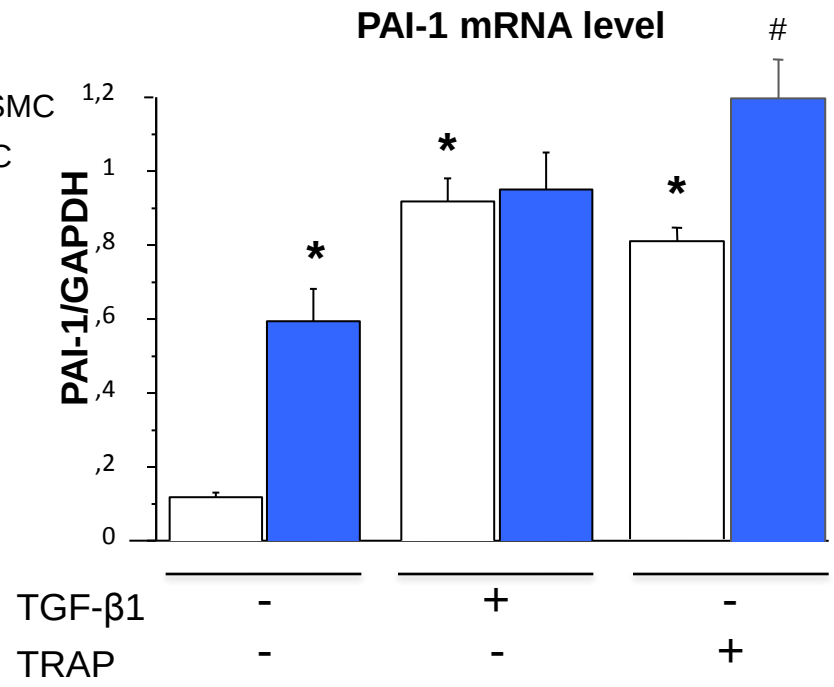



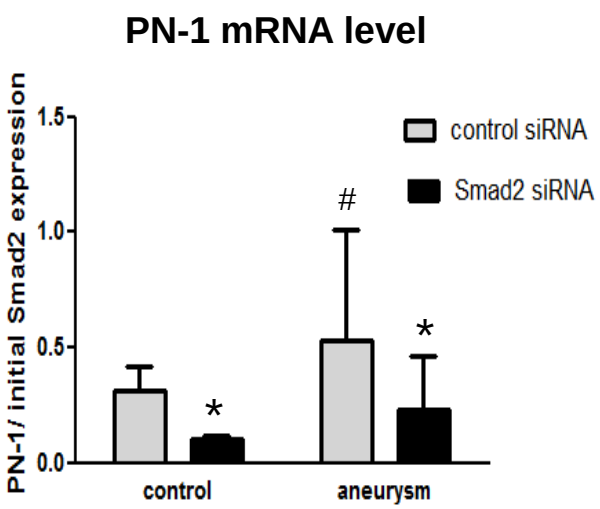



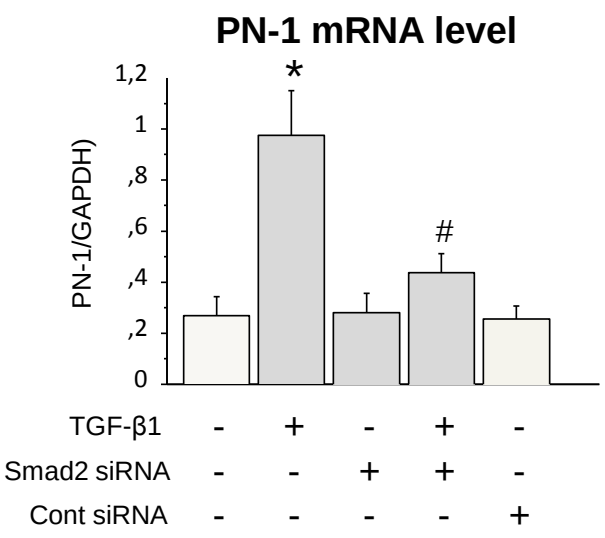



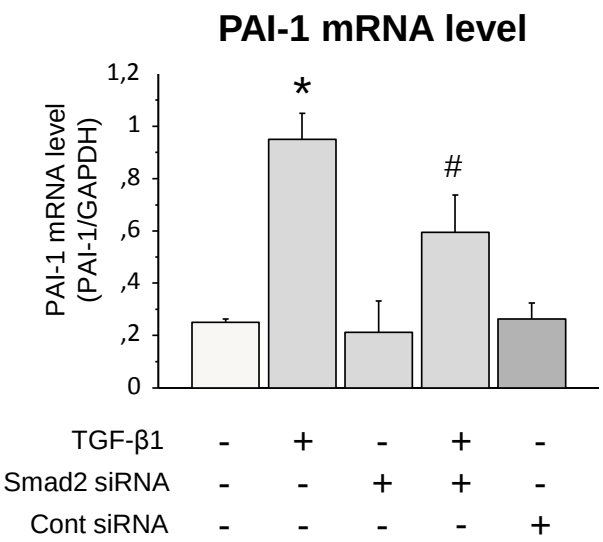
# Epigenetic control of antiprotease overexpression in TAA



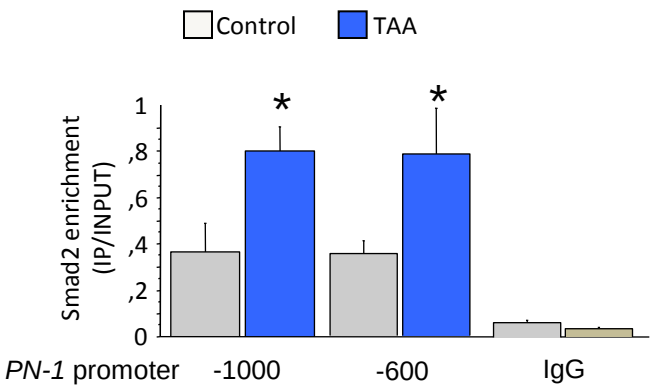



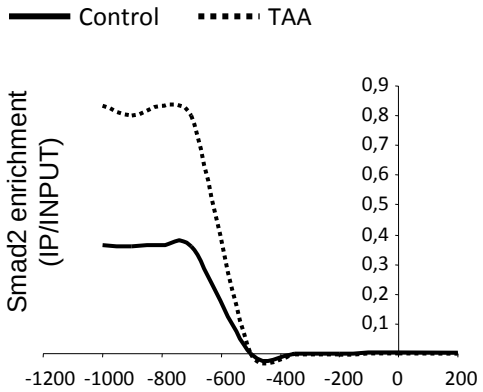
# Epigenetic control of antiprotease overexpression in TAA

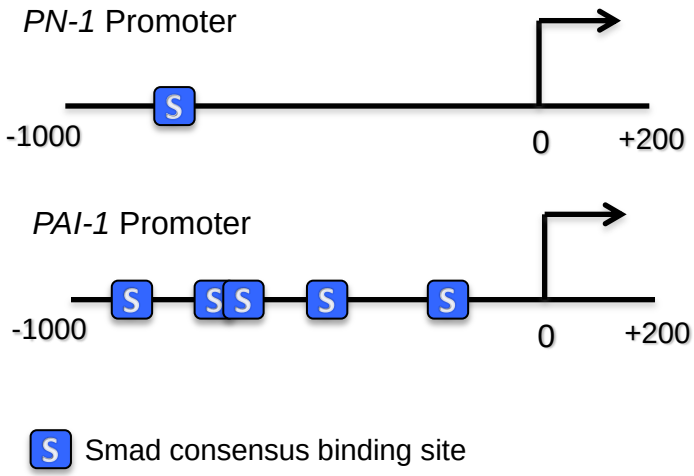
PUTATIVE SMAD BINDING SITES

| Gene | sequence | position | strand |
|---|---|---|---|
| PN-1 | CGTCTGCCT | -834 | + |
| PAI-1 | GTCTGTGT | -903 | + |
| | AGCCAGACA | -734 | - |
| | AGTCTGGAC | -686 | + |
| | AGACAGACA | -585 | - |
| | AGACAGACA | -281 | - |

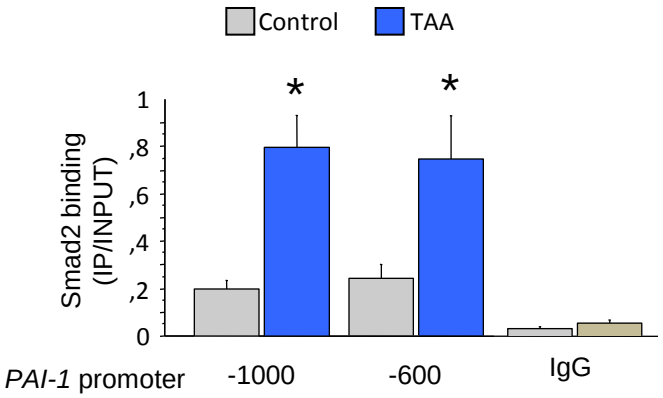
## Smad2 enrichment on the *PN-1* promoter

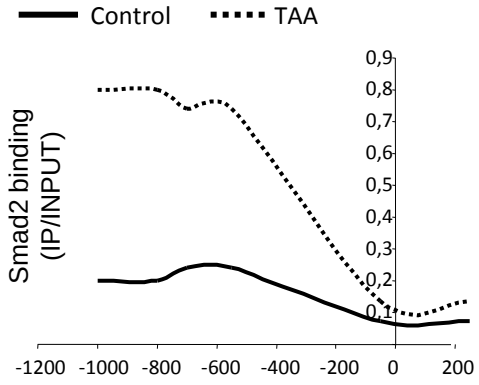


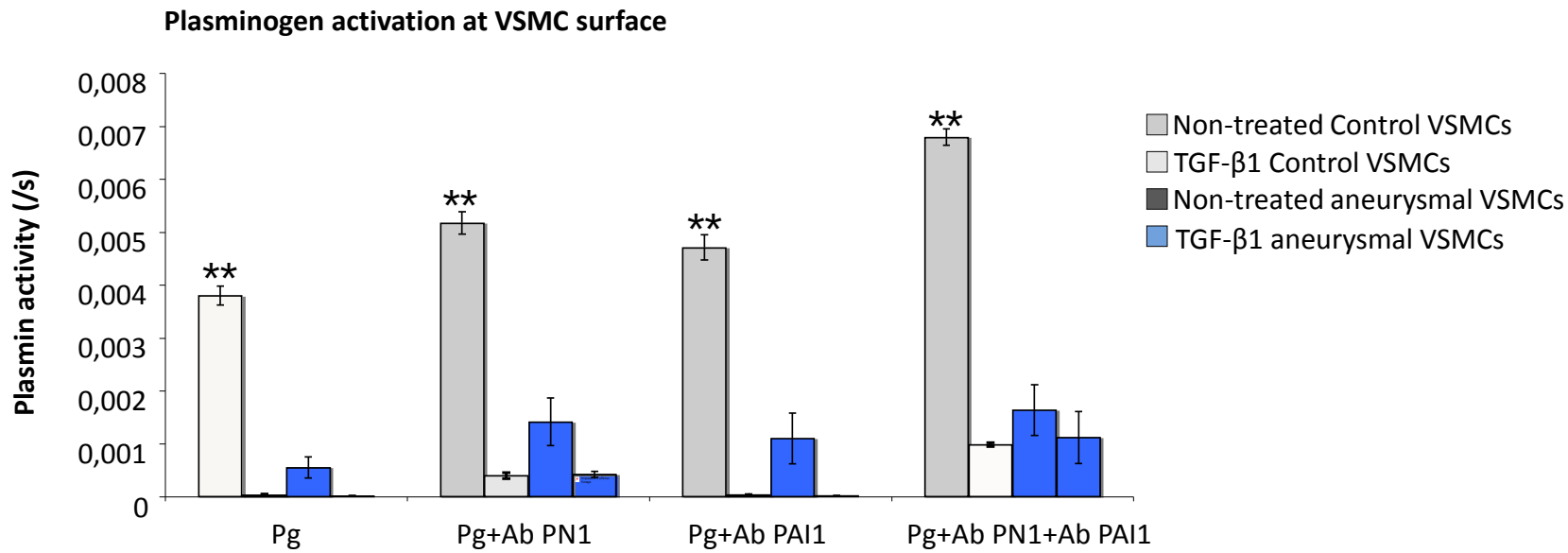



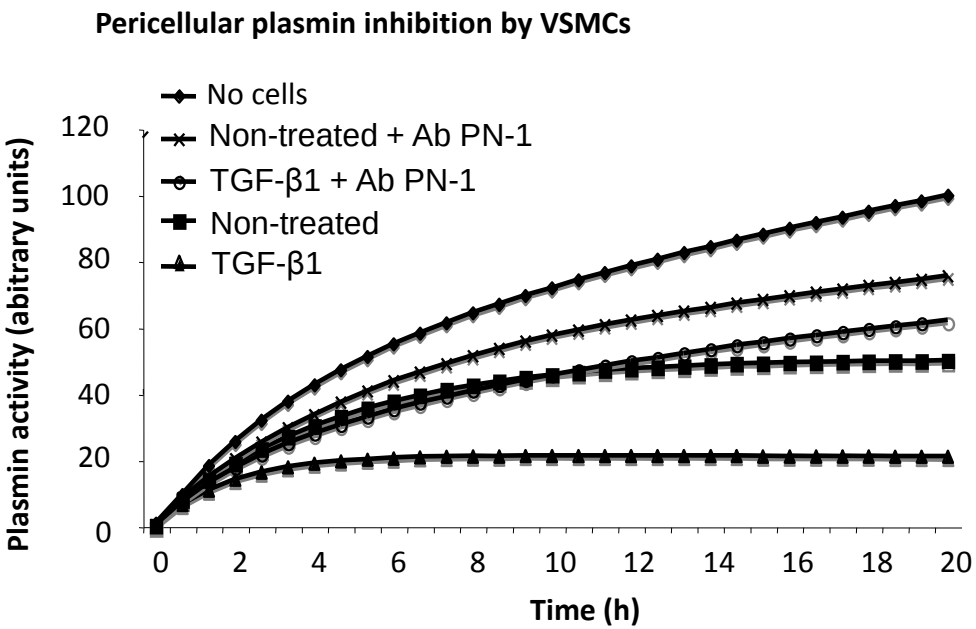

## Smad2 enrichment on the *PAI-1* promoter

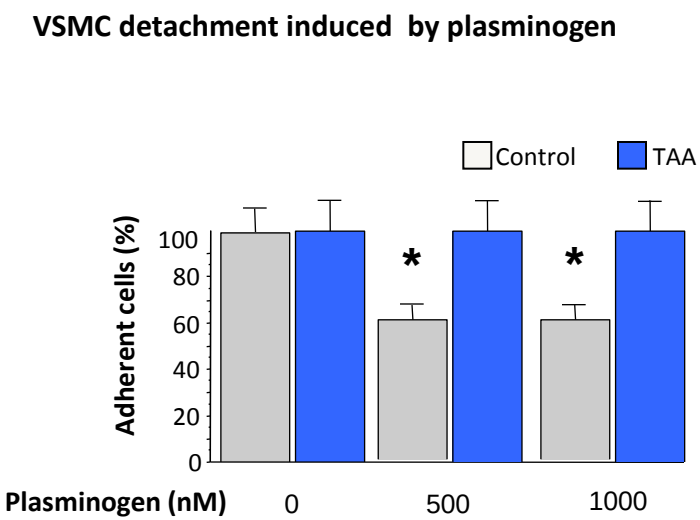


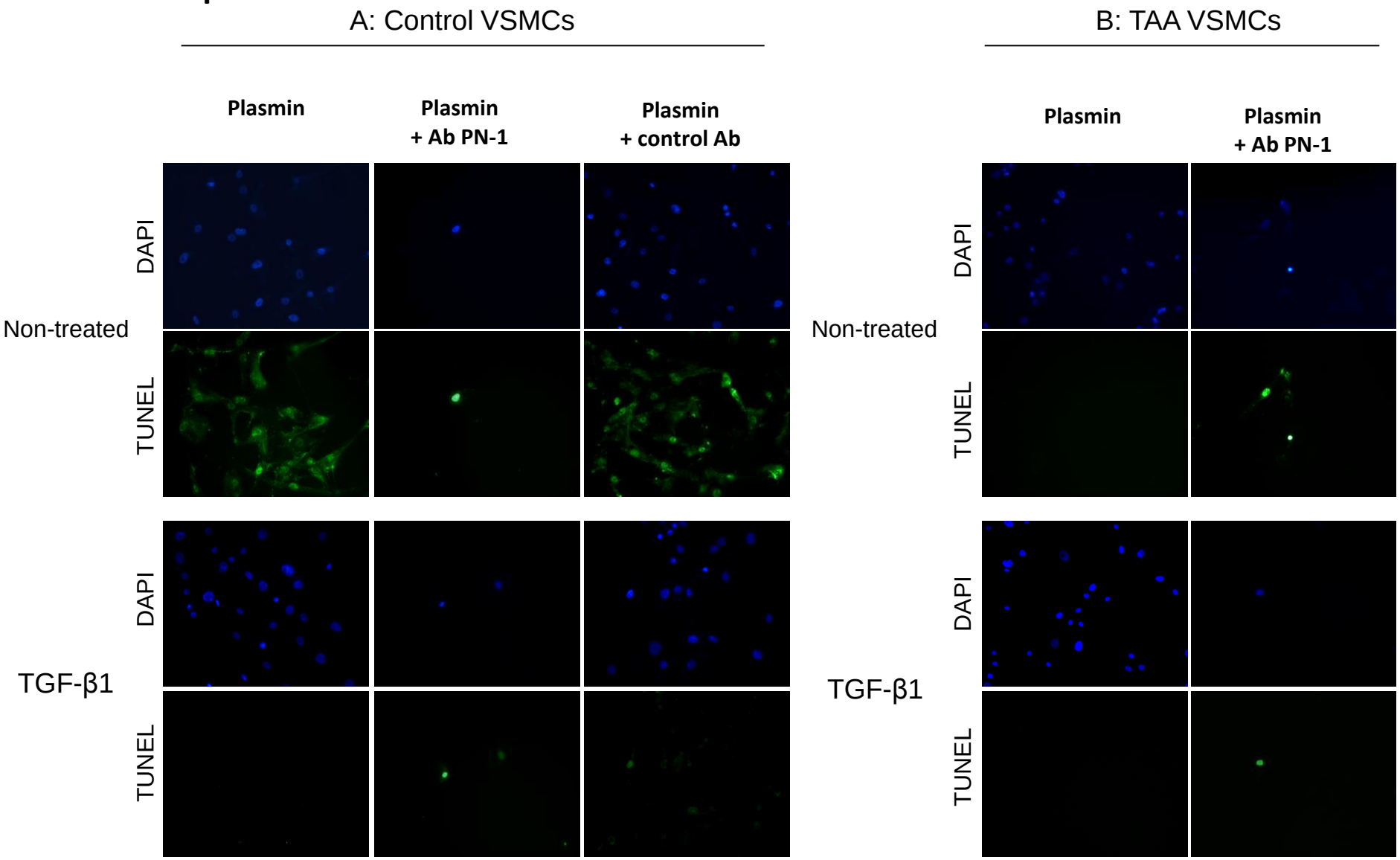
# VSMC consequences

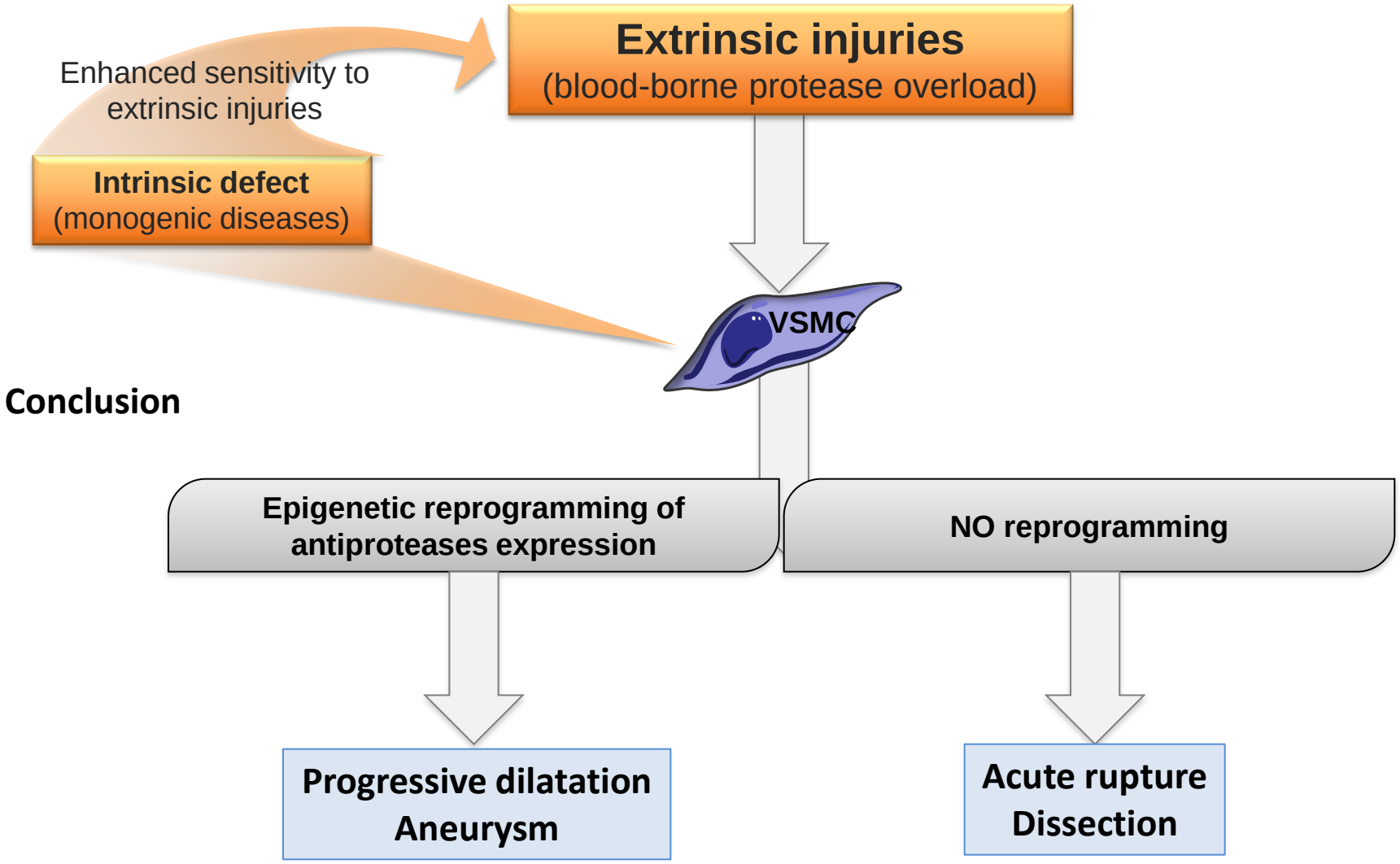


# VSMC consequences




Extrinsic injuries
(blood-borne protease overload)
Enhanced sensitivity to extrinsic injuries
Intrinsic defect
(monogenic diseases)
VSMC
Conclusion
Epigenetic reprogramming of antiproteases expression
NO reprogramming
Progressive dilatation
Aneurysm
Acute rupture
Dissection