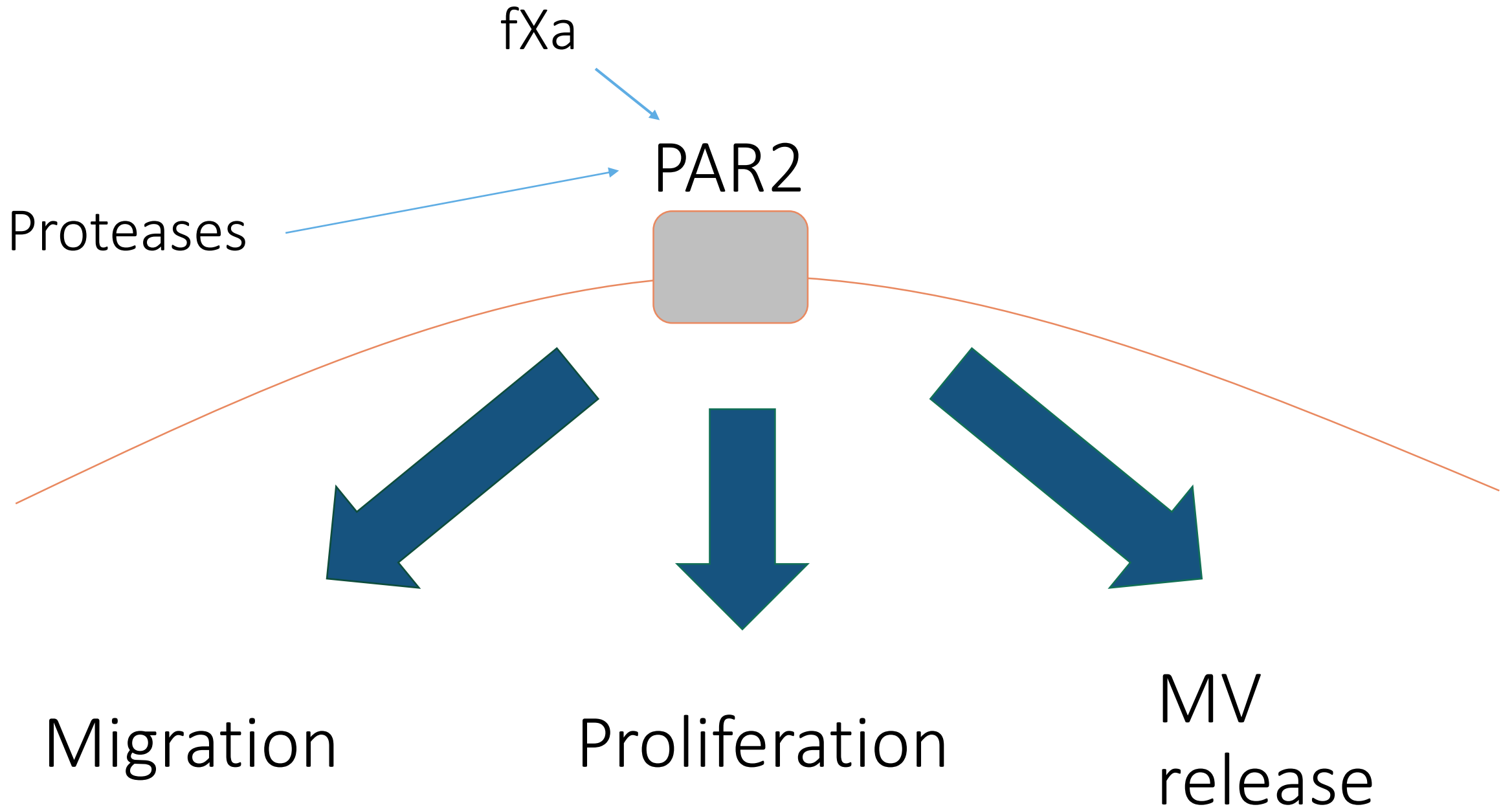


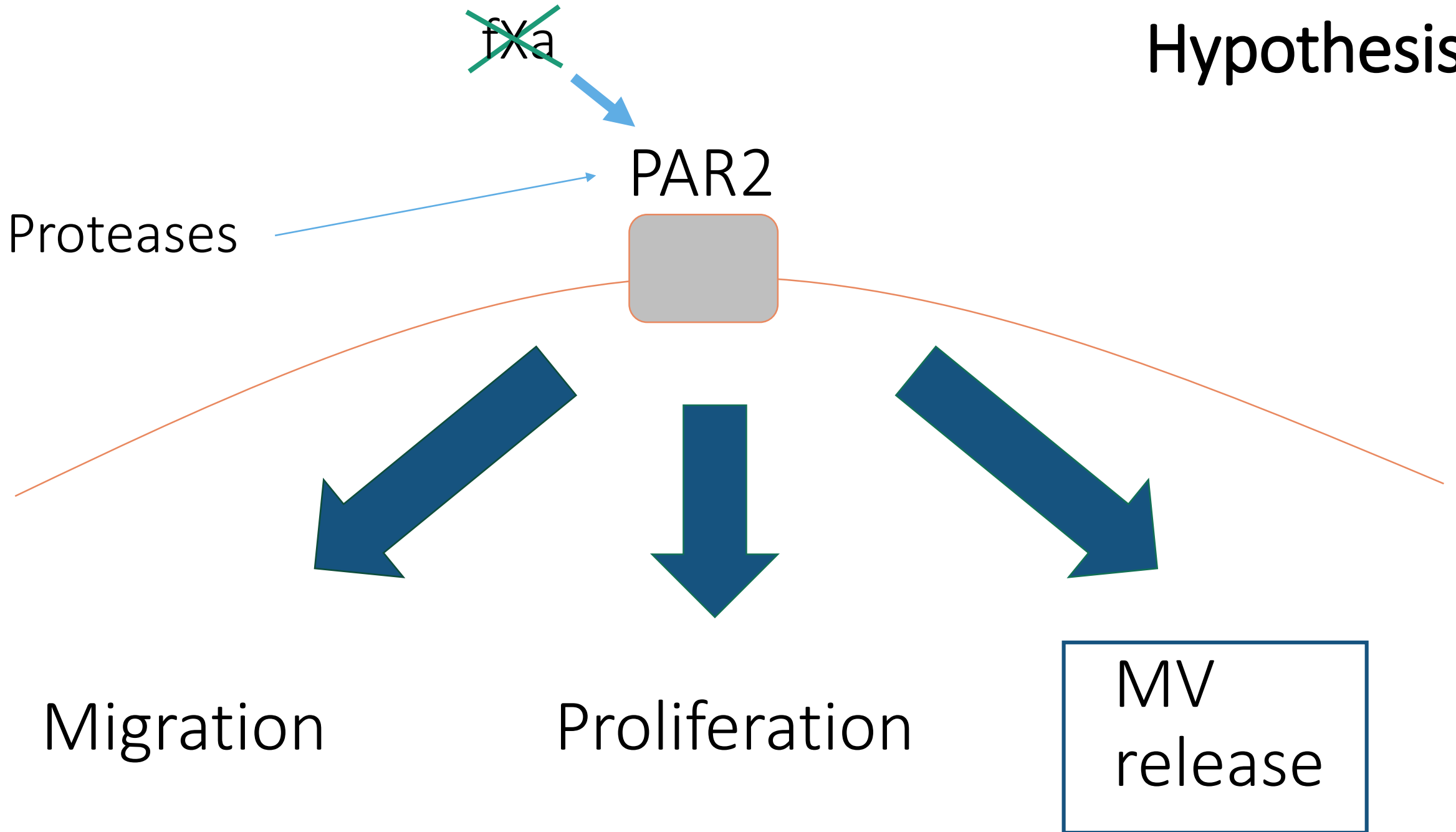
Apixaban and Rivaroxaban
Reduce the Release of TF-
Bearing Microvesicles from fXa
Activated Cancer Cell Line.

Disclosures

- This project has been funded in part by:
 - Bristol-Mayer-Squib
 - The Castle Hill Hospital Cancer Trust Fund

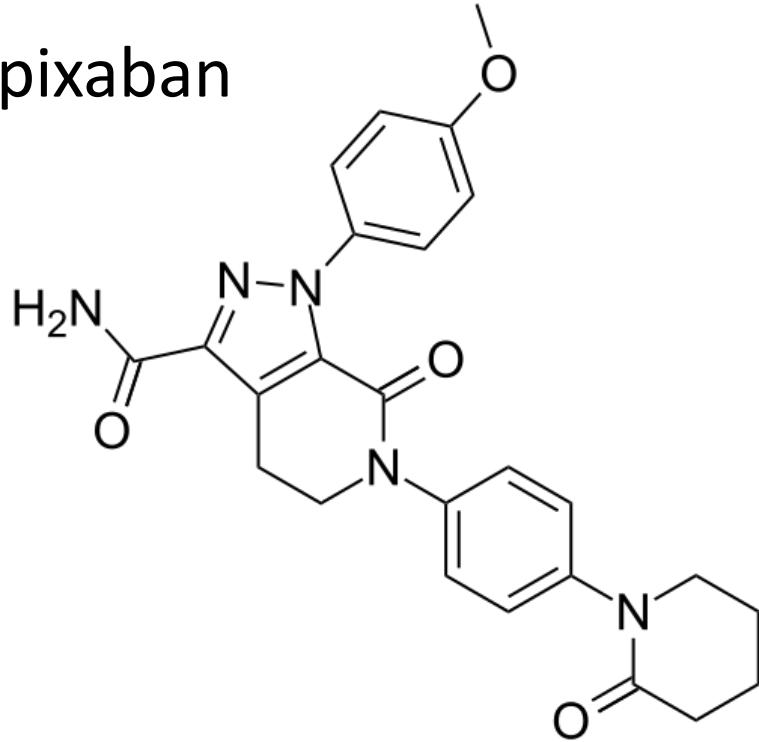


Hypothesis



fXa inhibitors – pure compounds

Apixaban



Pharmacokinetic

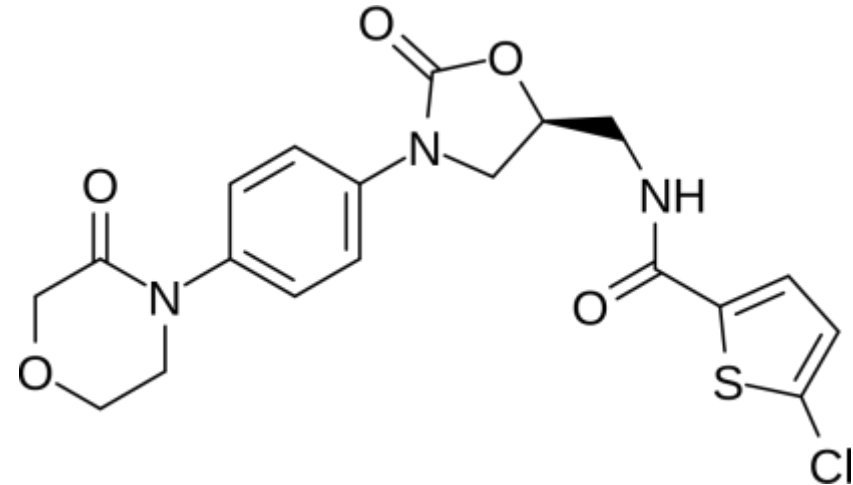
Mean blood concentrations

0.72-0.05 µg/ml

Concentrations used

1 µg/ml

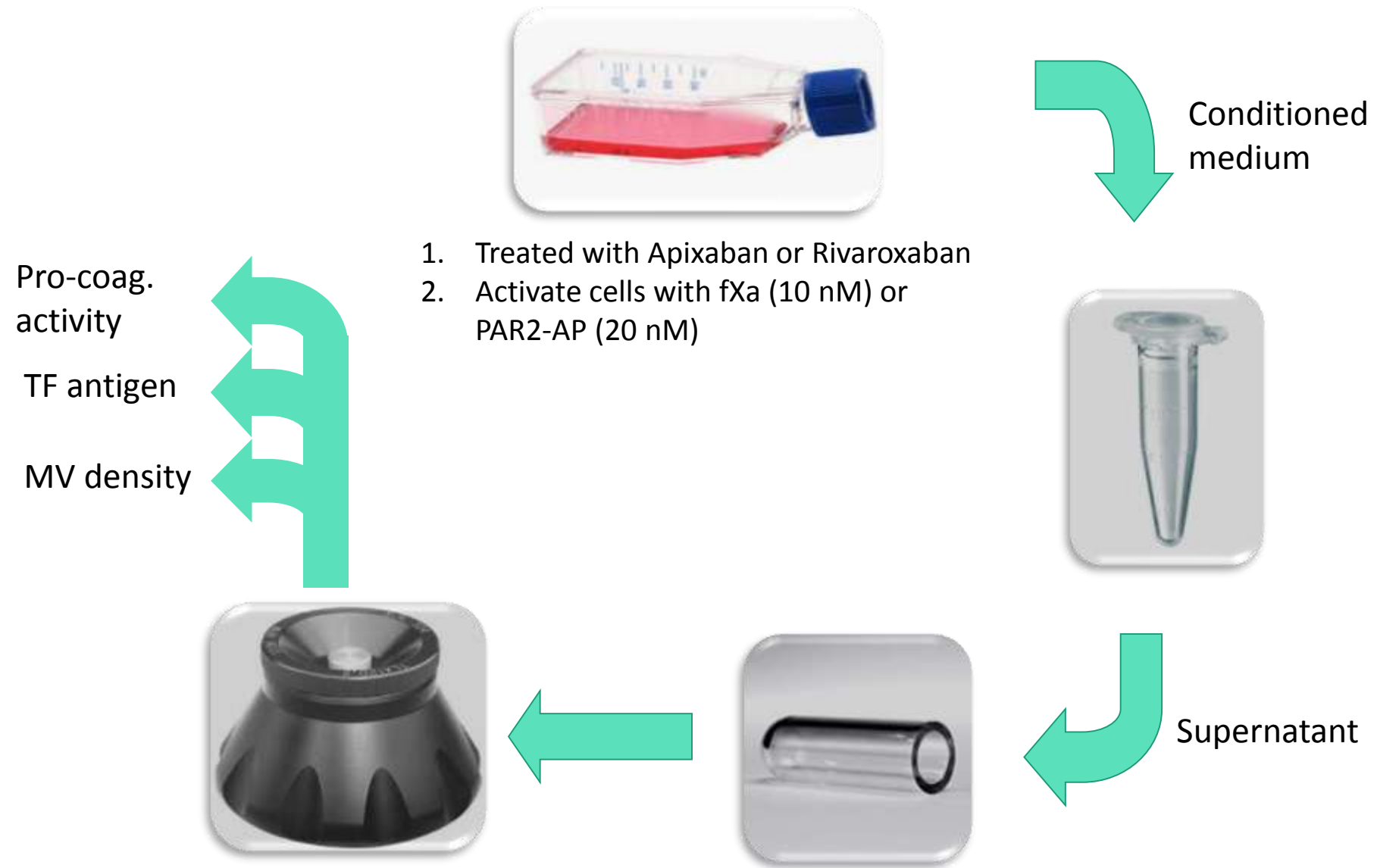
Rivaroxaban



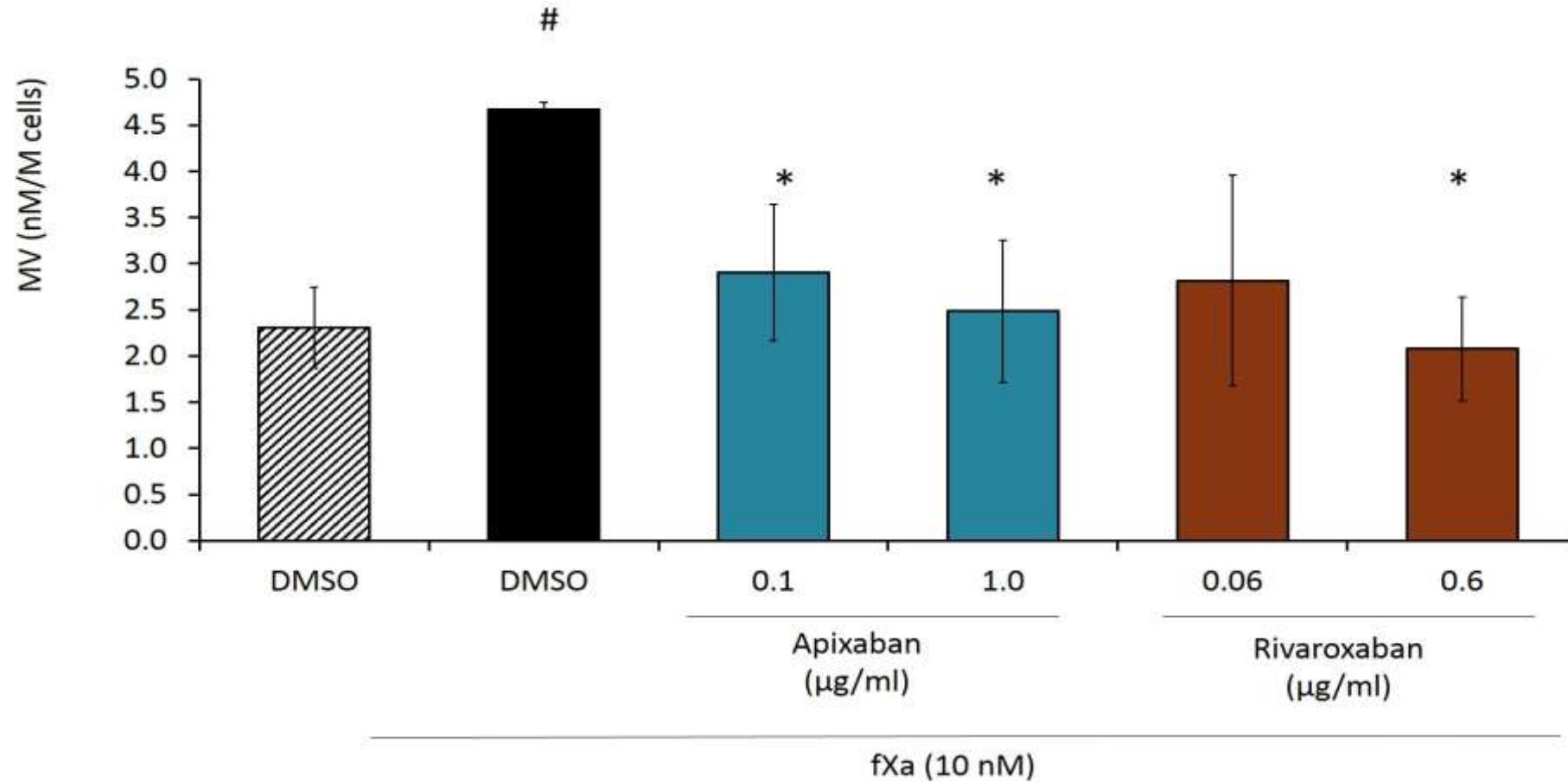
0.46-0.10 µg/ml

0.6 µg/ml

Procedure: Preparation of microvesicles

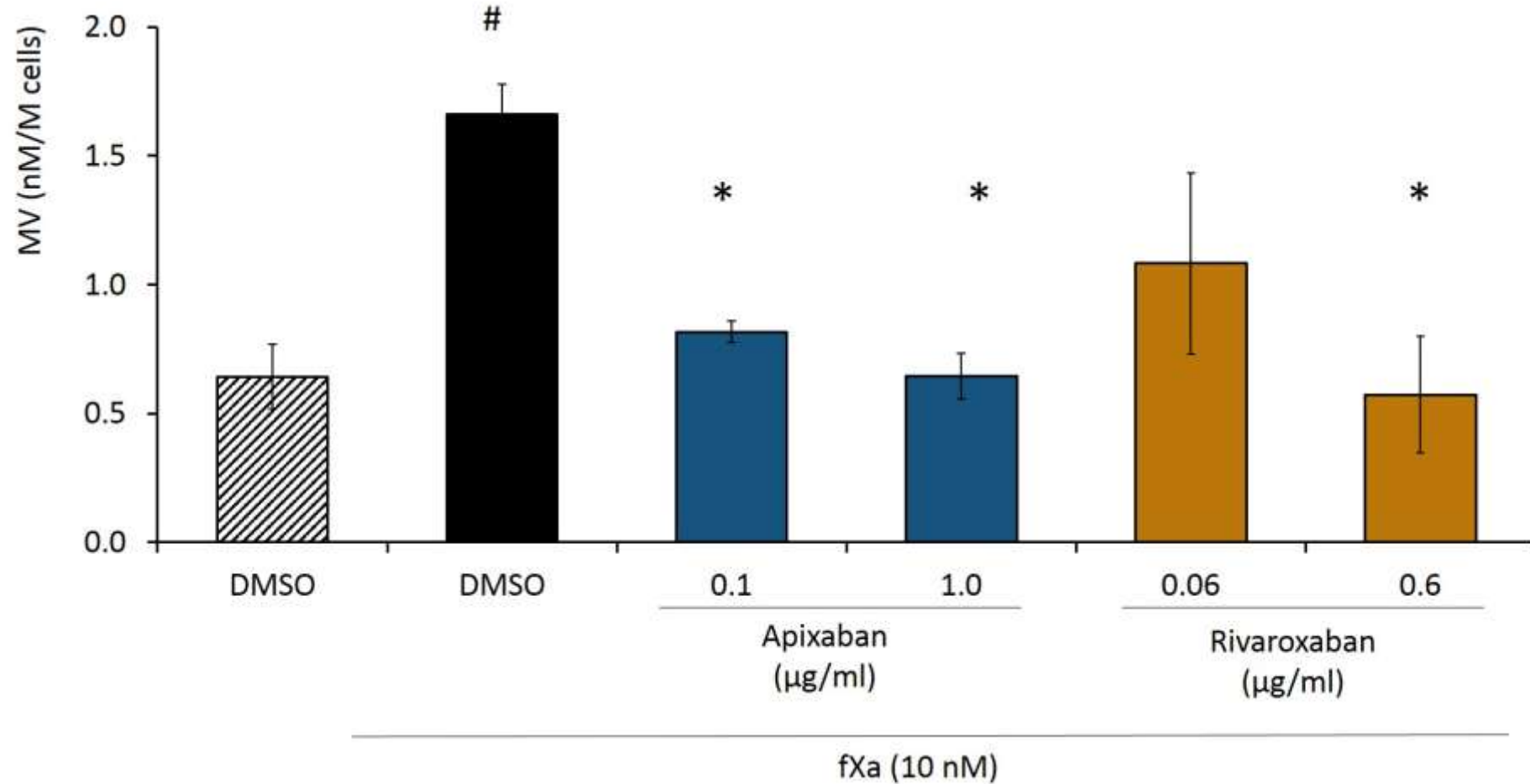


DOACs suppress fXa-mediated MV release from MDA-MB-231 cells



n= 3, error bars = SEM
- P vs DMSO only < 0.05
* - P vs DMSO + fXa < 0.05

DOACs suppress fXa-mediated MV release from AsPC-1 cells

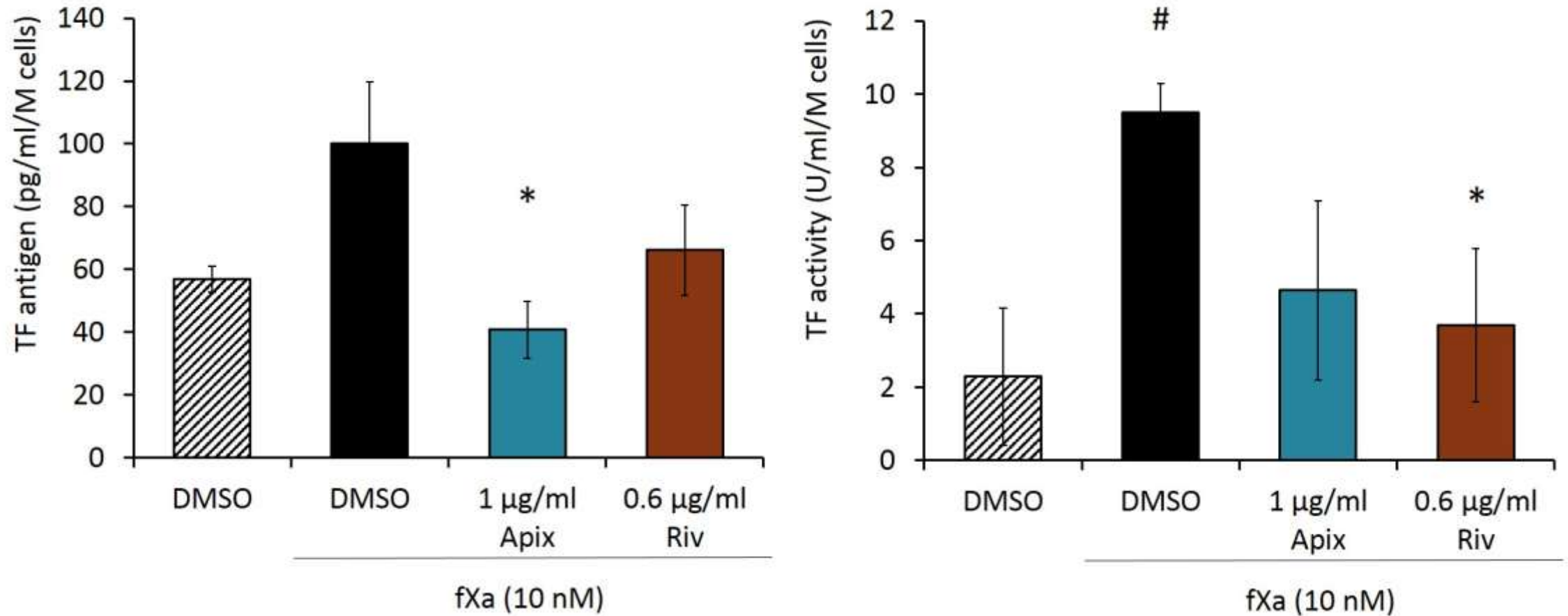


n= 4, error bars = SEM

- P vs DMSO only < 0.05

* - P vs DMSO + fXa < 0.05

Influence of DOACs on fXa-mediated TF release and activity from MDA-MB-231 cells

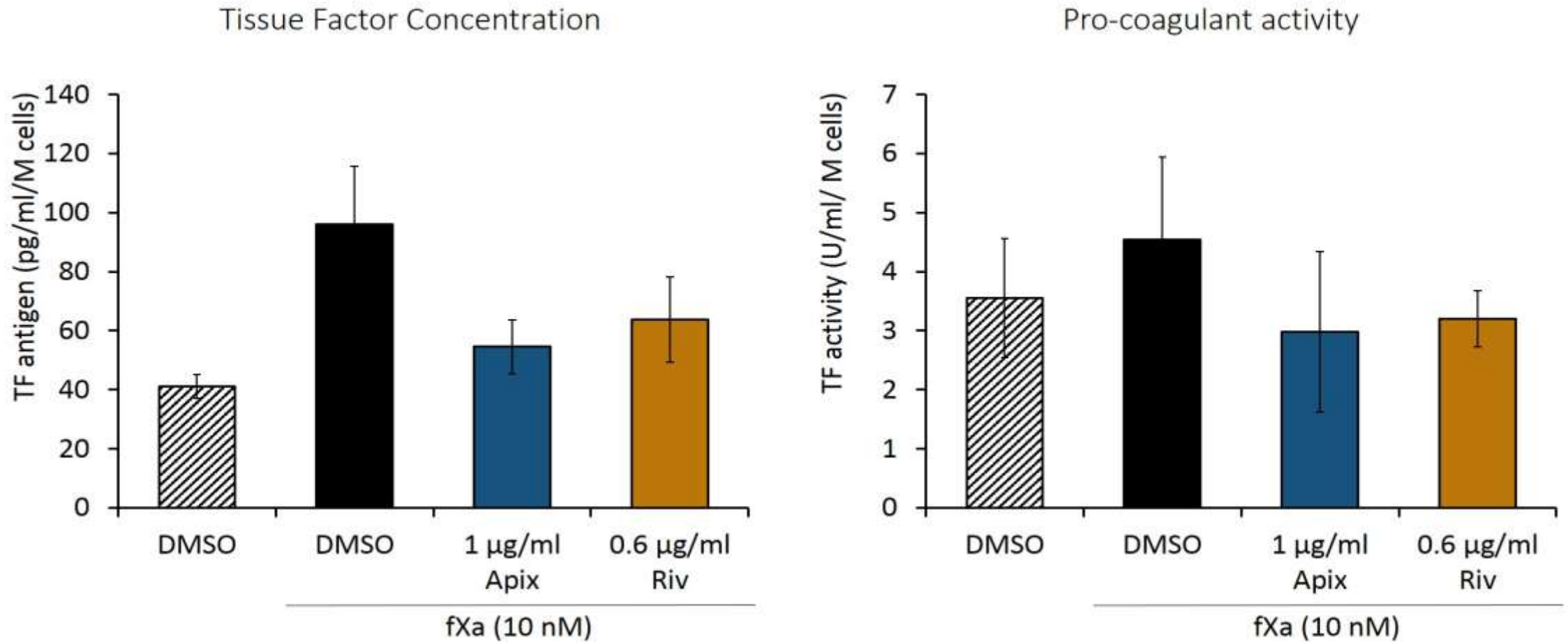


n= 3, error bars = SEM

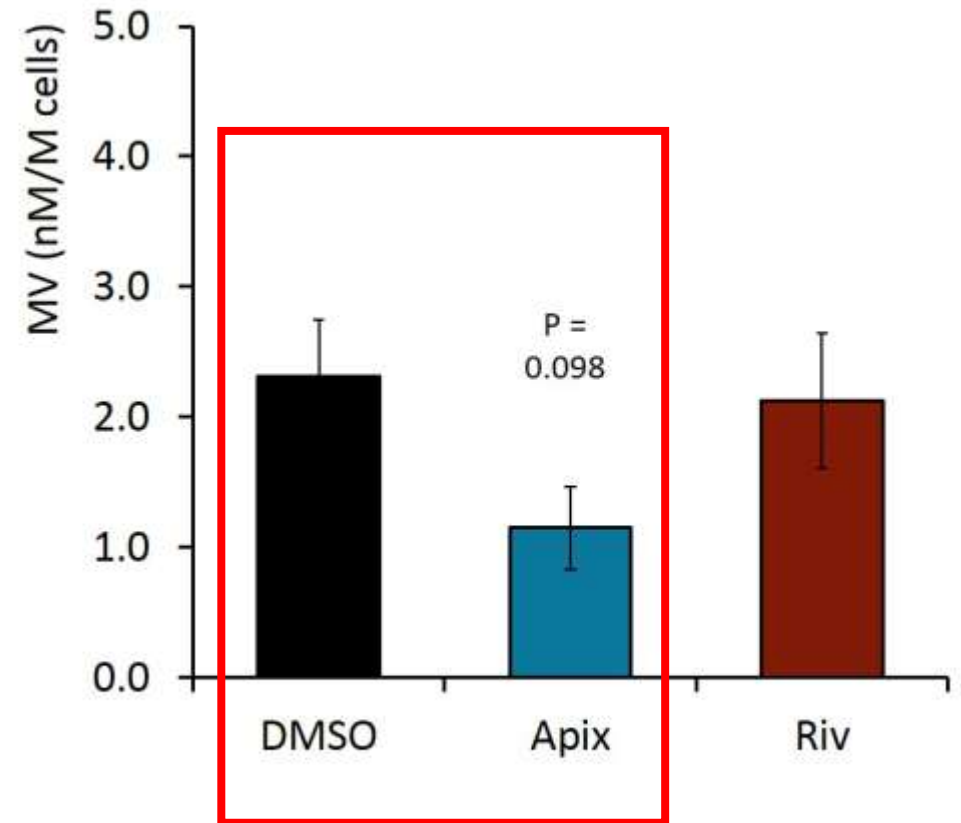
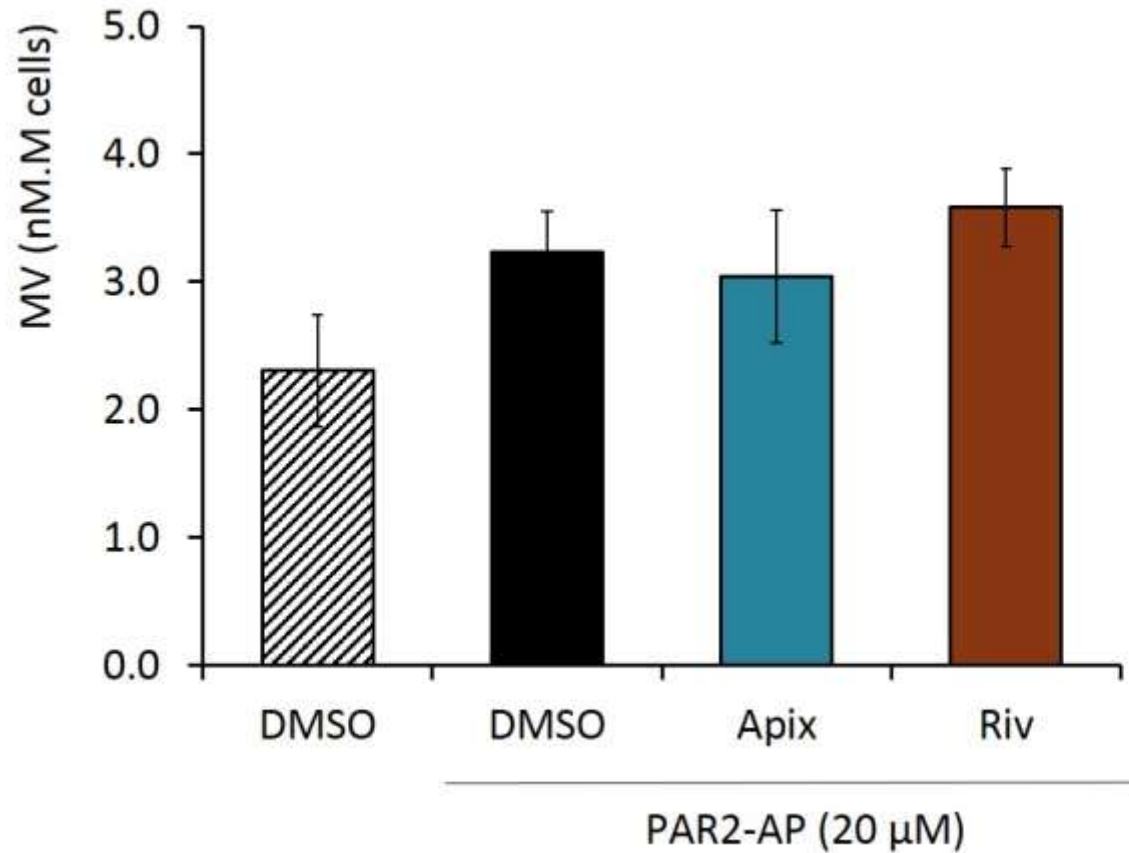
* = P vs DMSO + fXa < 0.05

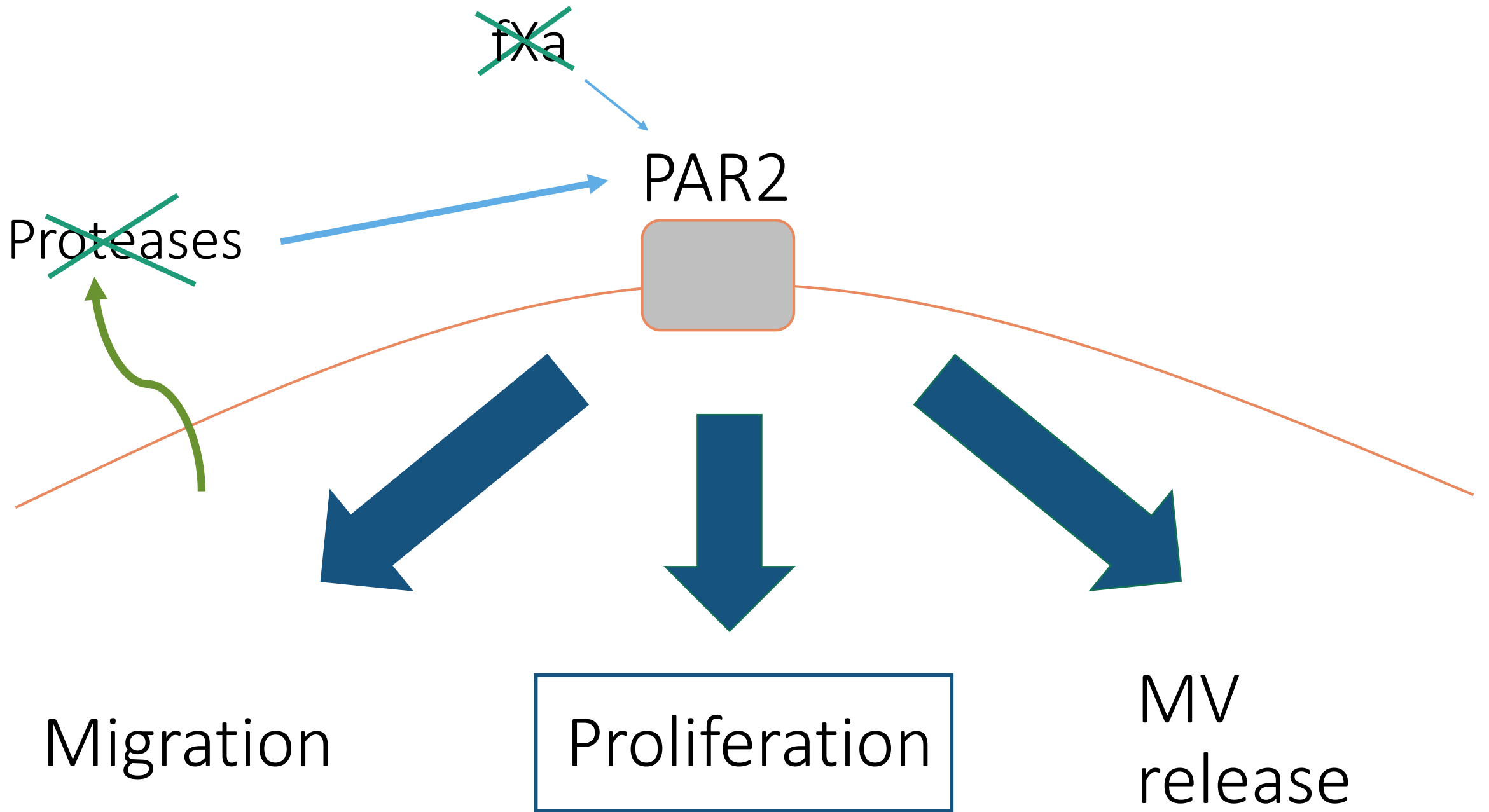
= P vs DMSO only < 0.05

Influence of DOACs on fXa-mediated TF release and activity from AsPC-1 cells

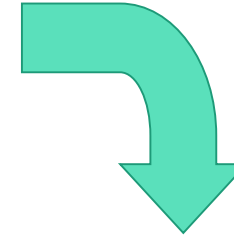


DOACs do not interfere with protease-independent (PAR2-AP) MV release from MDA-MB-231 cells

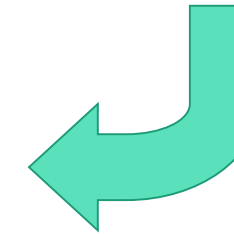
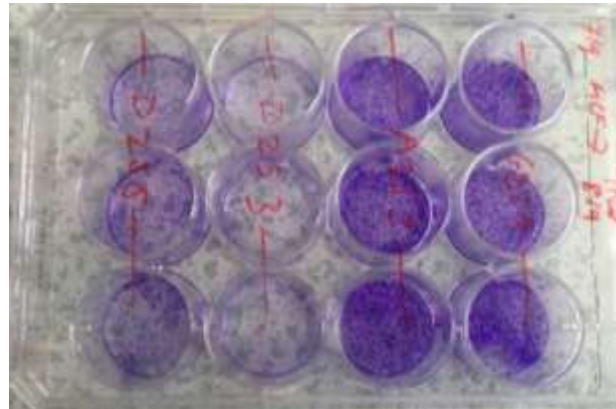




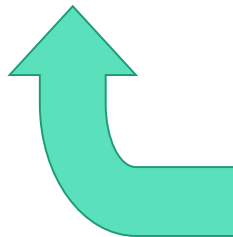
Procedure: Crystal violet proliferation assay



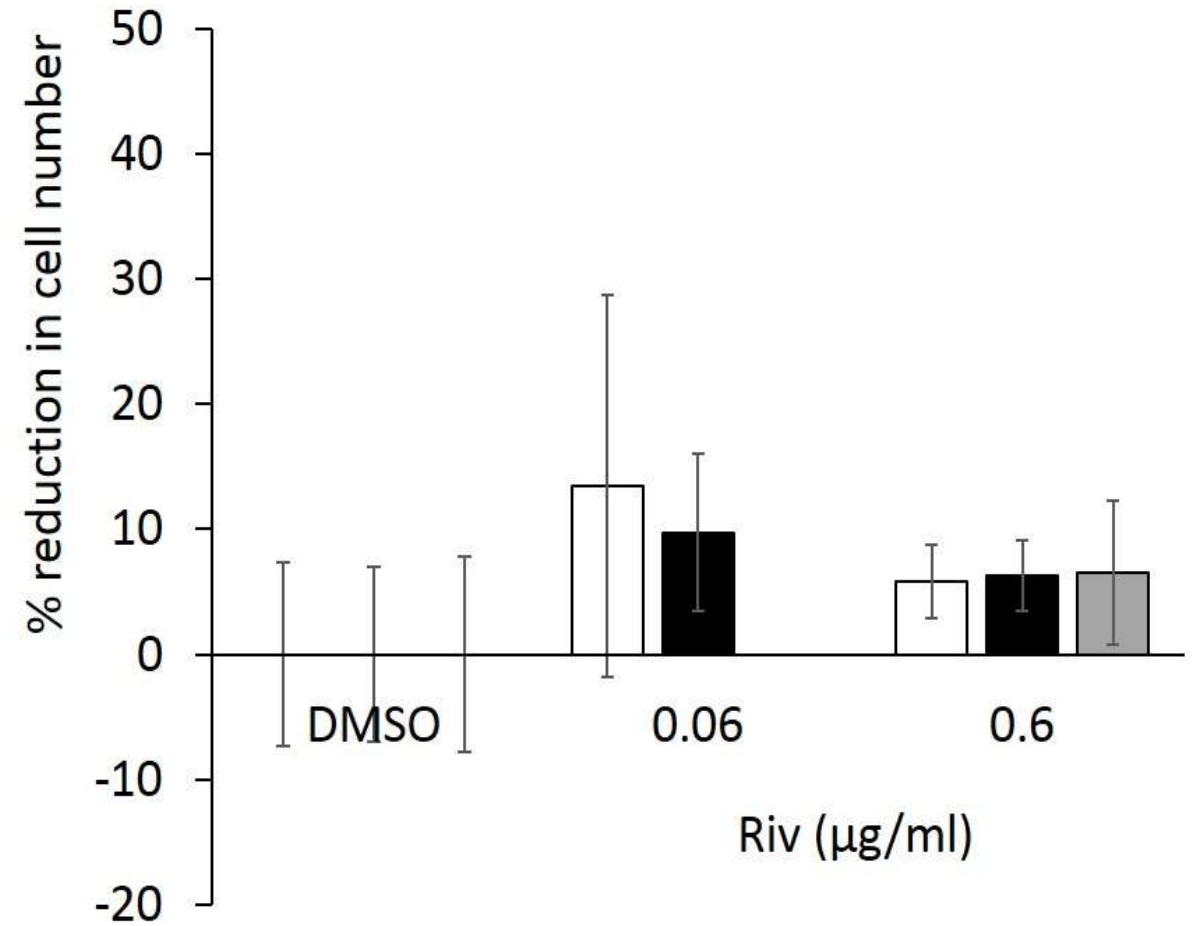
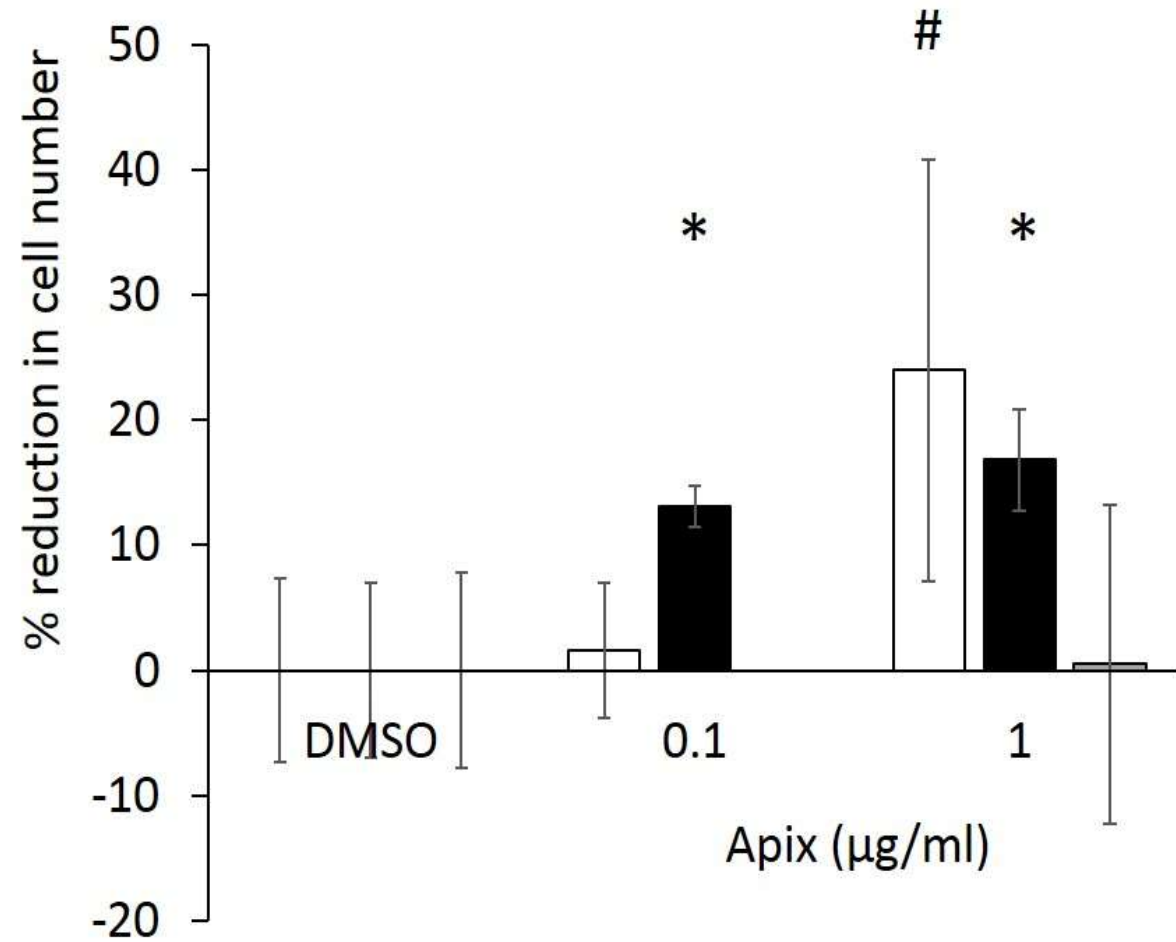
+ Apixaban or
Rivaroxaban



72 h



DOACs suppress cancer cell proliferation



n= 4, error bars = SEM

* - P vs DMSO treated AsPC-1 <0.05

- P vs DMSO treated MDA <0.05

□ MDA-MB-231 ■ AsPC-1 ■ Endo

Conclusions

- Apixaban and Rivaroxaban reduce fXa induced TF₊MV release.
- Apixaban reduces TF₊MV release from resting cells.
- Apixaban reduces cancer cell proliferation but not endothelial cell proliferation.

Acknowledgements

Dr Camille Ettelaie

Prof Anthony Maraveyas



Thank you for listening

- Any Questions?

fXa activation in presence of PAR2 inhibitor antibody

