



# JCET

Jagiellonian Centre  
for Experimental Therapeutics

## ENDOTHELIAL PROFILING OF DRUG CANDIDATES

CLINICALLY-RELEVANT EFFICACY STUDIES

PREDICTIVE SAFETY ANALYSIS

EXPLORATORY STUDIES ON NEW INDICATIONS

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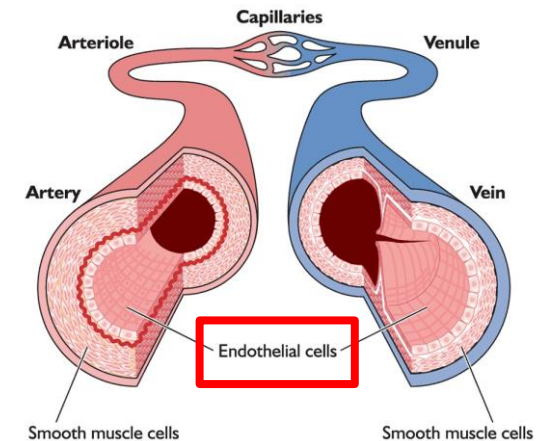
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## WHY ENDOTHELIAL PROFILING?

- vascular endothelium - the largest interface for systemic drugs
- **drug-induced endothelial/vascular dysfunction** - notable clinical failures – yet neglected in drug development
- endothelial dysfunction **predicts cardiovascular events**
- **endothelial function profiling** can detect vascular toxicity
- but also identify **favourable vasoprofile** of drug candidates



Lonza Bioscience



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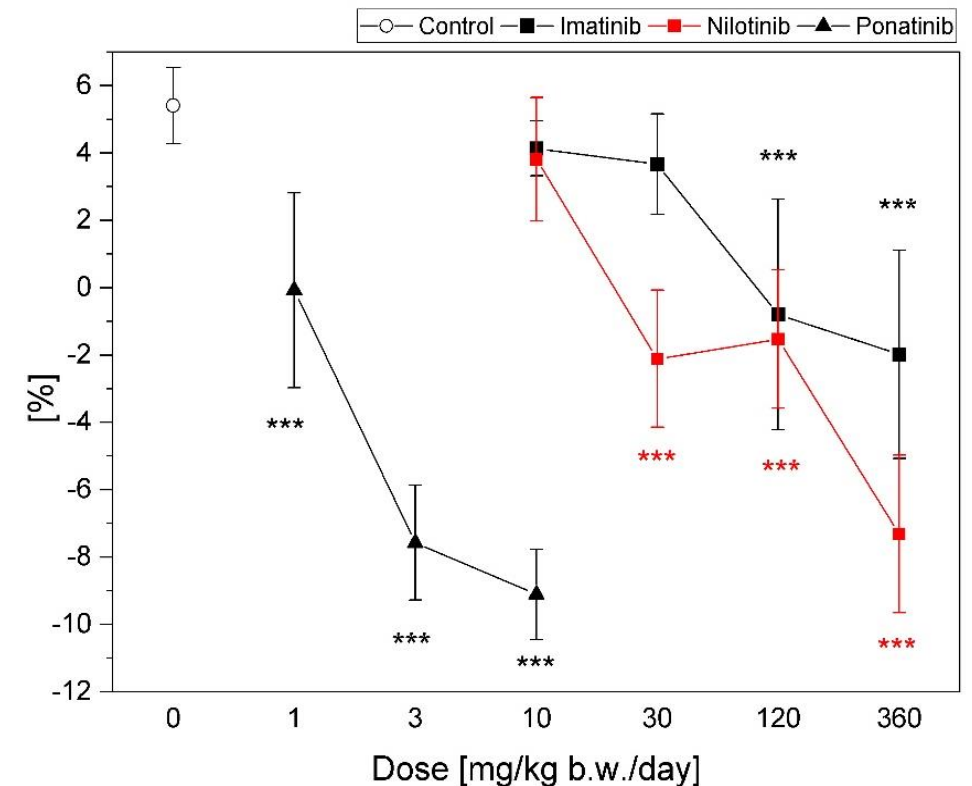
# ENDOTHELIAL PROFILING OF DRUG VASOTOXICITY

## SIGNIFICANCE FOR DRUG DISCOVERY AND DEVELOPMENT

- demonstration of drug-induced endothelial **function impairment *in vivo*** in mice
- direct evidence of **subtle, yet differentiating** endothelium-dependent response
- dose-dependent endothelial dysfunction at clinically-relevant dosing
- track record of studies based on our state-of-the-art 3D MRI method *in vivo*
- **your compound could be next!**

## USE CASES FOR VASOTOXICITY PROFILING *IN VIVO*

- **risk assessment** for new compounds
- **understanding the mechanisms** of toxicity
- lead selection and **candidate nomination**
- managing clinical development risk
- improved out-licensing data package
- deeper in-licensing due diligence





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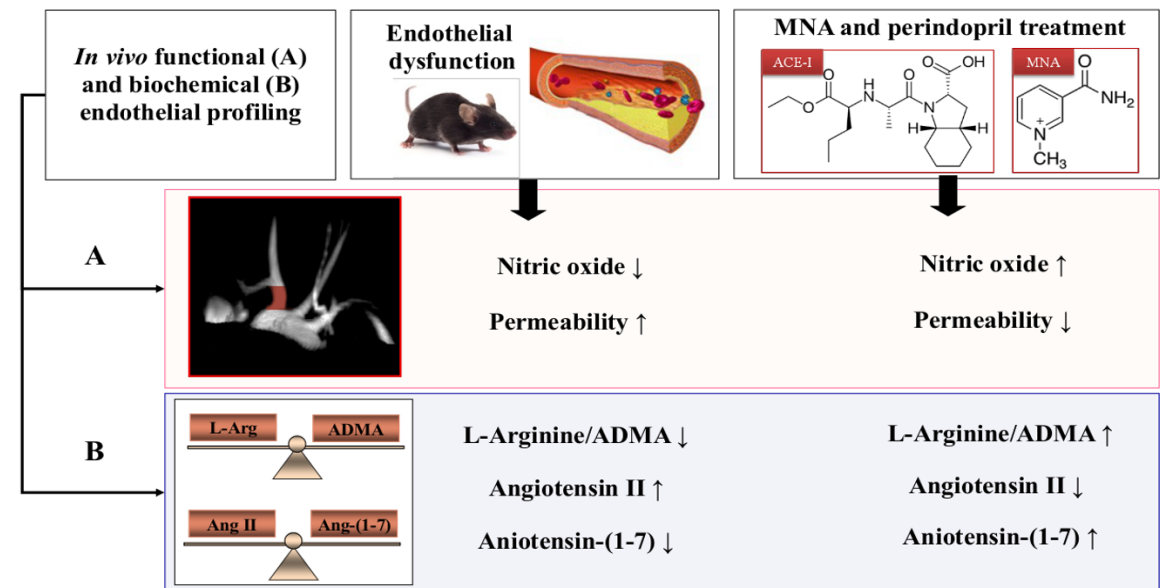


## ENDOTHELIAL PROFILING OF DRUG EFFICACY SIGNIFICANCE FOR DRUG DISCOVERY AND DEVELOPMENT

- demonstration of drug-induced **improvement in endothelial function** *in vivo* in mice
- based on a number of **clinically-relevant animal models** operated by JCET
- efficacy can be **directly compared** to approved drugs/competitive compounds
- track record of studies based on our state-of-the-art 3D MRI method *in vivo*
- **your compound could be next!**

# ENDOTHELIAL/VASCULAR PROFILING OF *IN VIVO* EFFICACY

- detection of **vasoprotective profile**
- understanding the protective mechanisms
- exploring **new therapeutic areas**
- **drug repurposing/repositioning**
- improved out-licensing data package
- deeper in-licensing due diligence





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## ENDOTHELIAL PROFILING AT JCET

- scientific expertise - **centre of excellence in endothelial research**, 40+ top-tier publications in 2021
- original experimental approach based on **internal know-how and experienced team** [1]
- methodology successfully used and validated in a **number of indications/animal models** in large vessels [2-7], as well as in recently-developed approach to study **microvasculature** [8]

[1] Bar et al. (2016) *NMR in Biomedicine*, 29(8):1088

[2] Sternak et al. (2018) *Frontiers in Pharmacology*, 9, 178

[3] Bar et al. (2019) *Vascular Pharmacology*, 106581

[4] Bar et al. (2019) *Journal of the American Heart Association*, 8(6), e011171

[5] Bar et al. (2020) *Journal of the American Heart Association*, 9(21), e016929

[6] Proniewski et al. (2021) *Cells*, 10(6), 1448

[7] Mohaisen et al. (2021) *Cardiovascular research*, cvab306

[8] Kwiatkowski et al. (2021) *Scientific reports*, 11(1):18915

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