EFMC-YMCS
Young Medicinal Chemists' Symposium
Virtual Event
September 9-10, 2021

UNIVERSITÀ DEGLI STUDI DI TORINO
POLITECNICO MILANO 1863
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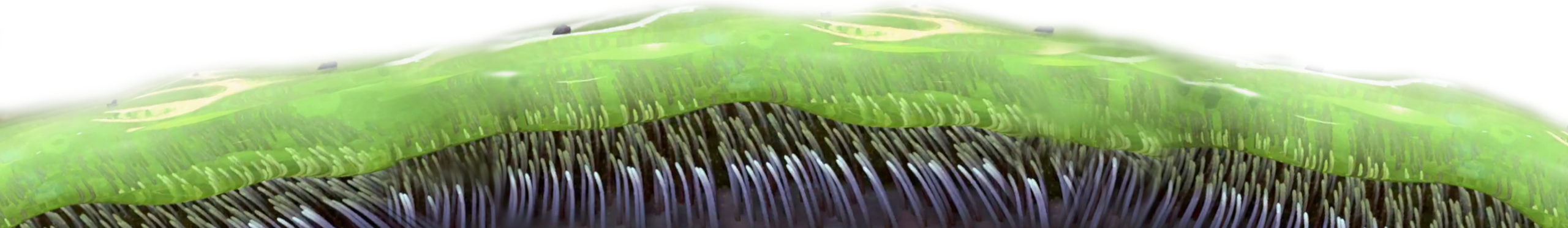
Untie the skein: deciphering the mechanism governing the interaction of drugs with mucus using a biosimilar mucus model

Cosmin Butnarasu, Daniela Peneda Pacheco, Sebastiao van Uden, Paola Petrini, Livia Visai, Giulia Caron, Sonja Visentin

Introduction | mucus protect us

Mucus is the
body's first line of defense



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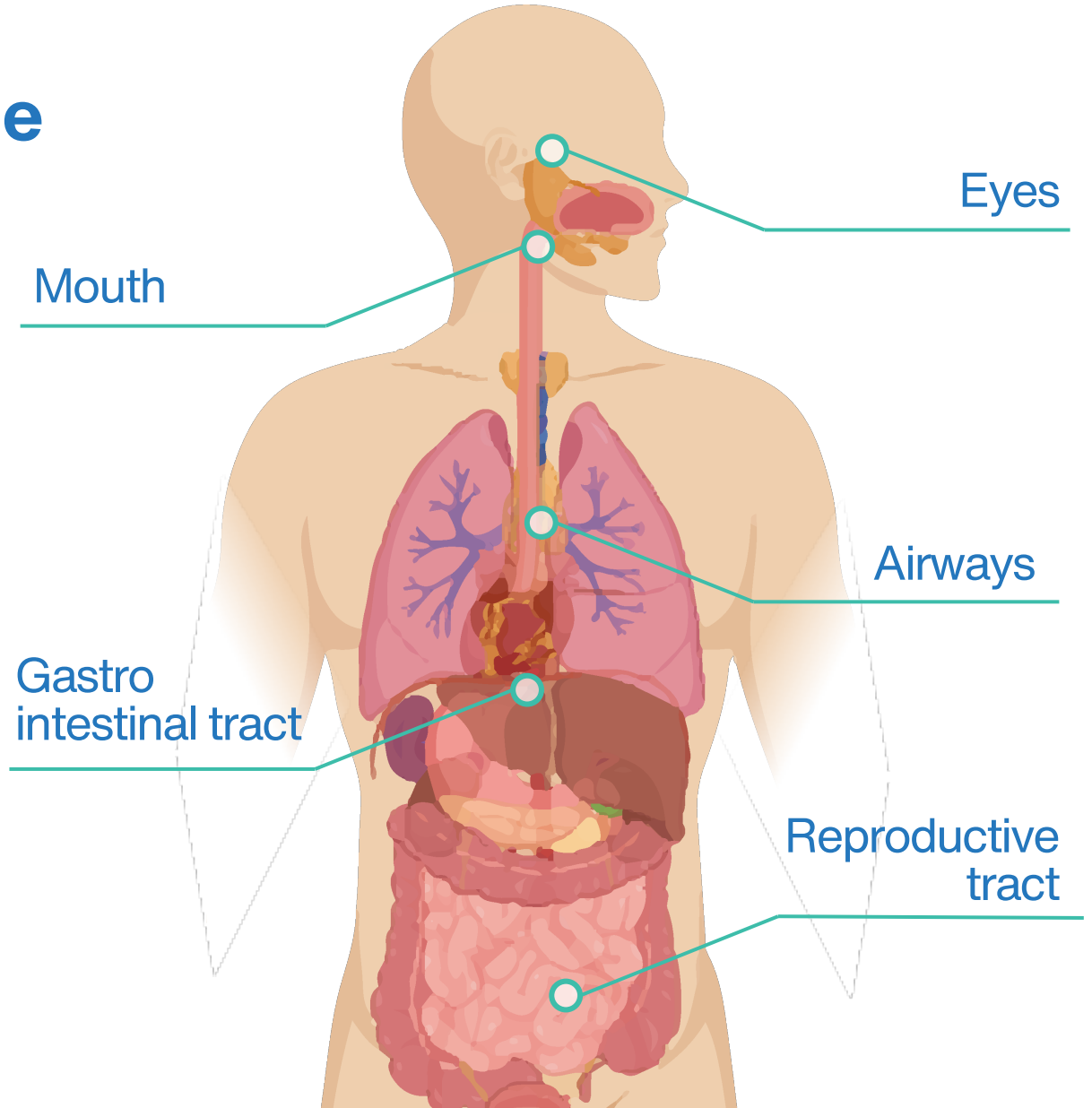
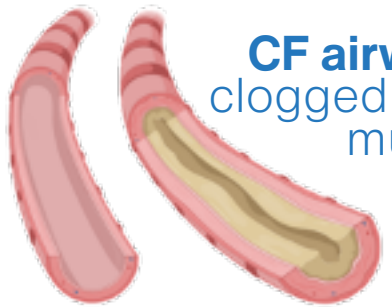


Introduction | mucus can be a barrier for the absorption of drugs

Mucus is the **body's first line of defense**

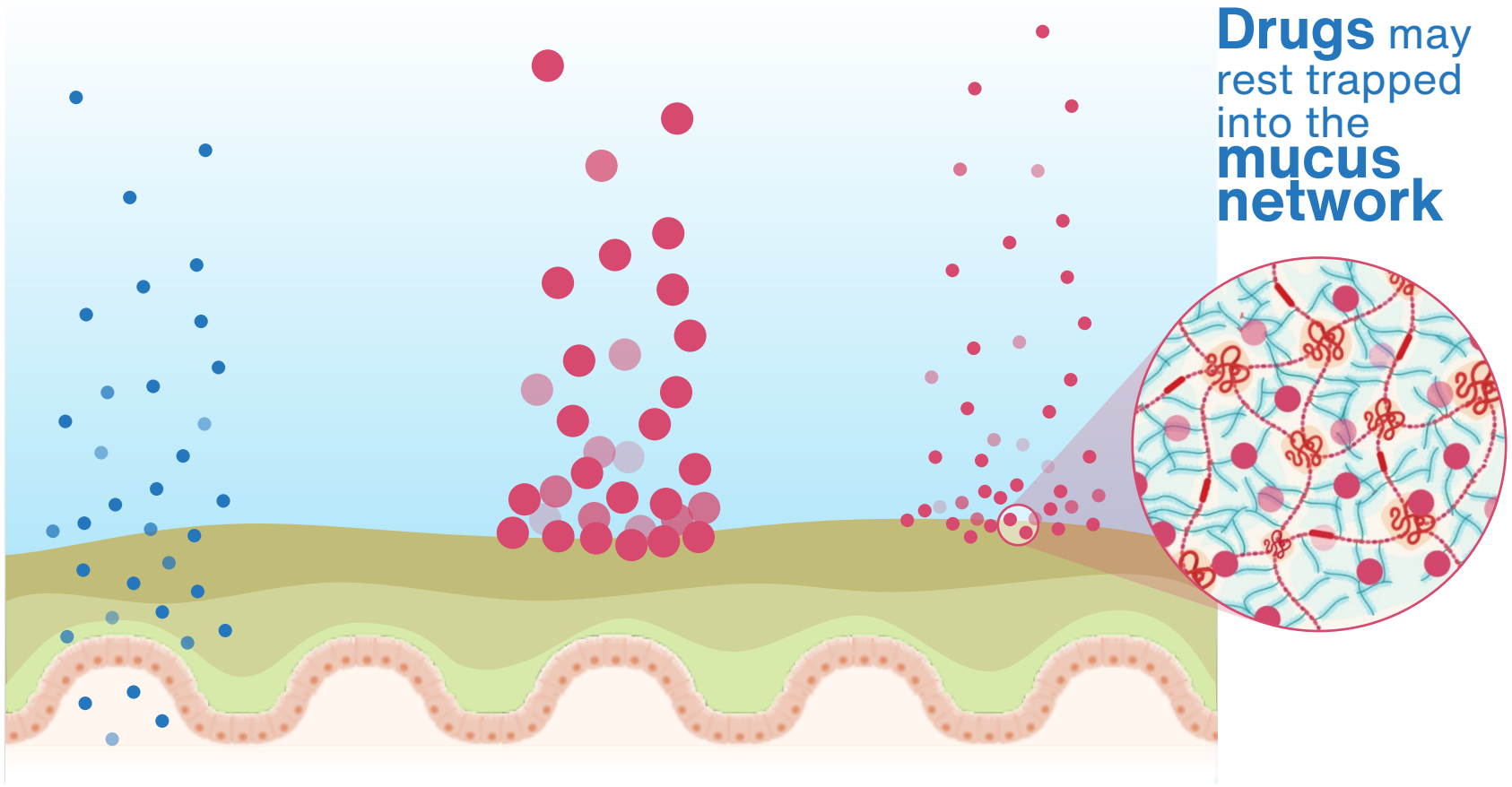
Disorders associated with mucus overproduction

- Cystic fibrosis
- COPD
- Asthma



CF airways clogged with mucus

Normal Cystic fibrosis



[1] Leal J., et al., Int. J. Pharm, Vol. 532, (2017), 136-144, DOI 10.1016/j.ijpharm.2017.09.018

Aim | a biosimilar mucus model to study the diffusion of drugs

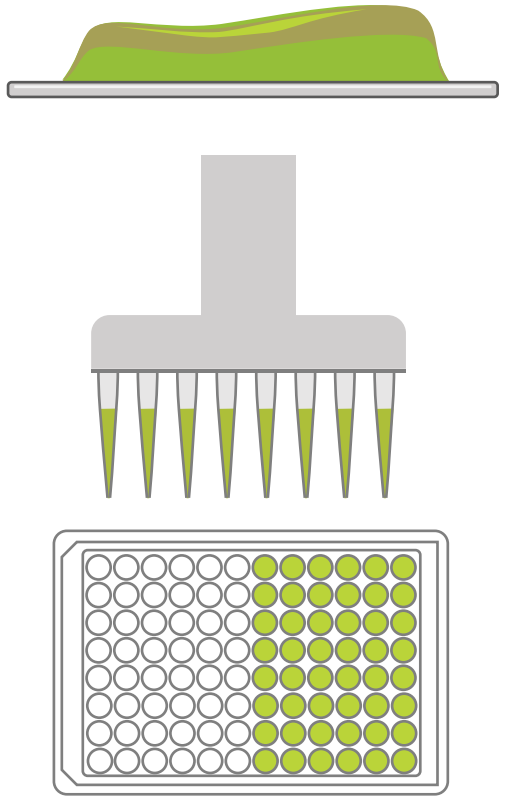
What we need

Realistic 3D *in vitro* mucus model

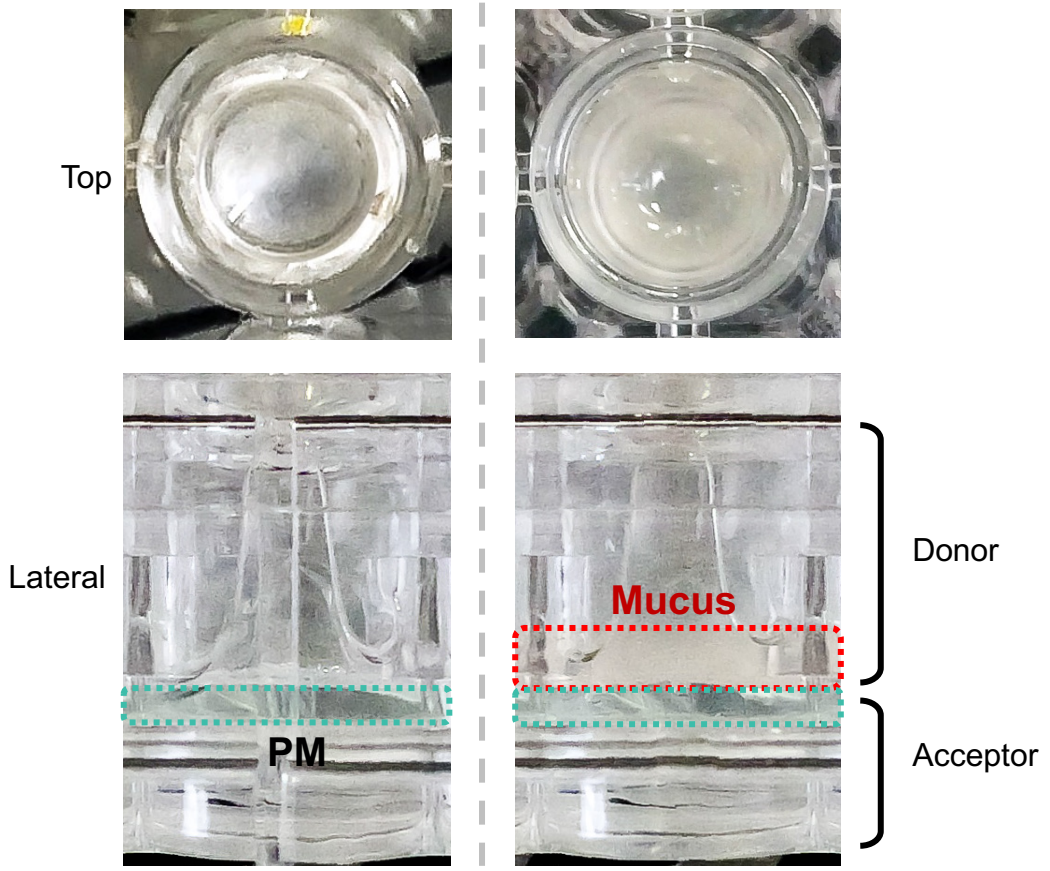
Standardized model suitable for HTS purposes

Reduce ineffective drug candidates

Cystic fibrosis
mucus model



PAMPA plate



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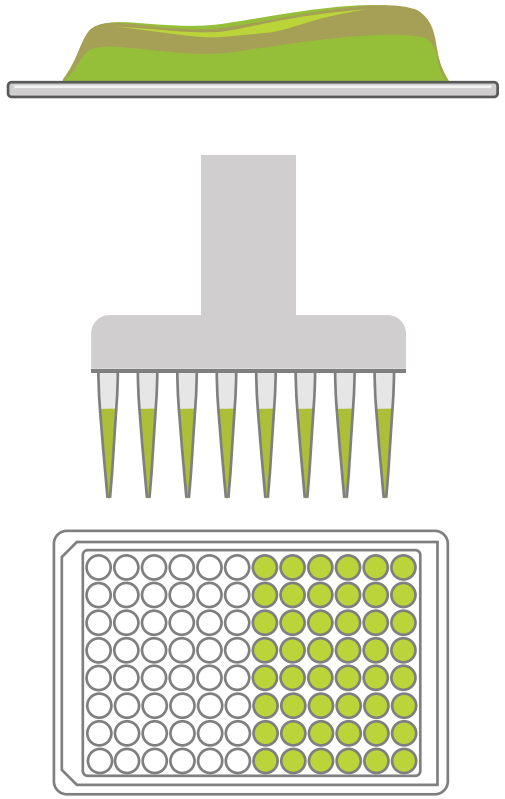

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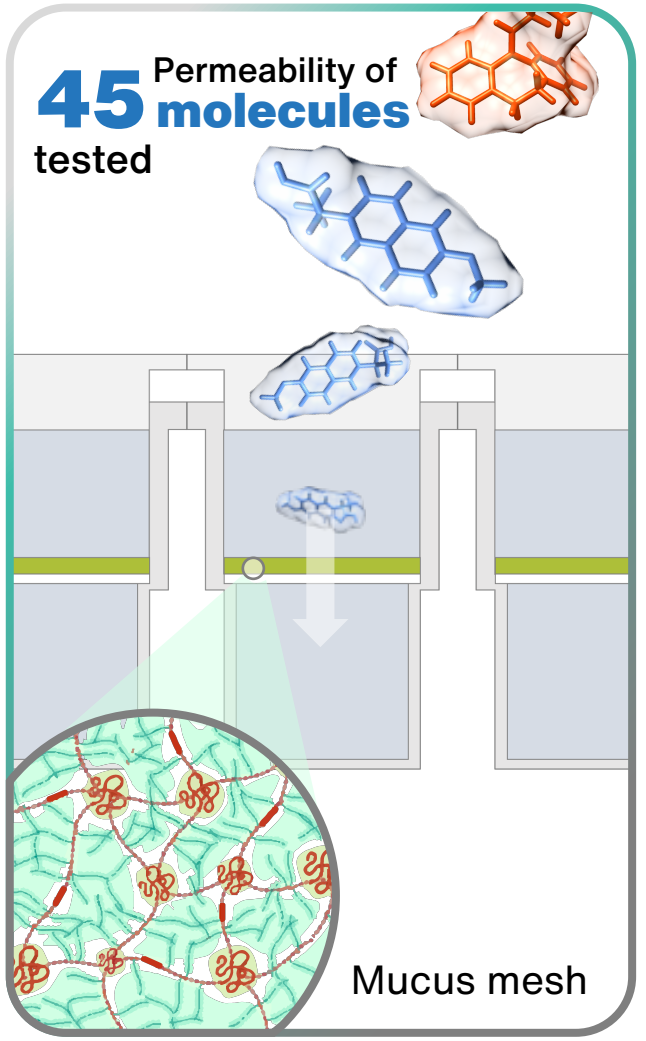
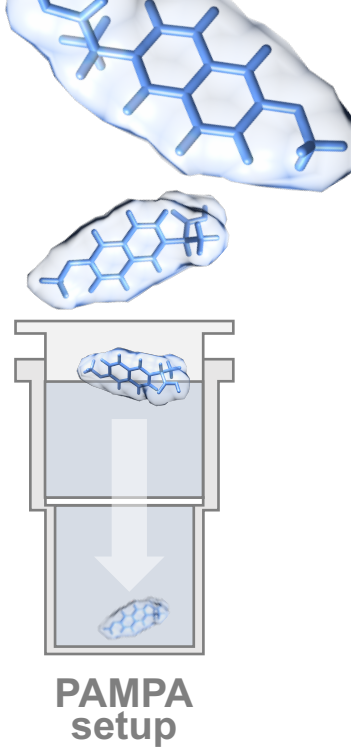
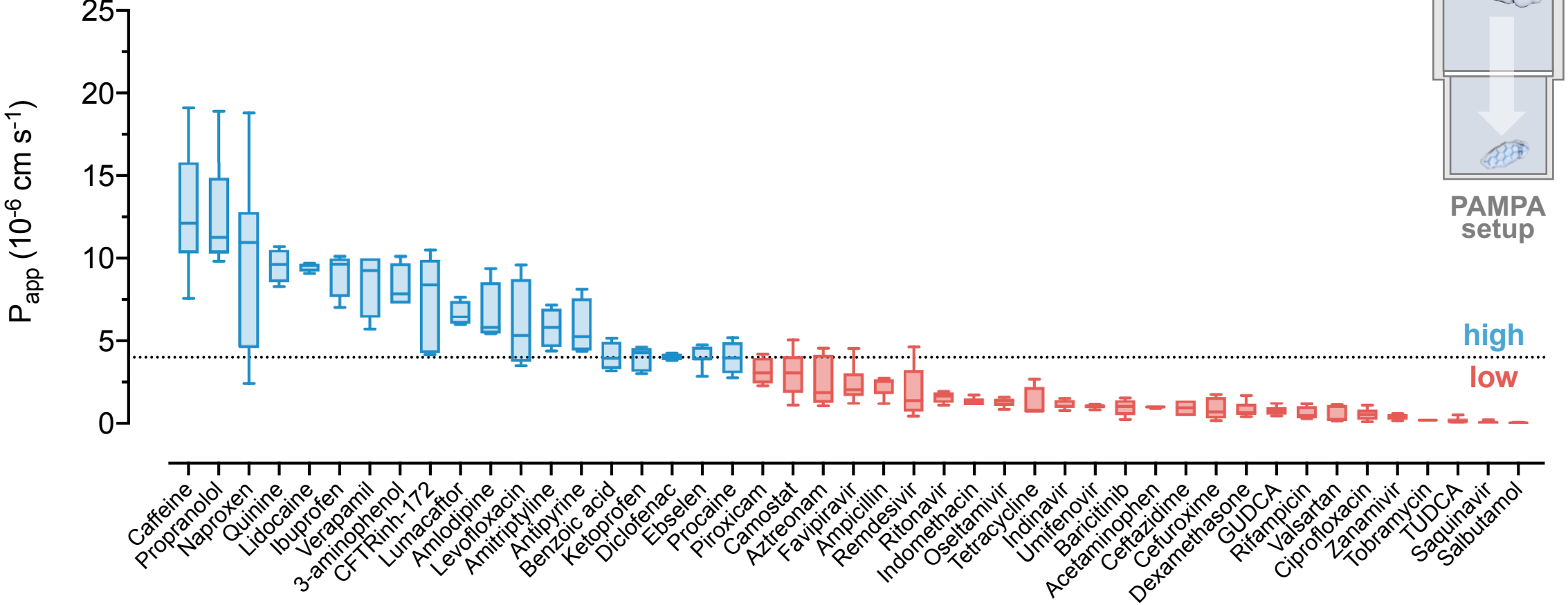


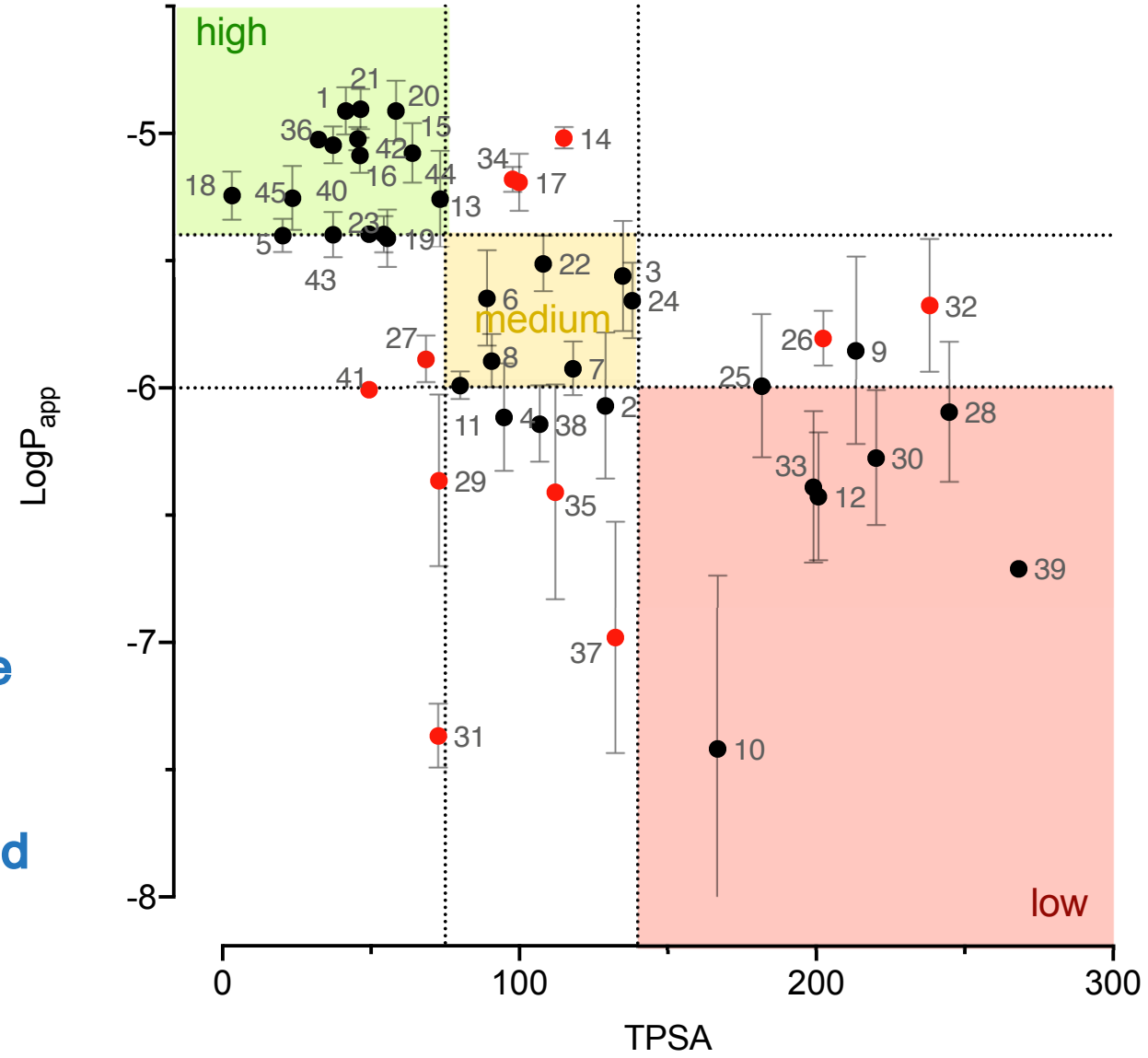
Results| Validation of the permeability setup



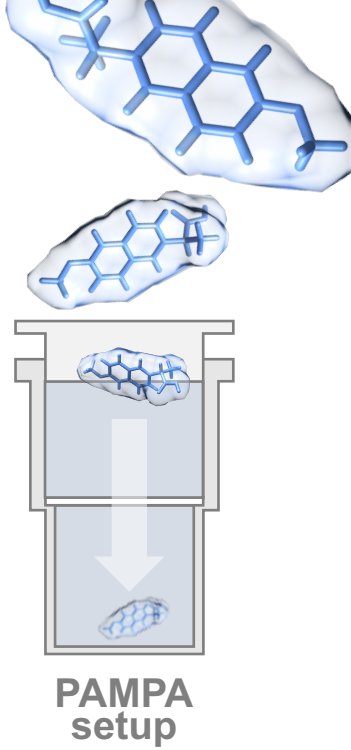


Results| Validation of the permeability setup

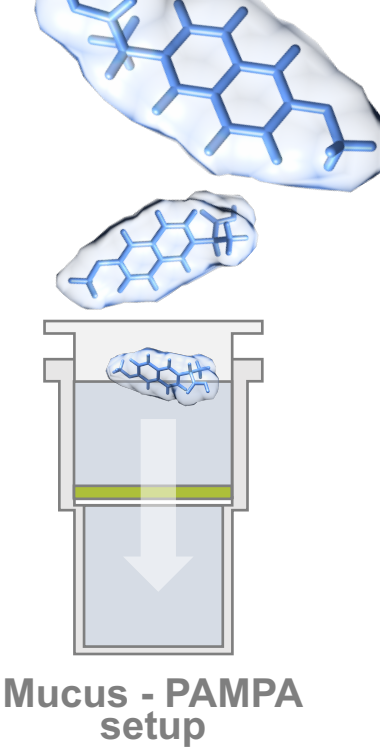
Good correlation of P_{app} with TPSA



80% of the drugs had the P_{app} correctly predicted based on the TPSA



Results| The mucus model is an interactive barrier

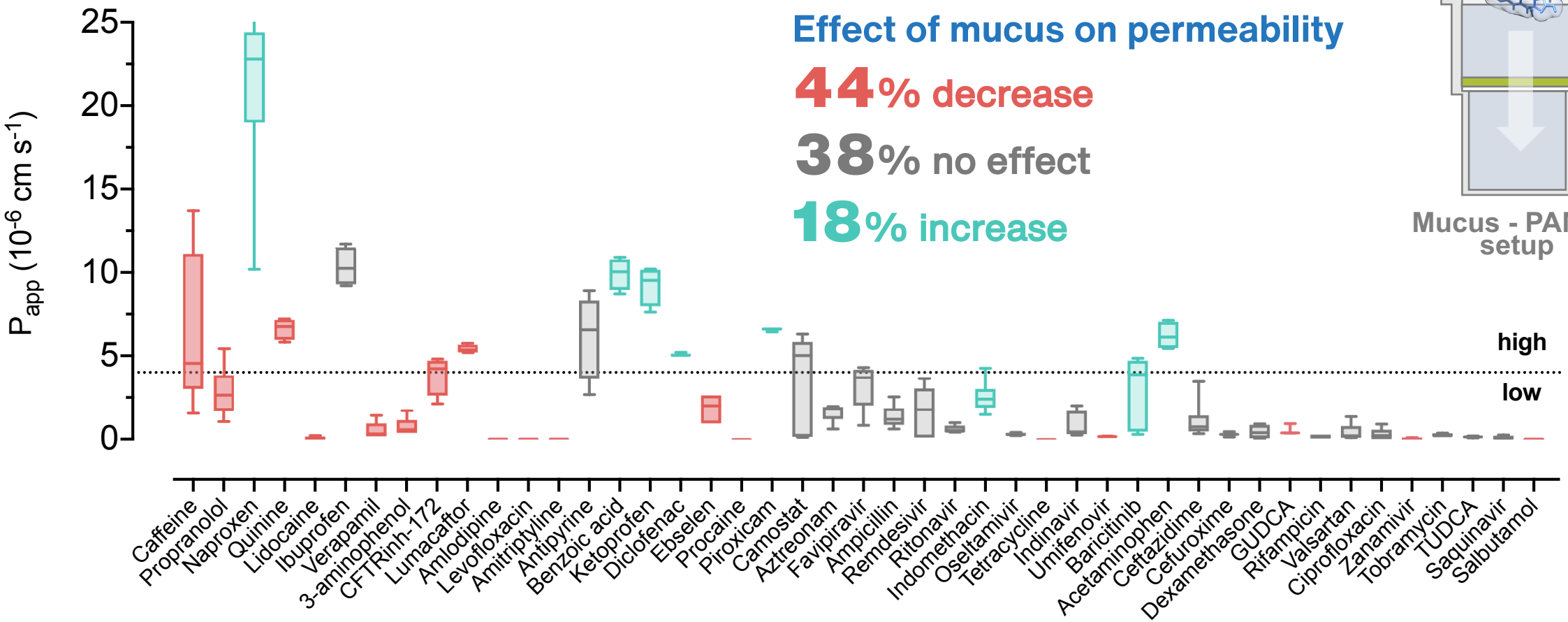


Effect of mucus on permeability

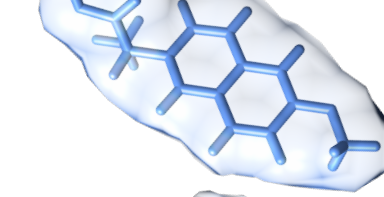
44% decrease

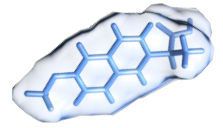
38% no effect

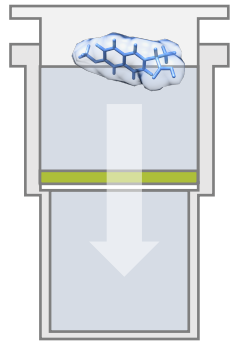
18% increase



Results| The mucus model is an interactive barrier

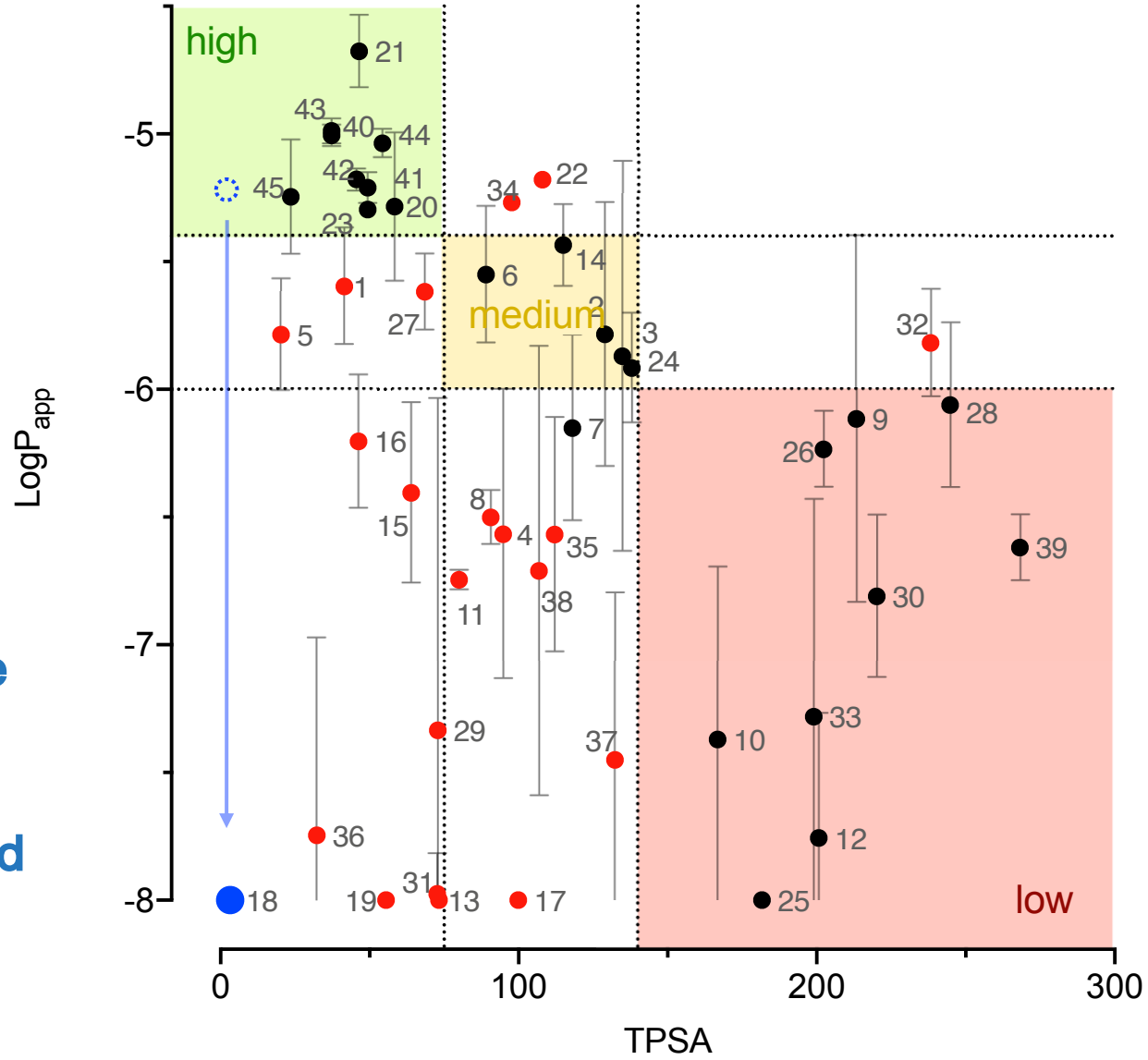




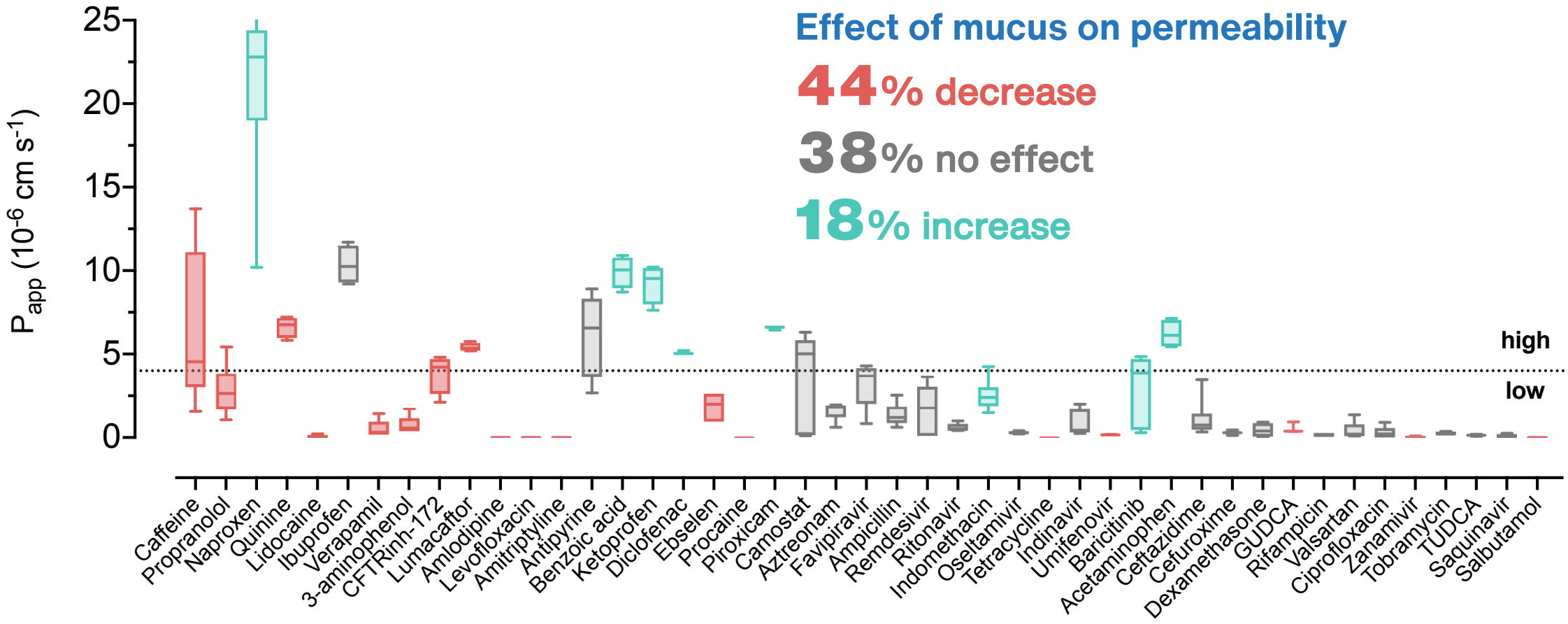


Mucus - PAMPA setup

57 % of the drugs had the P_{app} correctly predicted based on the TPSA



Results| On the increased permeability in presence of mucus



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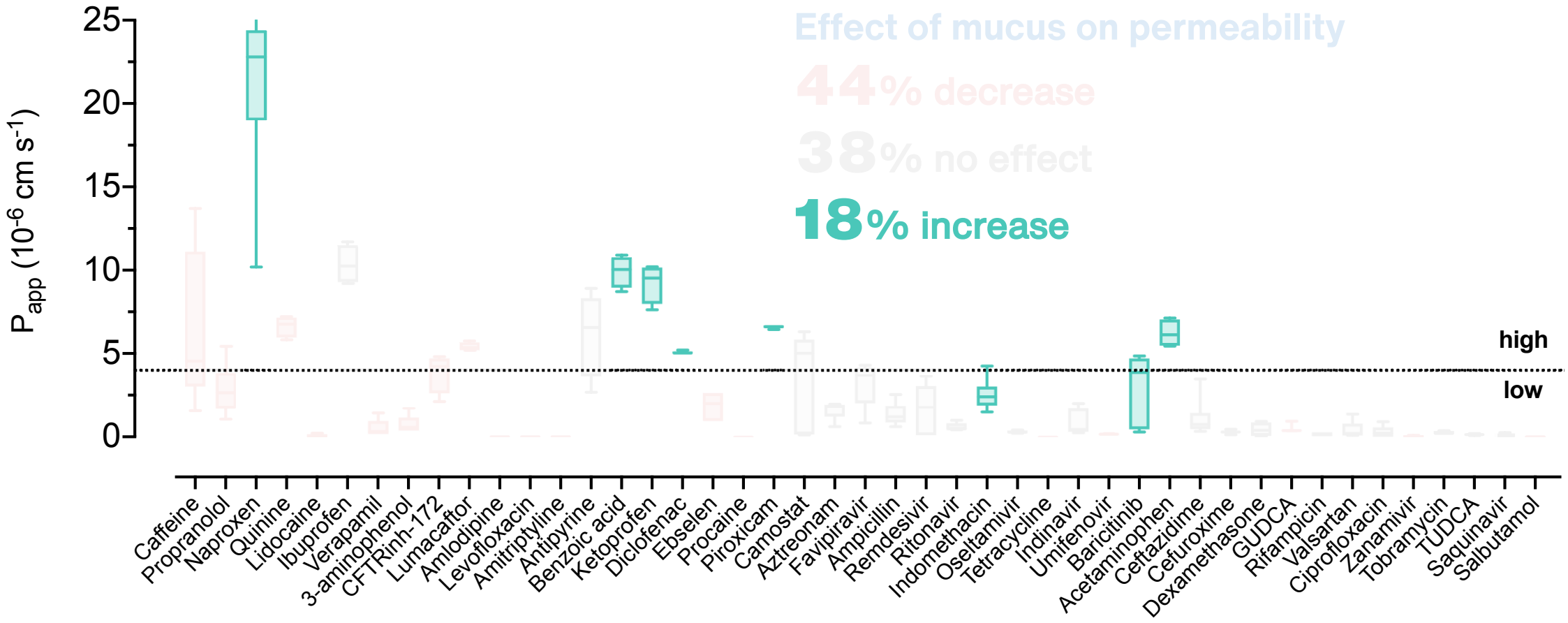
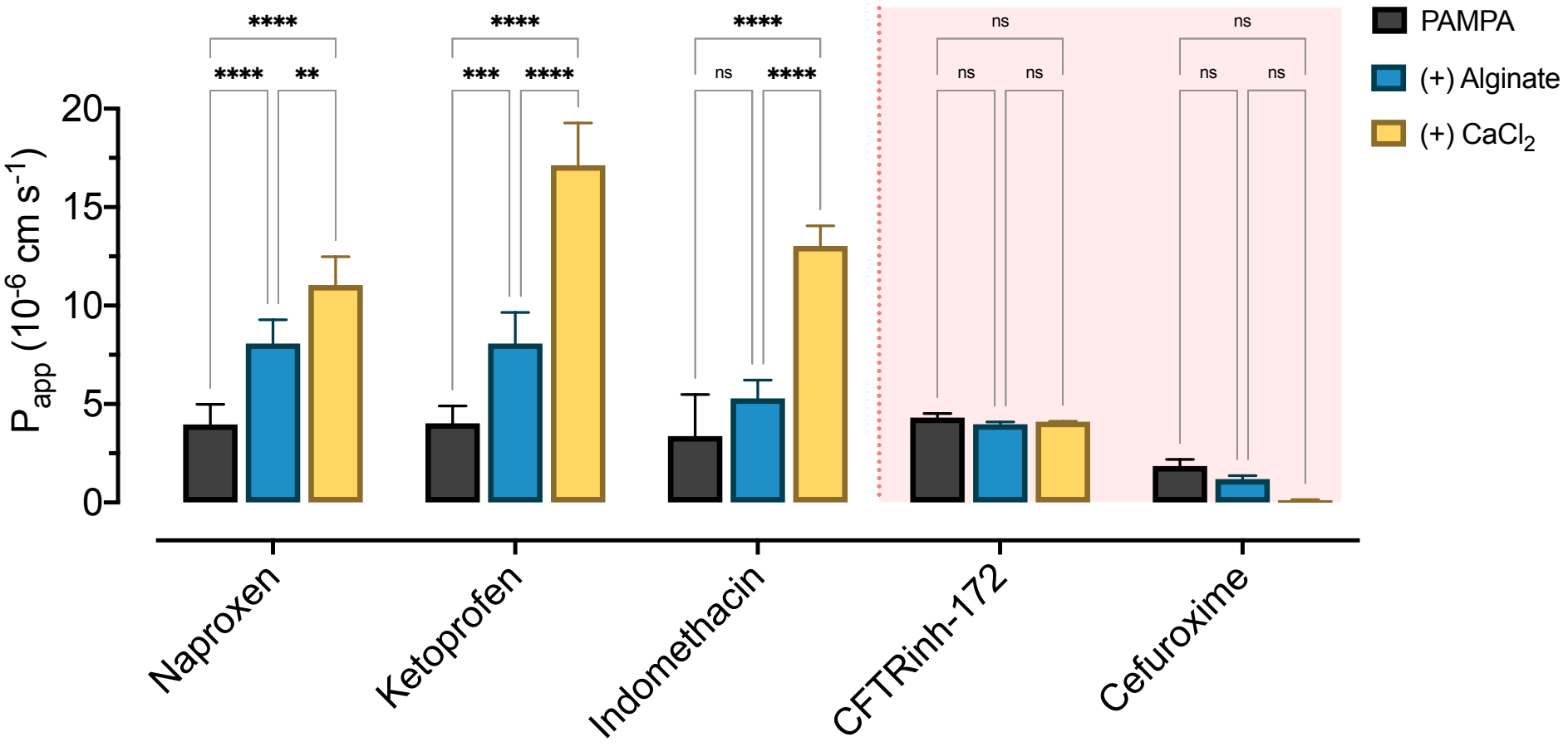


Results| Calcium-drug salts increase drug permeability



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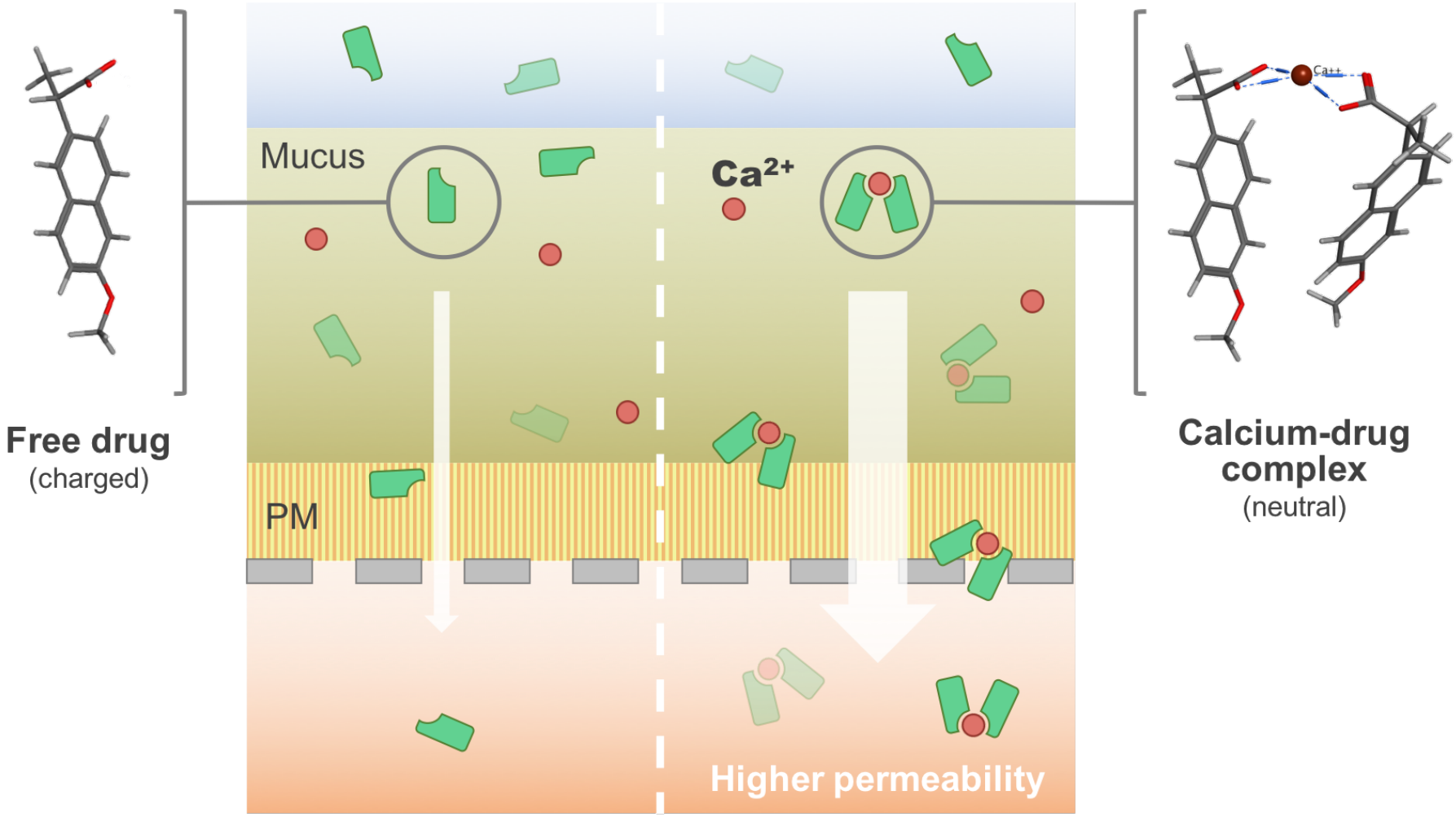

Conclusions

The effect of mucus is difficult to predict in pathological conditions and the PAMPA system is a too simplistic model

Retention within mucus is a complex phenomenon. Permeability can be decreased by mucus, but even increased when drug-calcium salts are formed

A fast screening of highly retained compounds can be assessed with the herein presented *in vitro* mucus model