

XXIX Symposium on bioinformatics and computer-aided drug discovery  
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**A NEW TARGET TO OVERCOME ABC  
TRANSPORTER ACCOSITED  
CHEMORESISTANCE OF TUMOR CELLS**

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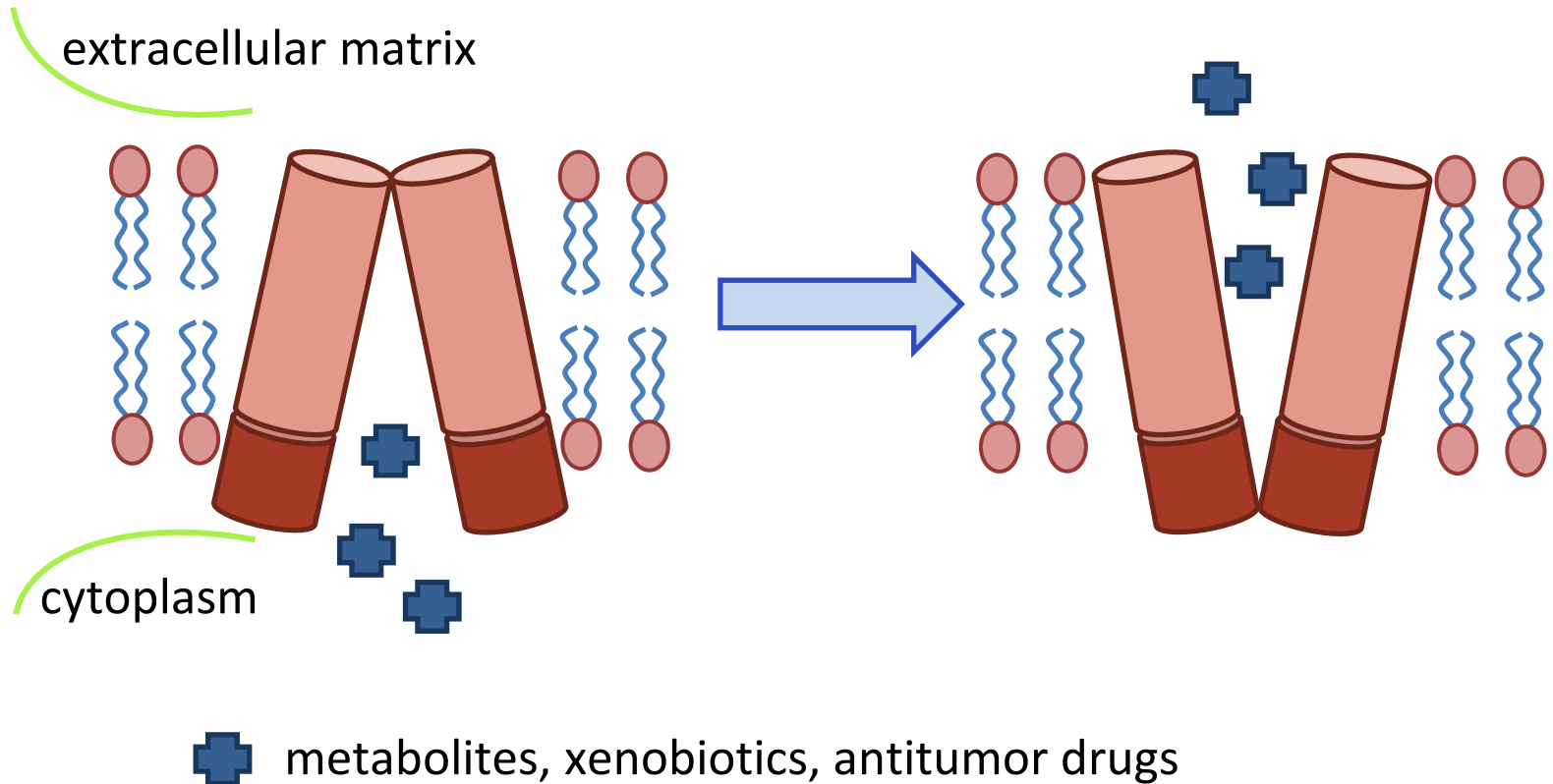
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# Chemoresistance of tumor cells



Chemoresistant cell

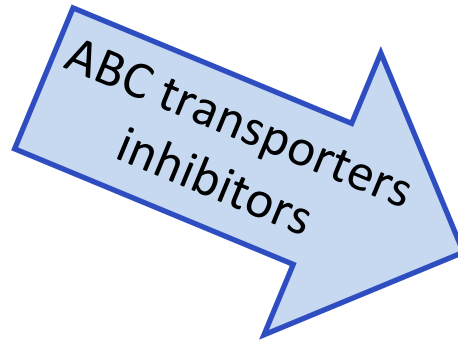
# ABC transporters activity (P-gp, BCRP)



# ABC transporter associated tumor cells chemoresistance overcoming



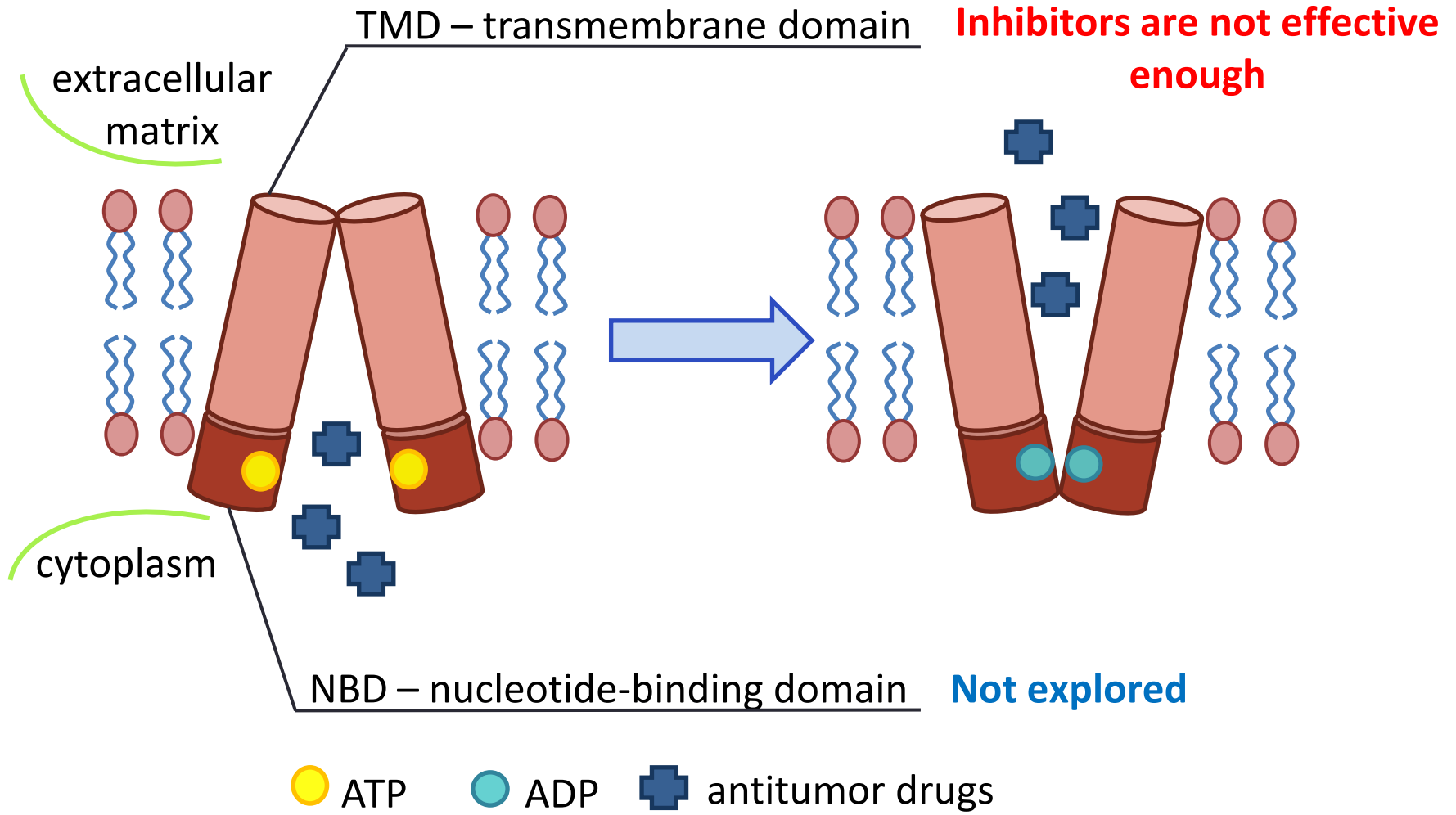
Chemoresistant cell



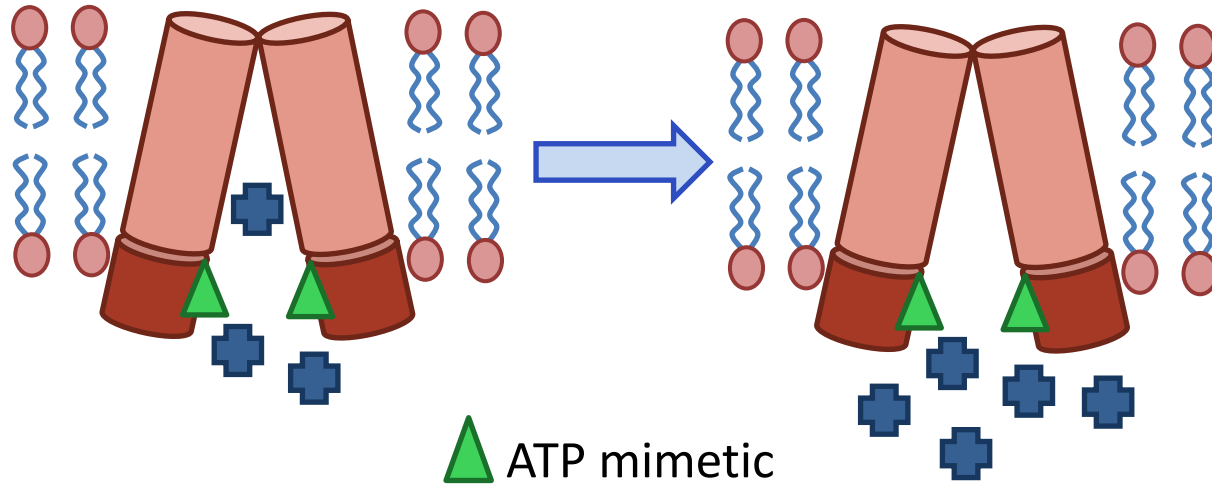
Chemosensitive cell



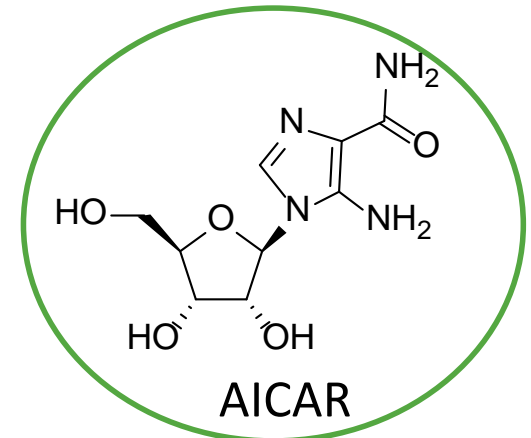
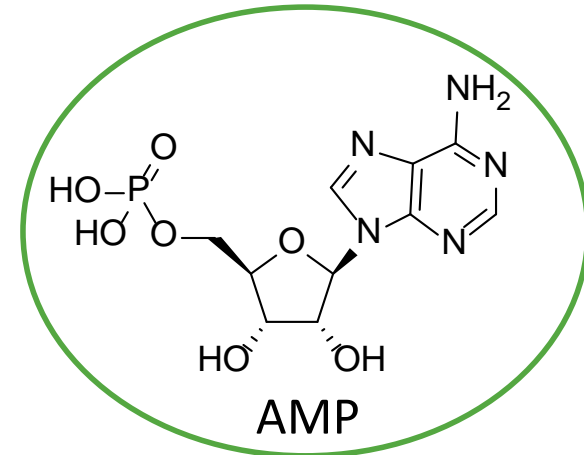
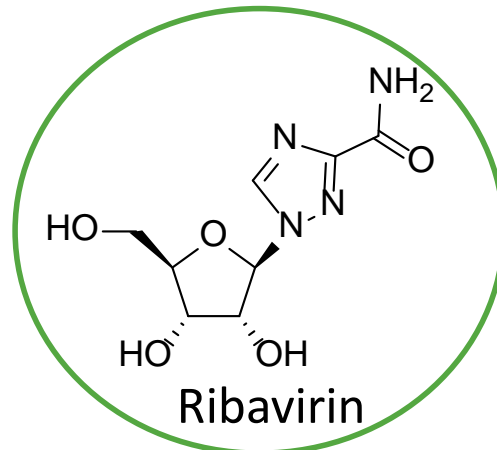
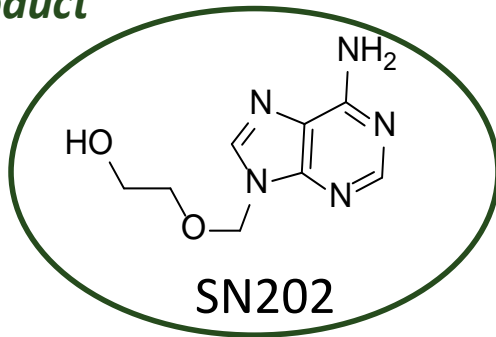
# ABC transporters inhibition



# ABC transporters inhibition by NBD binding

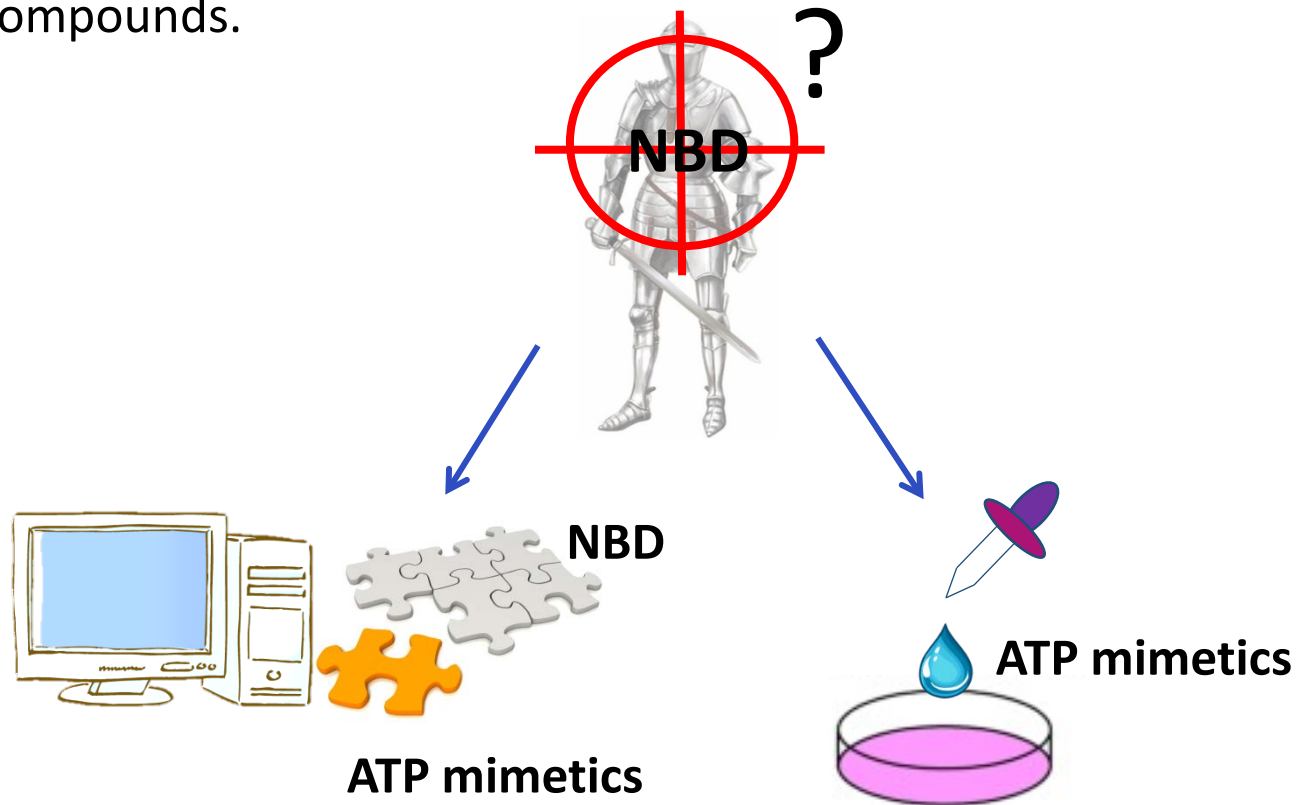


*Laboratory of  
Molecular  
Pharmacology  
product*



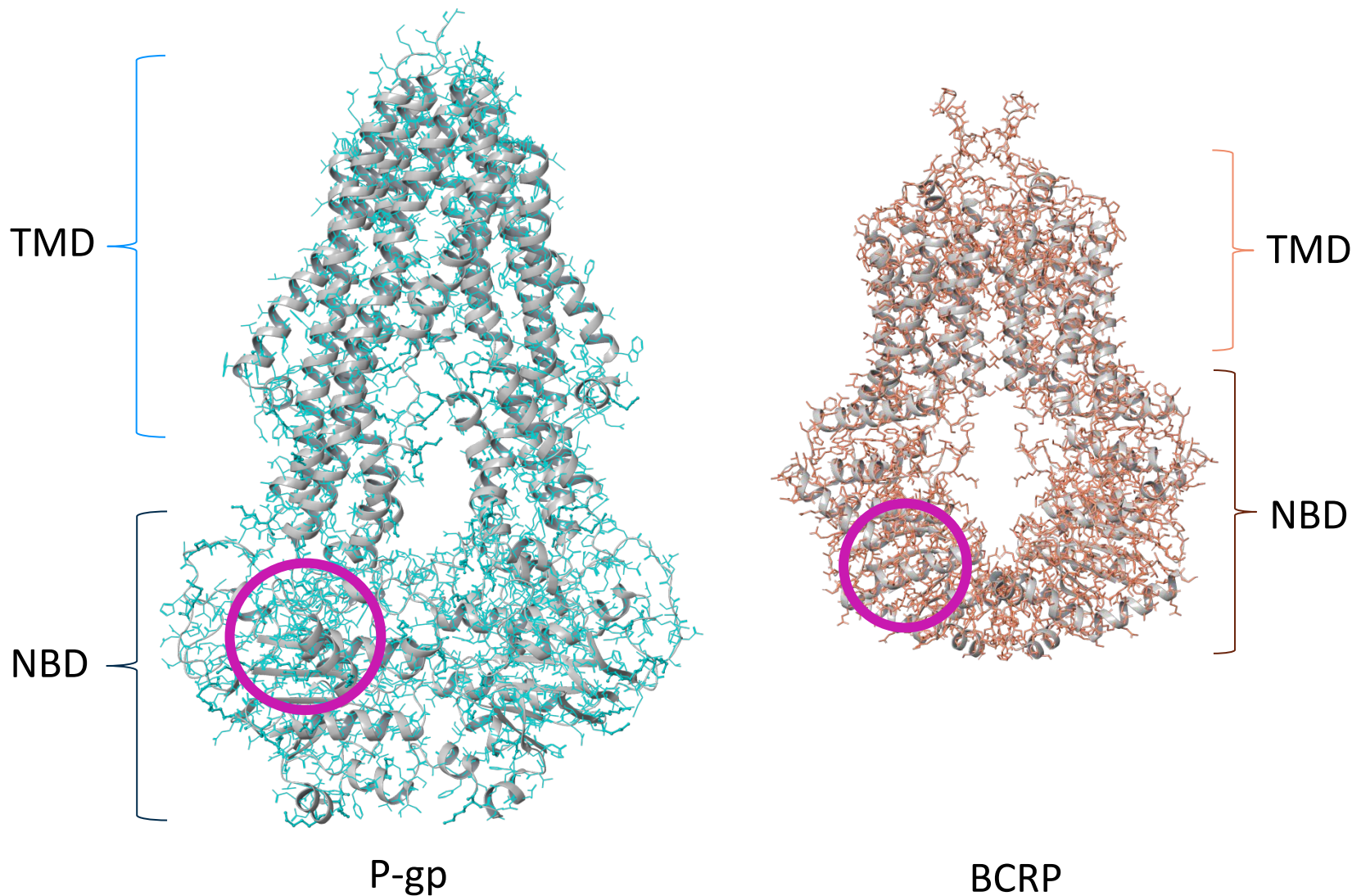
# The aim of the work

NBD validation as a new target for ABC transporters inhibition by studying interaction of ATP mimetics with ABC transporters and evaluating biological activity of compounds.



# *In silico* ATP mimetics interaction with NBD

P-gp and BCRP structures from the PDB





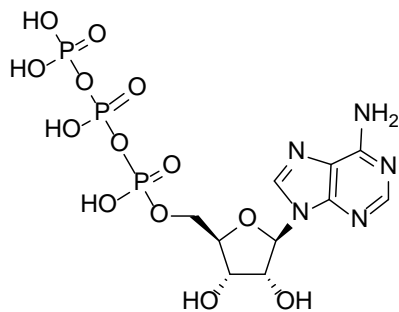
# *In silico* ATP mimetics interaction with ABC transporters

P-gp

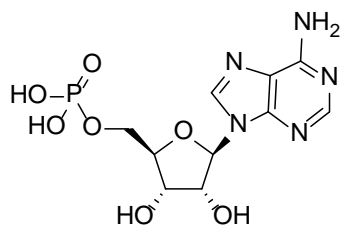
Ligand	NBD	TMD
ATP	-8,2	-7
AMP	-6,8	-5,7
AICAR	-6,9	-5,3
Ribavirin	-6,3	-5,5
SN-202	-6,0	-4,7

BCRP

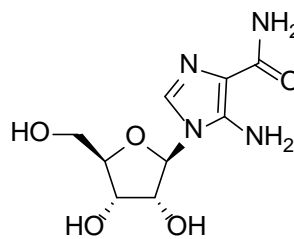
Ligand	NBD	TMD
ATP	-9,0	-7,4
AMP	-9,2	-7,4
AICAR	-6,3	-5,9
Ribavirin	-6,3	-5,9
SN-202	-5,7	-5,4



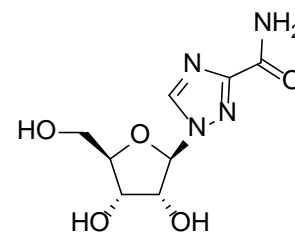
ATP



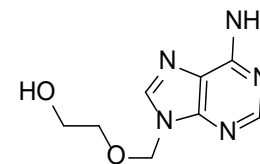
AMP



AICAR



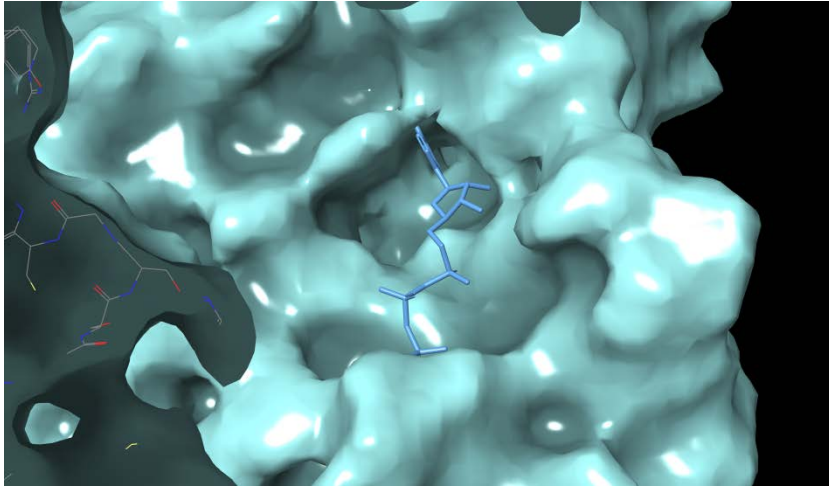
Ribavirin



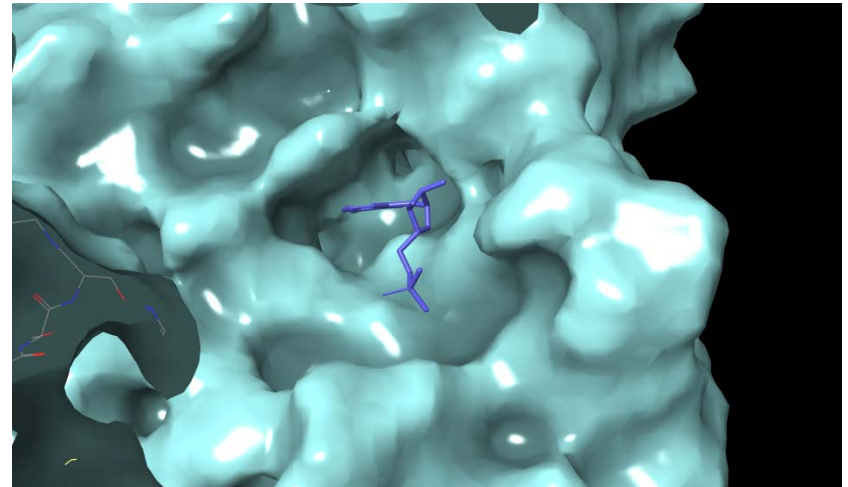
SN202

# *In silico* ATP mimetics interaction with P-gp NBD

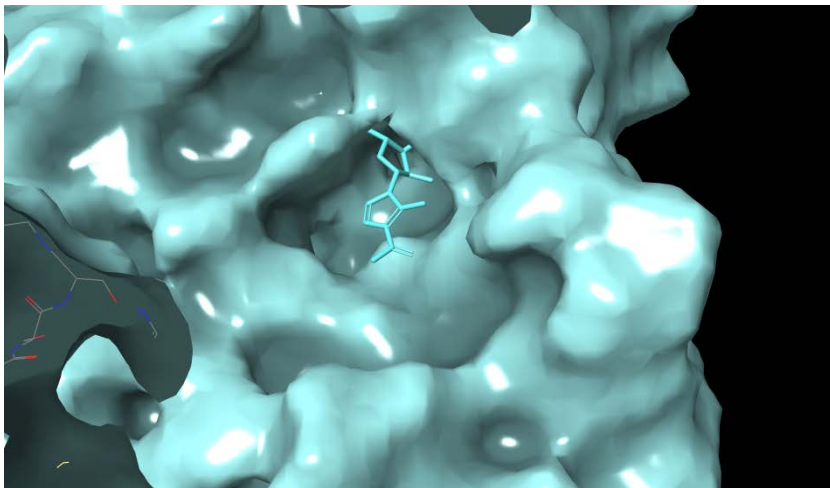
ATP



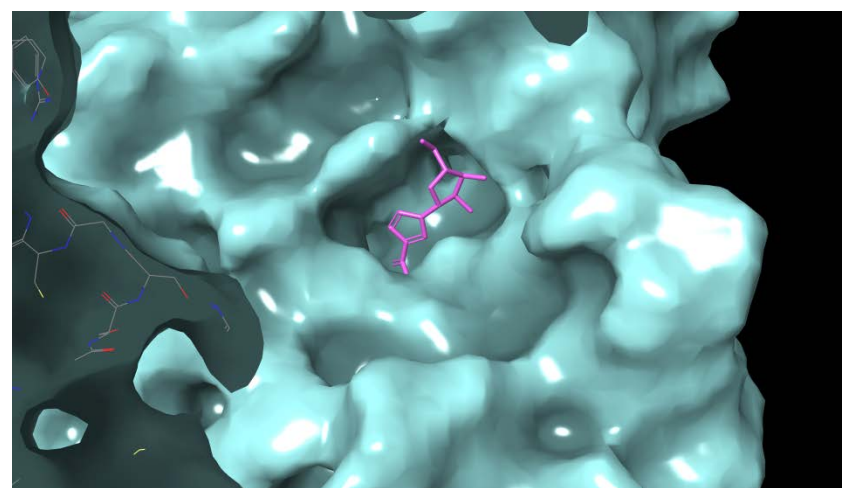
AMP



AICAR

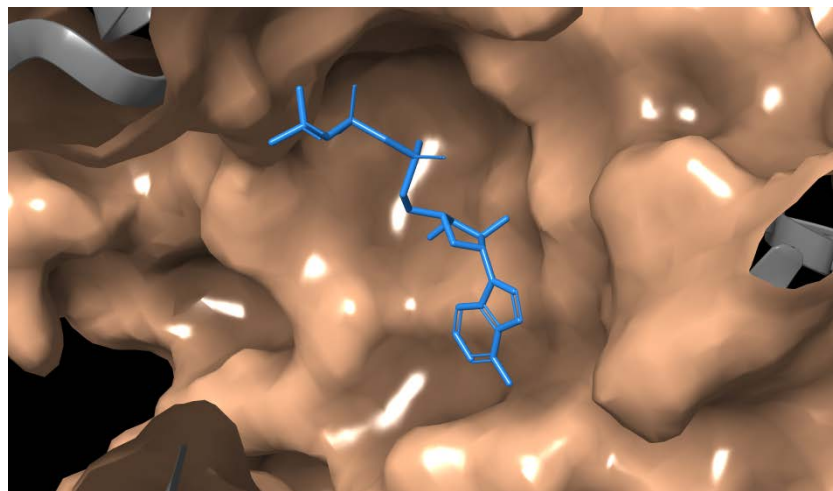


Ribavirin

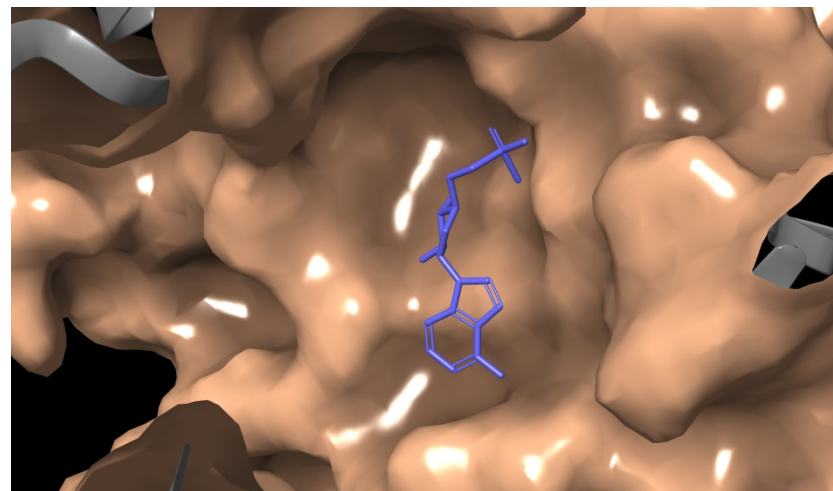


# *In silico* ATP mimetics interaction with BCRP NBD

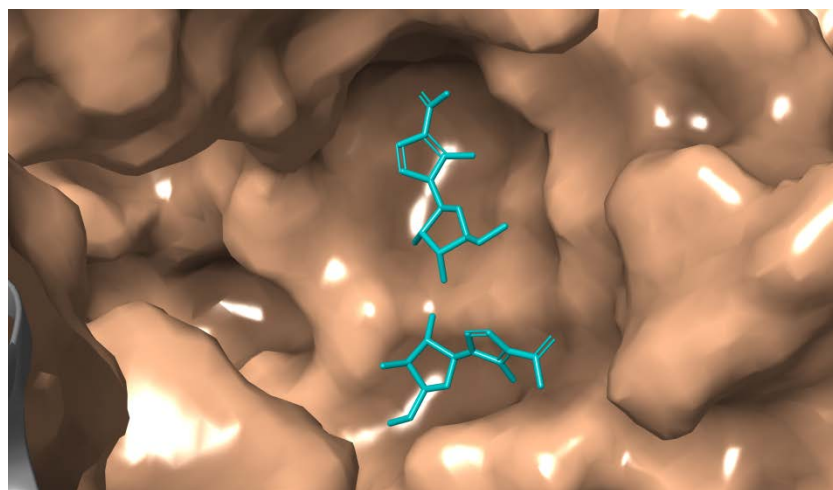
ATP



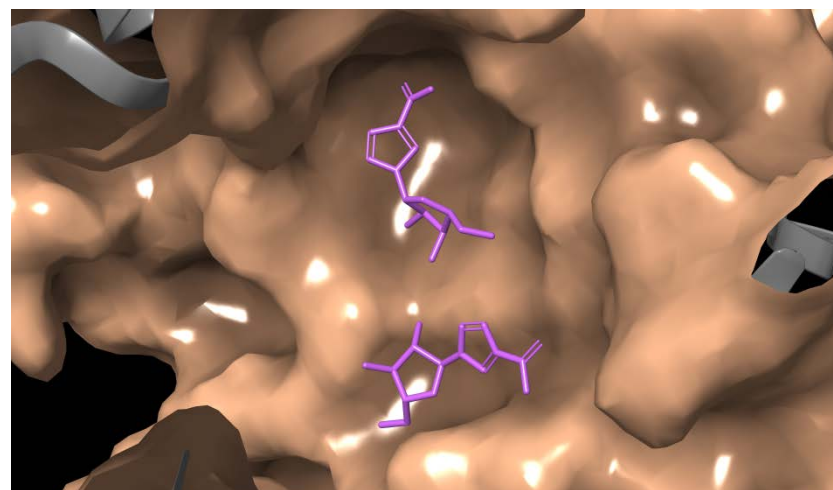
AMP



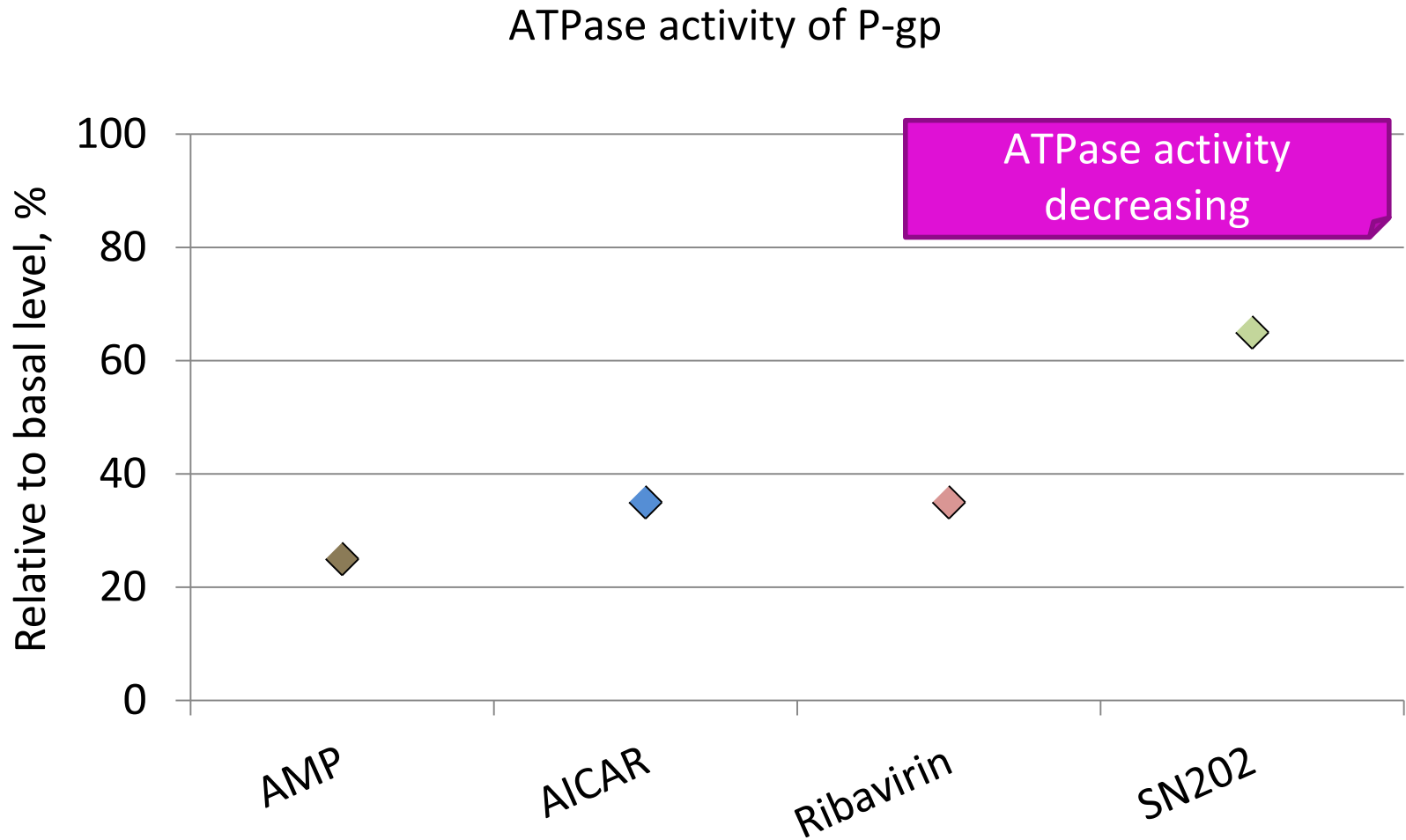
AICAR



Ribavirin

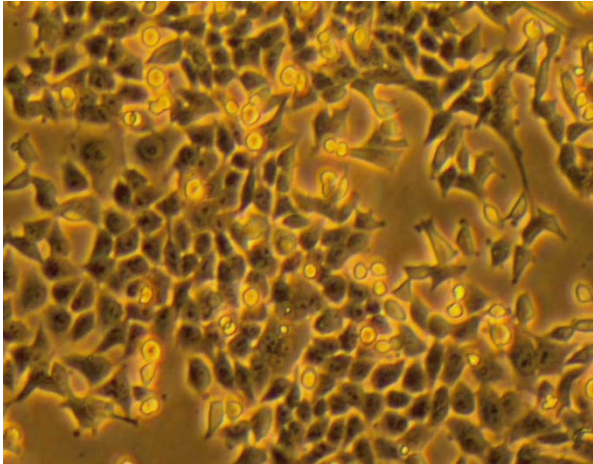


# Effect of ATP mimetics on ABC proteins ATPase activity

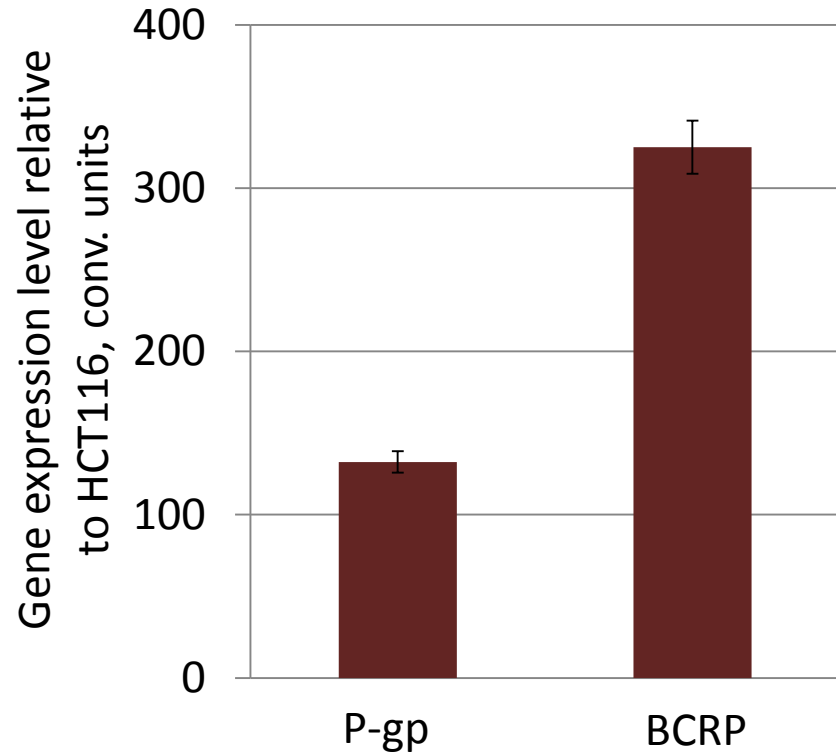
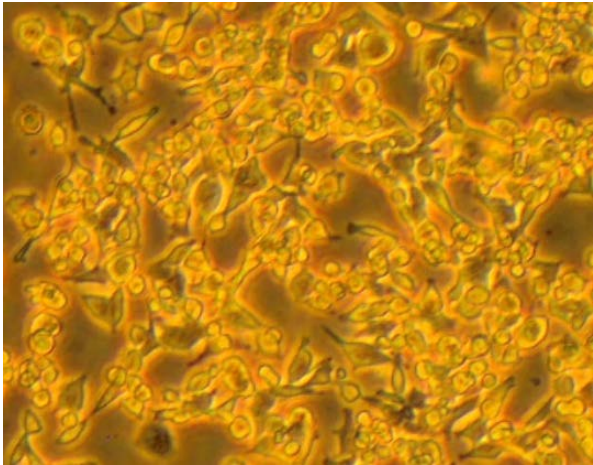


# Cancer cell line resistant to taxol

HCT116, wild type

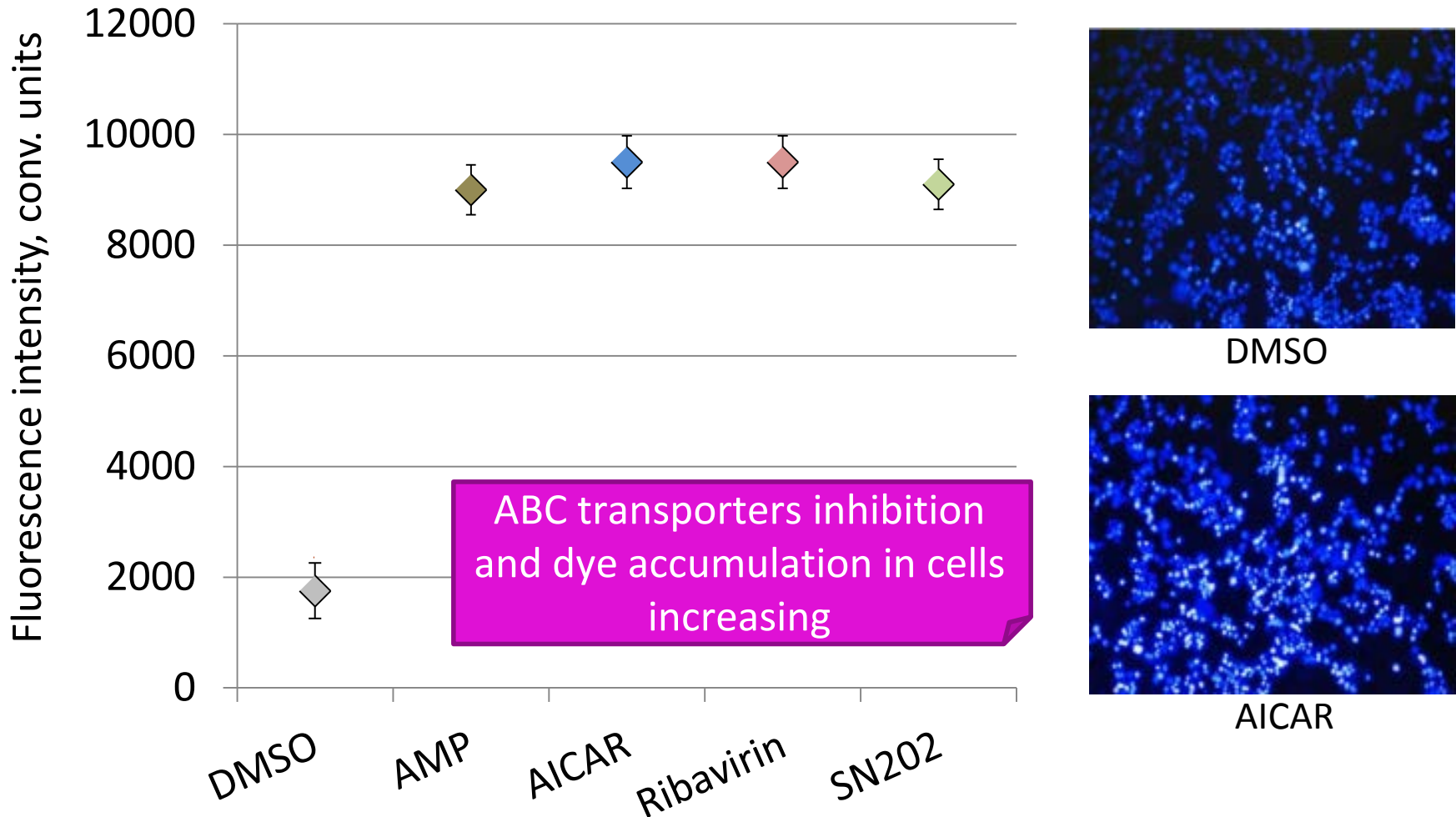


HCT116tax, resistant to taxol



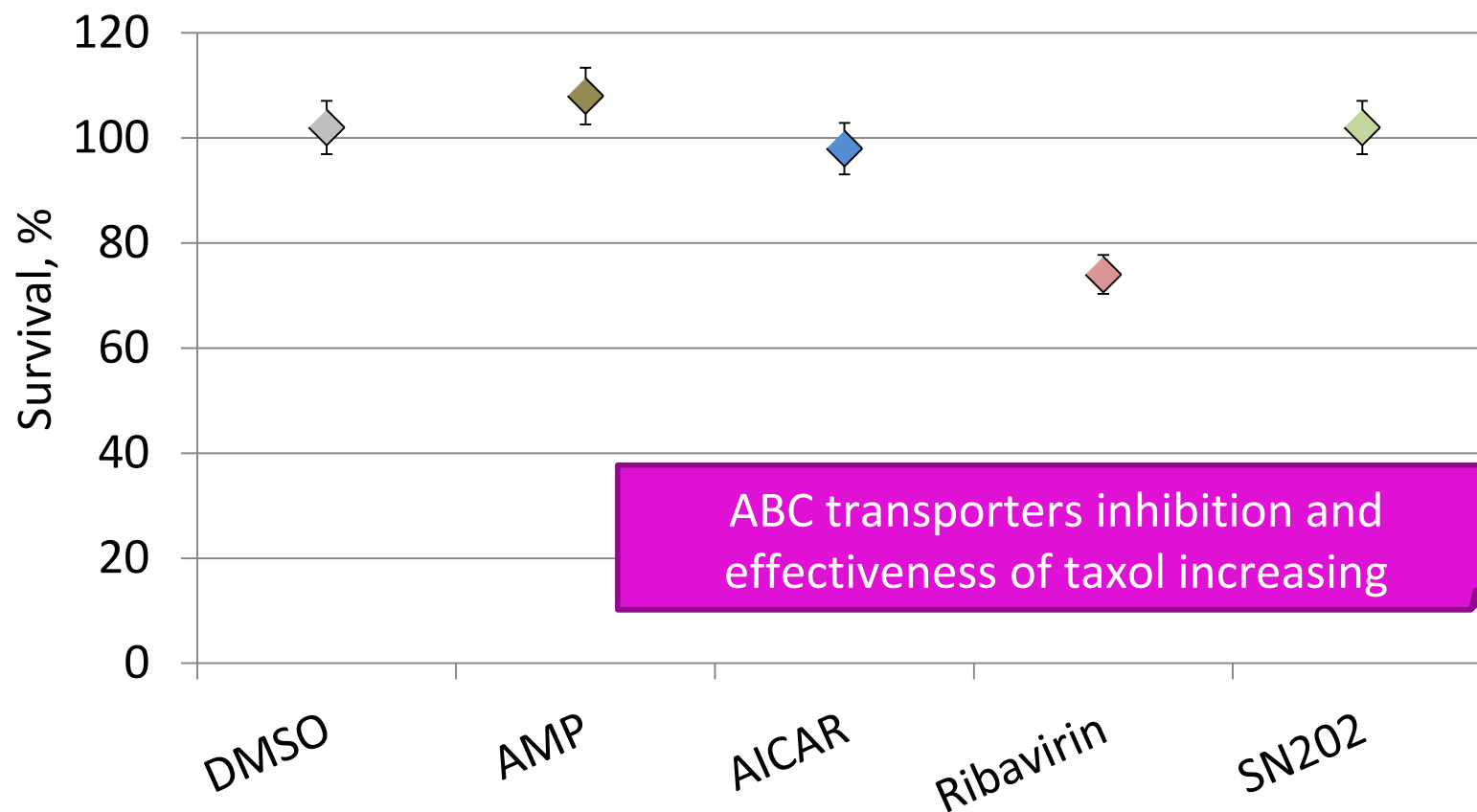
# Effect of ATP mimetics on ABC proteins transport activity

Hoechst 33342 accumulation in HCT116tax

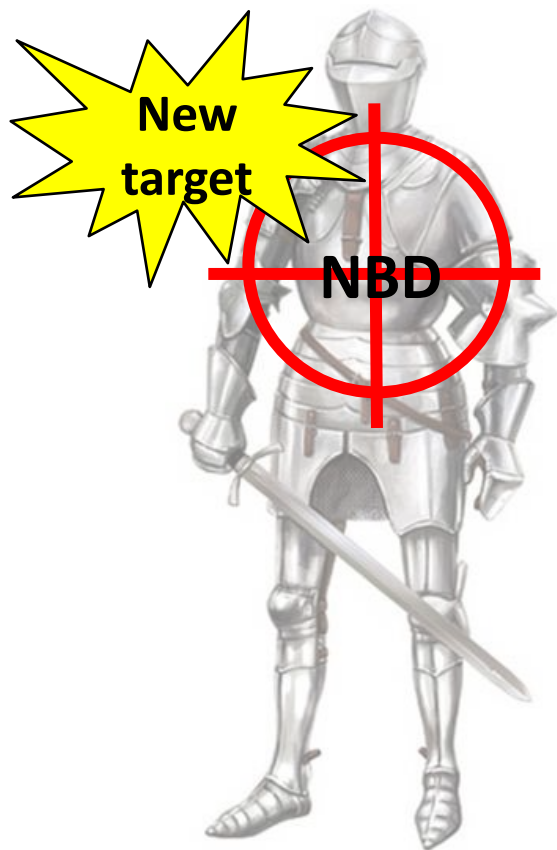


# Effect of ATP mimetics on chemoresistant cells survival

Cells HCT116tax survival in presence of taxol



# Conclusions



Chemoresistant cell

- ❑ ATP and its analogues selectively bind to ABC transporters NBD;
- ❑ ATP mimetics inhibit ABC transporters activity and increase sensitivity of chemoresistant cells to taxol.





We will be glad to have questions and comments!

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- Laboratory group VKontakte: <https://vk.com/molpharm>