Characteristics of antiviral peptides (AVPs) that inhibit flu and HIV viruses, using QDs for detection

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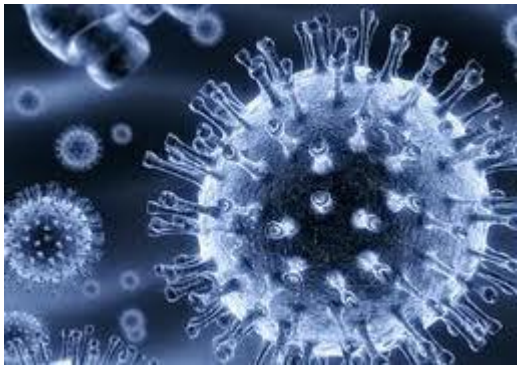
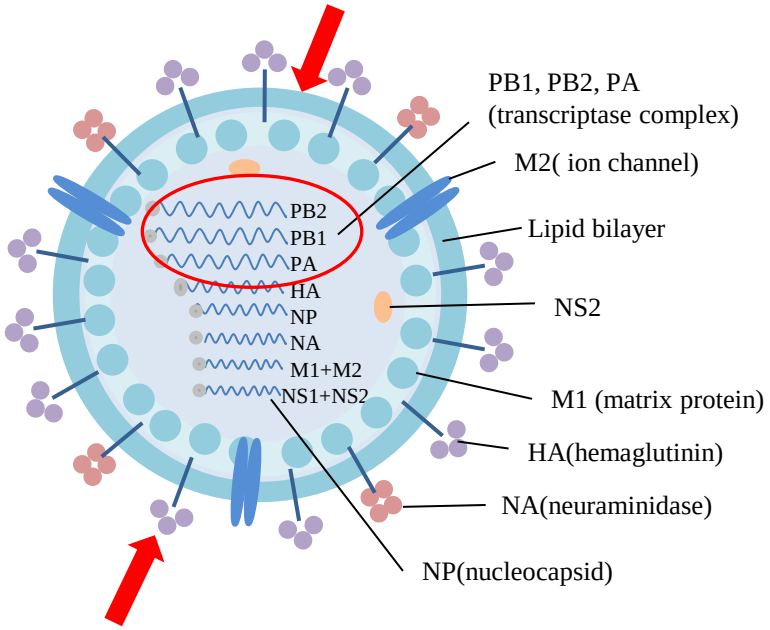
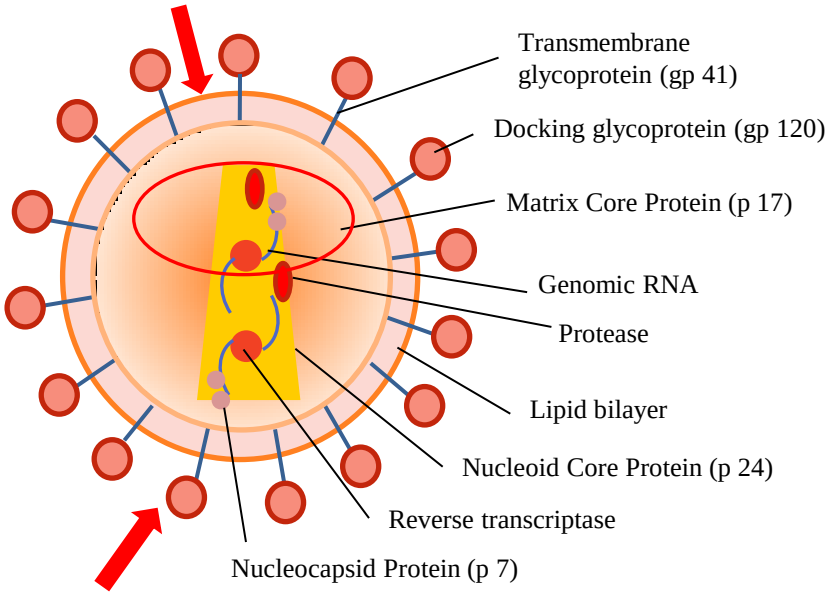


13.9.2013

Influenza and HIV viruses, their structure and target place for theraphy



Scheme of influenza virion



Scheme of HIV virion

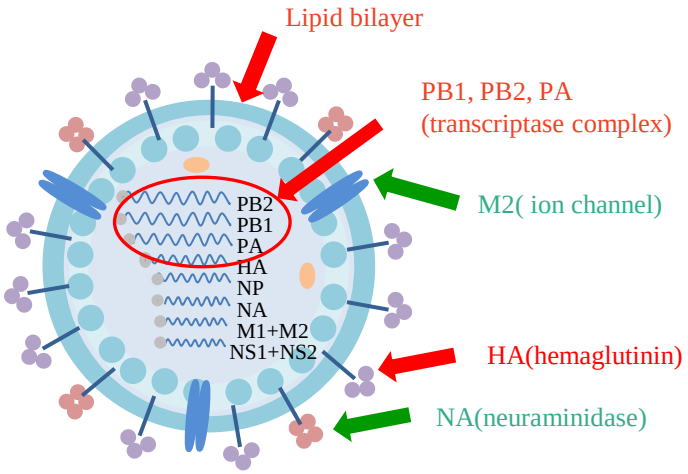
Targets for antiviral peptide therapy

Lipid bilayer

Surface proteins (antigens)

Complex for transcription and replication

Curent and potentional influenza therapy



Current antiviral therapy:

- Symptomatic treatment (antipyretics, vitamin C….)
- Blockers of M2 chanel (Amantadin, Rimantidin)
- Neureminidase inhibitors (Oseltamivir a Zanamivir)

! resistance increase (up to 80%)

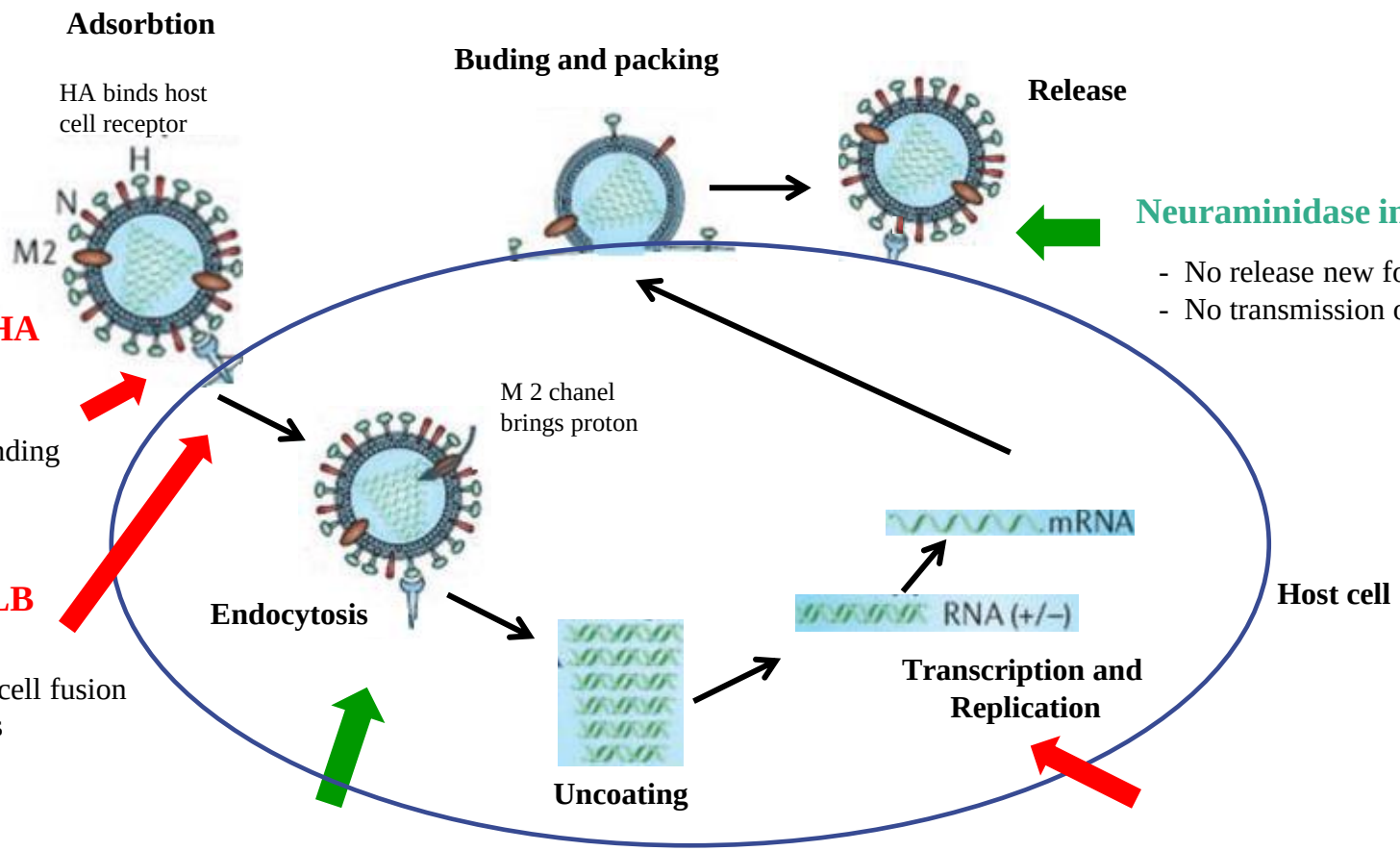
Future therapy:

Gene and/or Anti sense therapy

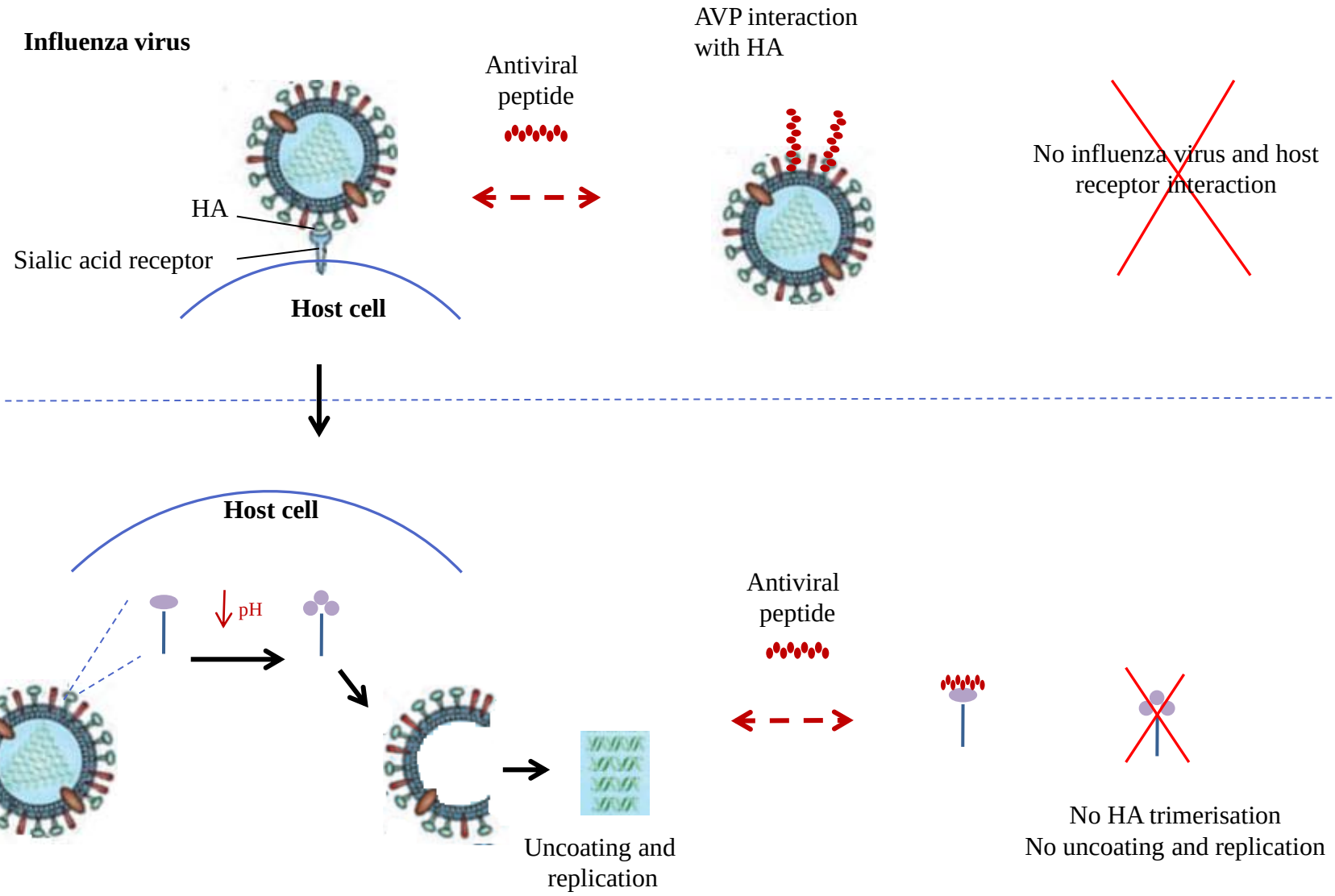
- ✓Minimal resistance
- ✓Selectivity
- ✓Variability
- ✓Easy to produce
- ✓Minimal side effects

Antiviral peptide therapy (lipid membrane, surface protein, replication)

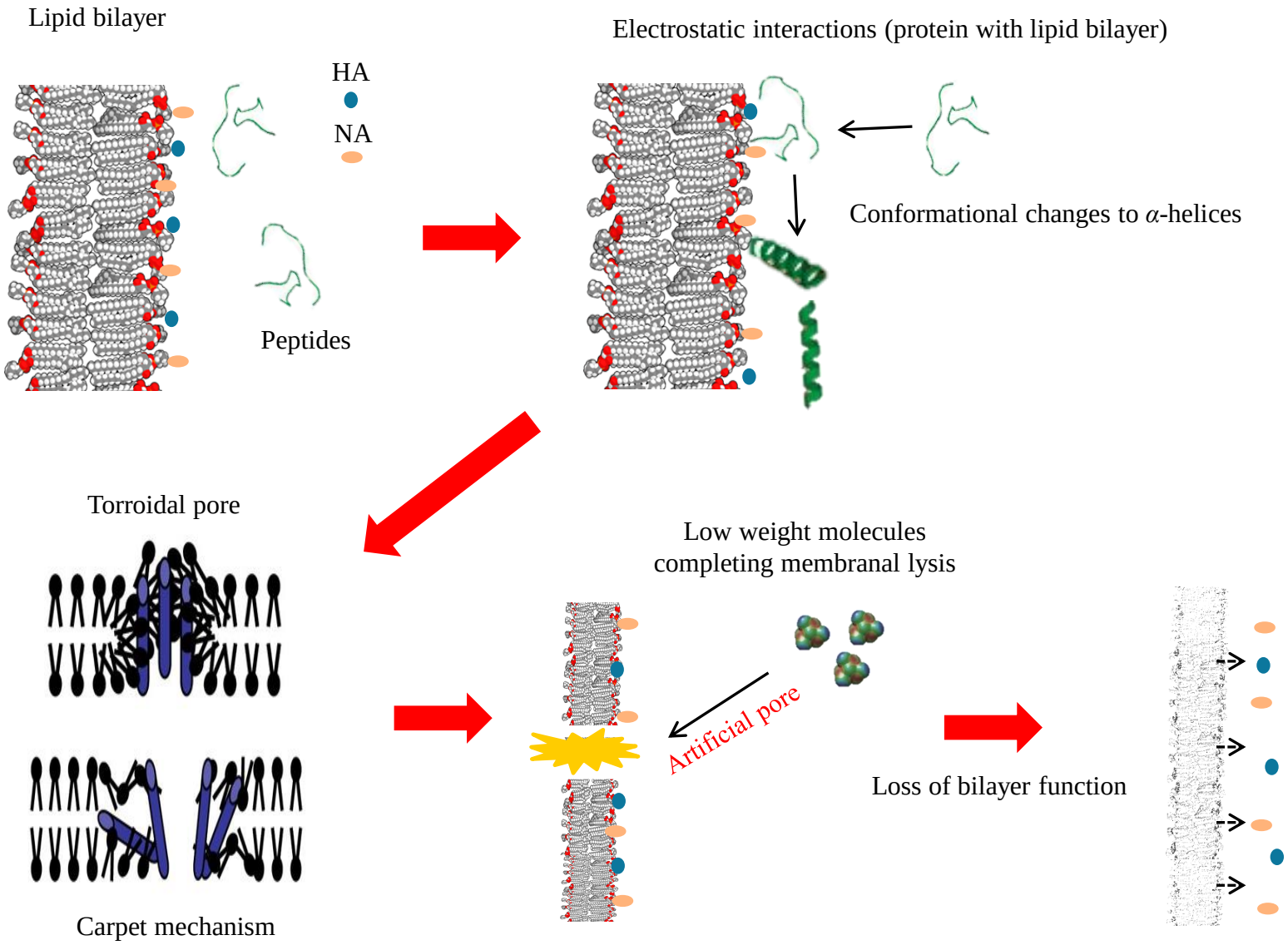
Influenza life cycle and target place for theraphy



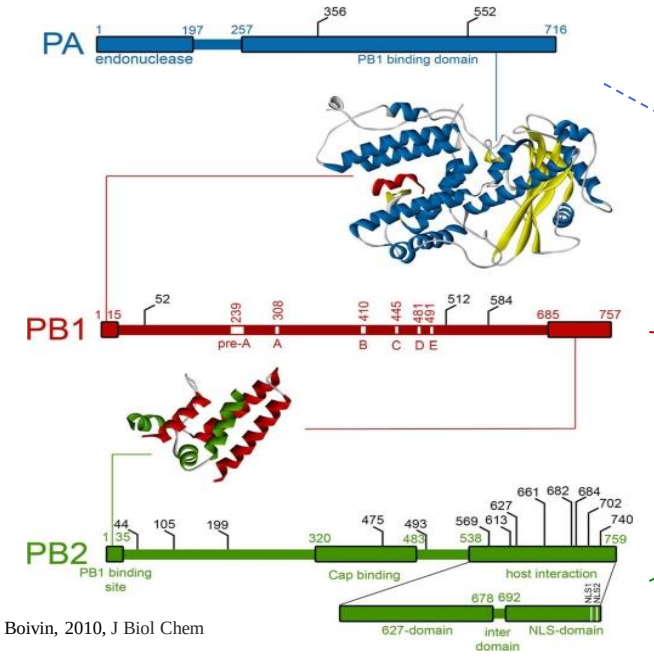
The principle effect of peptides targeting to the replication



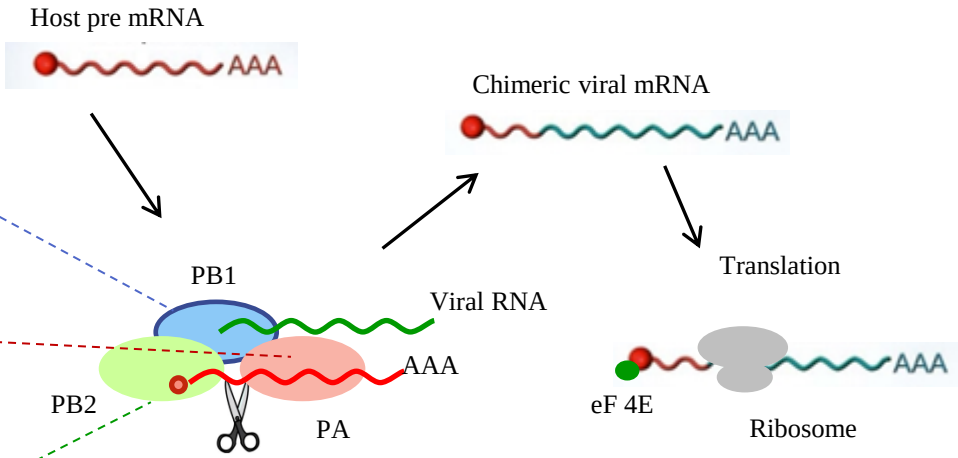
The principle effect of peptides targeting the lipid bilayer



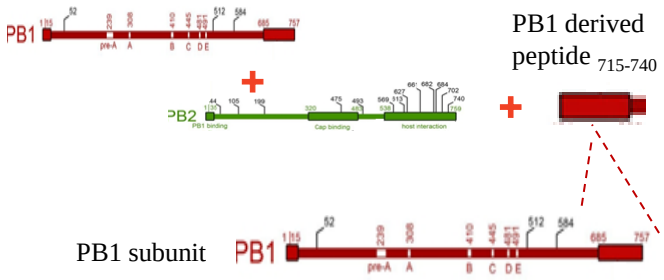
The principle effect of peptides targeting to the replication



Boivin, 2010, J Biol Chem



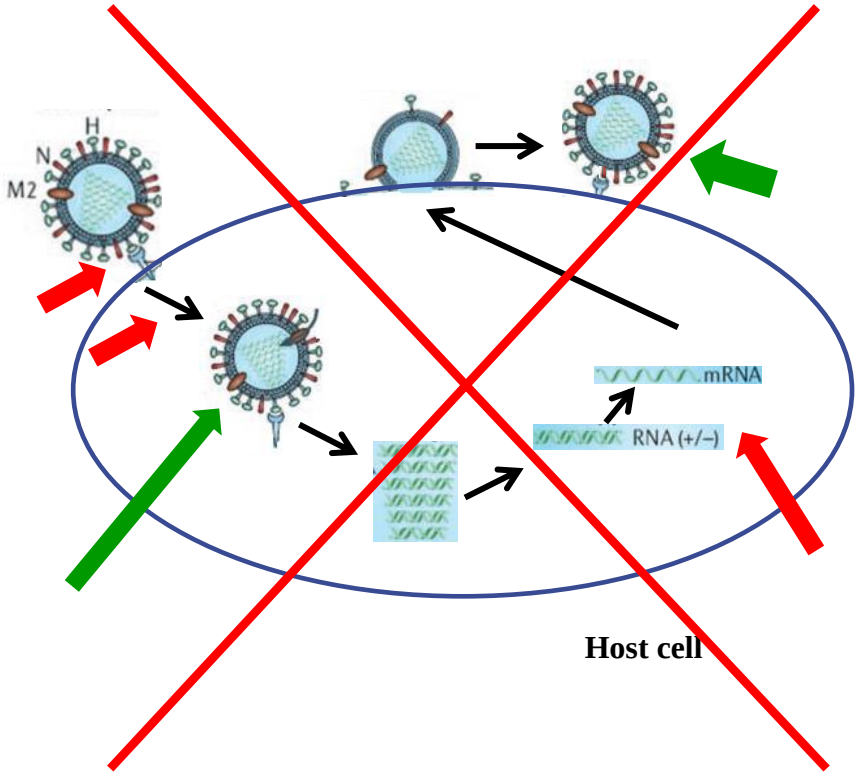
Antiviral peptide



Assembyl to polymerase complex:
interaction between PB1 and PA, PB1 and PB2, PA and PB2

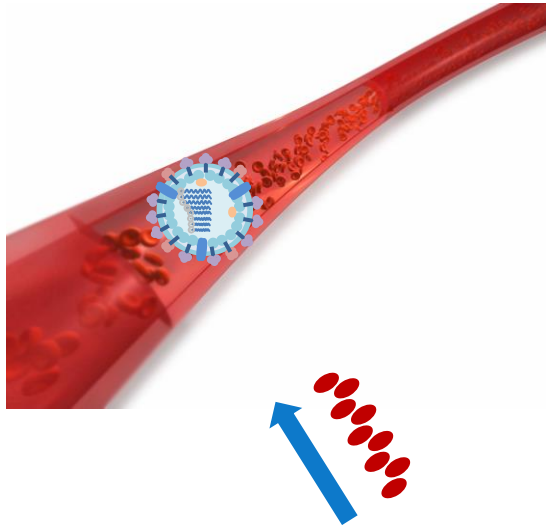
NO assembly PB1 and PB2 → NO transcription and replication

New strategy for peptide therapy



Current strategy

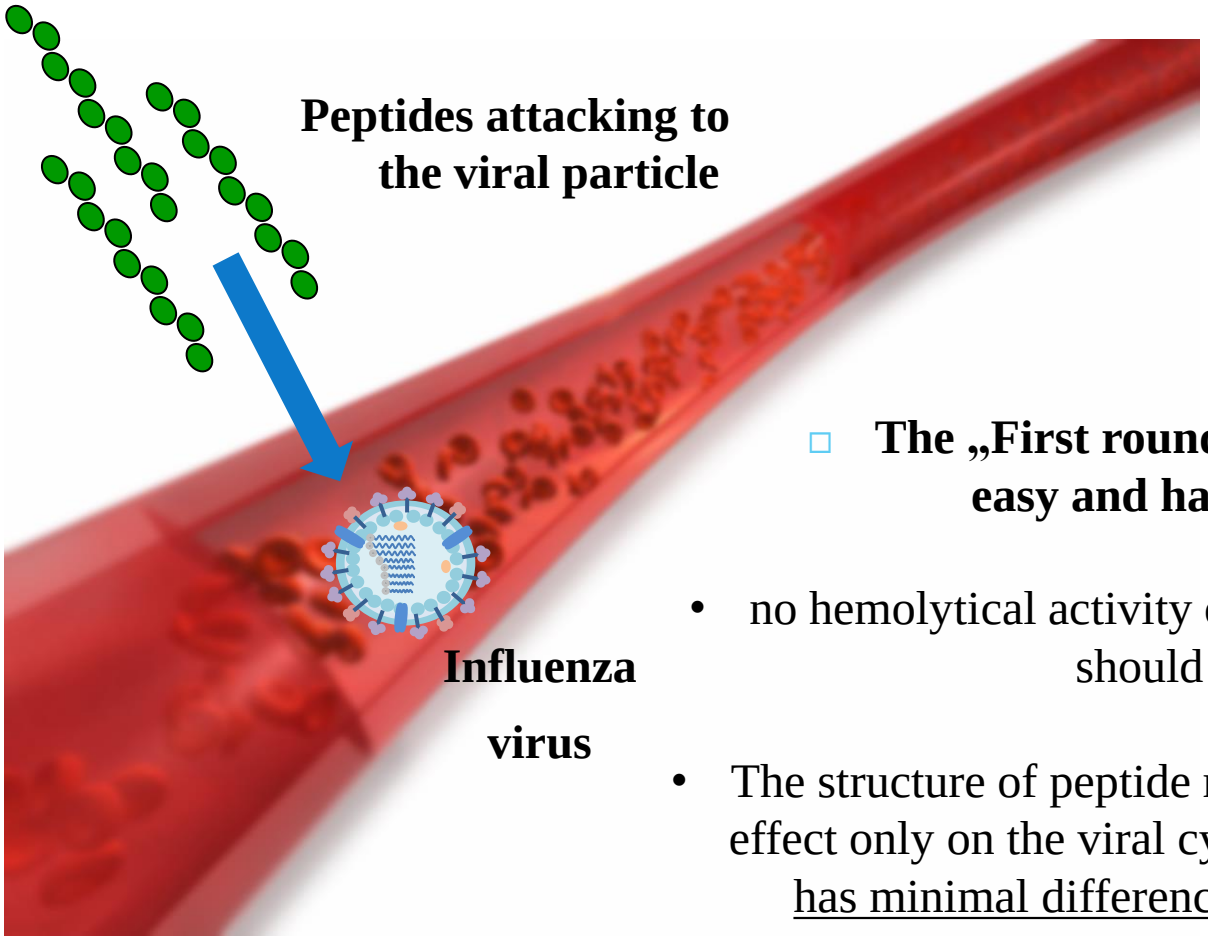
Is target on host cell interaction



New strategy

Is target on influenza viruses before interaction with host cell.

The „First round knockout strategy“



- **The „First round knockout strategy“ is not easy and has many requirements:**

- no hemolytical activity of peptide and no toxic effect should be occuring

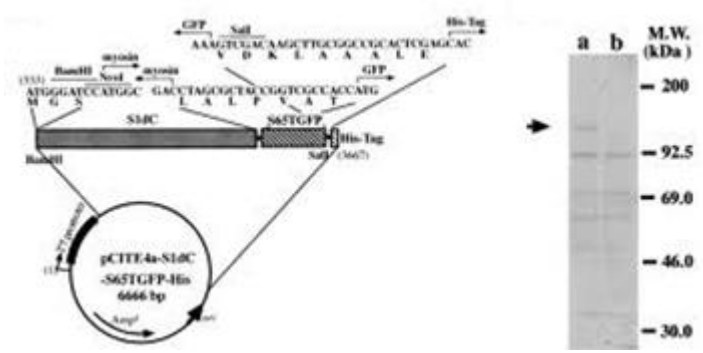
- The structure of peptide must be tuned to have specific effect only on the viral cytoplasmatic membrane <u>which has minimal difference to human cell membrane</u>

- The terapeutical concentration of „membrane affecting“ peptides is ussual too high and in the case of blood vessel environment there is high therapeutical index needed.

Our aims in preparation and testing of AVPs

- Production of AVPs and testing models in Vivo

(by recombinant protein)



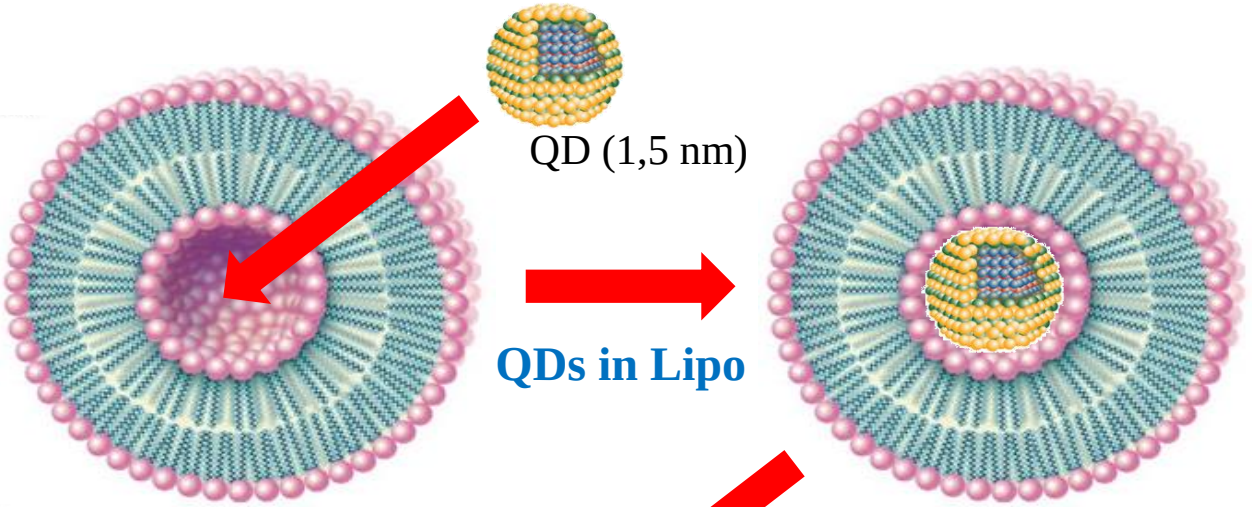
- Synthetic high purity production of AVPs

- One of our favorite peptide „now“ is **Melitin**, highlited part of peptide will by produced in **Yasara software** as computed variants…. We will tune it´s „**Net charge**“

GIGAVLKVLTTGL PALISWIKRKRQQ

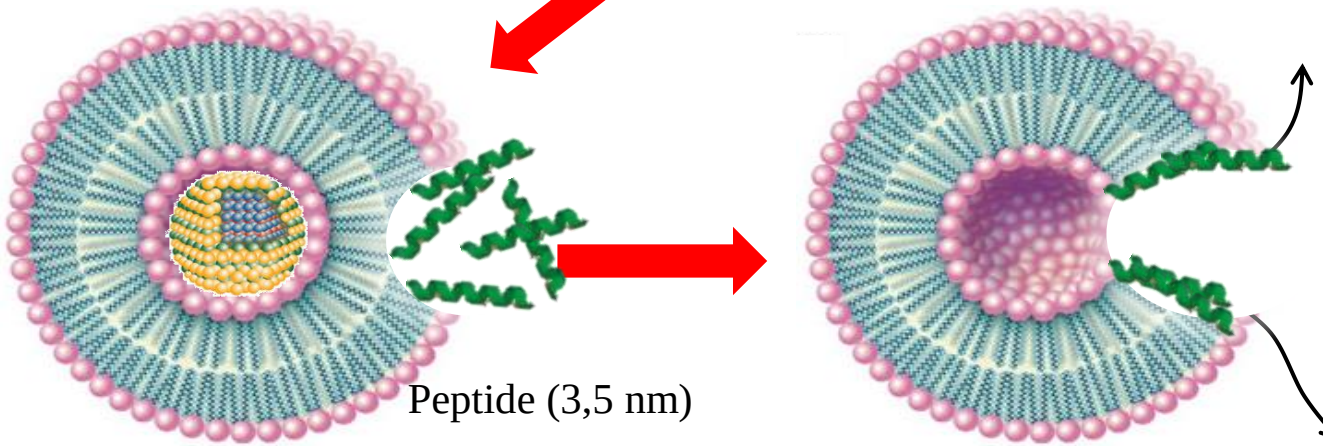
- Testing the hemolytical activity (is easy and neccesary stepp in case of all peptides)
- Testing of the efficiency of peptide variants on **lipid membrane or better directly on the model of particle of virus** **…. could be Quantum Dots useful for this????**

The „ QDs lipo-release“ testing concept

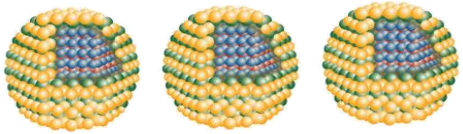


This QDs testing concept is dedicated only for rough *in vitro* testing …

Aplication of testing „battery“ of prepared AVP



Change in fluorescence – positive or negative (depends on aplication)



Easy monitoring in ELISA weels

If AVP works the QDs are released form Lipo

Conclusions: What we have…what we need:

- Are we able to prepare QDs? …**We are!!!**
- Are we able to prepare bilayered liposome? …**We shoud be.**
- Are we able to predict the sequence of peptide? … **We are´t!!!**
- Are we able to produce various peptides in high scale and purity? … **We will**

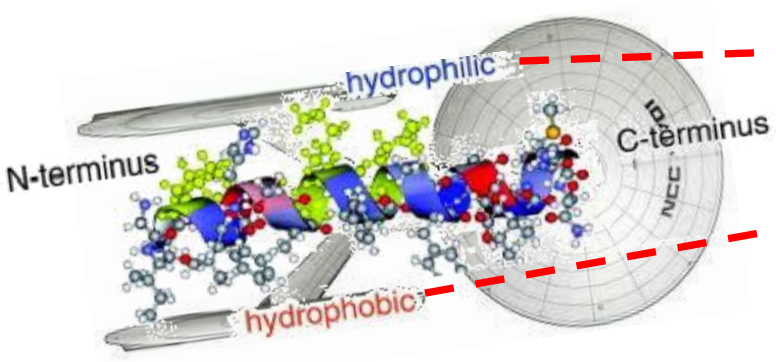
…these Antiviral peptides in range of our interest for future studies:

Peptide	Sequence
LL-37	LLGDFFRKSK EKIGKEFKRI VQRIKDFLRN LVPRTES
Lactoferrin	SKHSSLDCVLRP
Synthetic peptide	AGDDQGLDKC VPNSKEK
Synthetic peptide	NGESSADWAKN
Melittin	GIGAVLKVLT TGLPALISW IKRKRQQ

Thank you for your attention

Thanks for colaborators from Laboratory of Metalomics and Nanotechnologies…

…and the man (Prof. Rene Kizek), <u>who likes this kind of things</u>



The peptide aka …
…The Enterpries