

Instituto Politécnico Nacional  
Escuela Superior de Cómputo  
Bioinformatics

# Artificial Viruses

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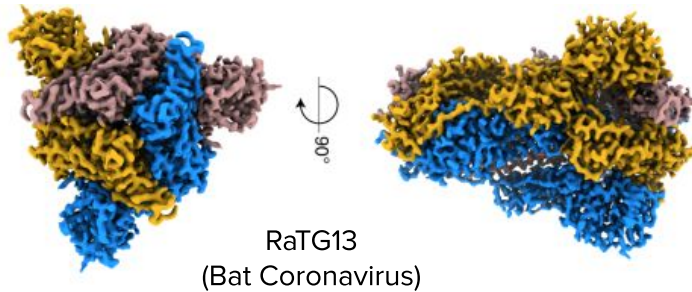
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Prof. Rosas Trigueros Jorge Luis  
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# Introduction: the COVID-19 controversy

## 1. Animal origin theory



Pangolin

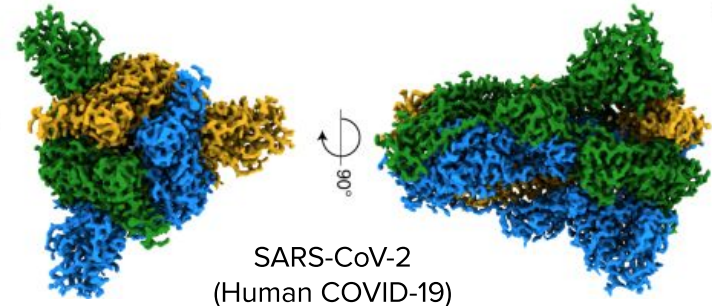


Bat

## 2. Lab origin theory



Dr. Li-Meng  
Yan

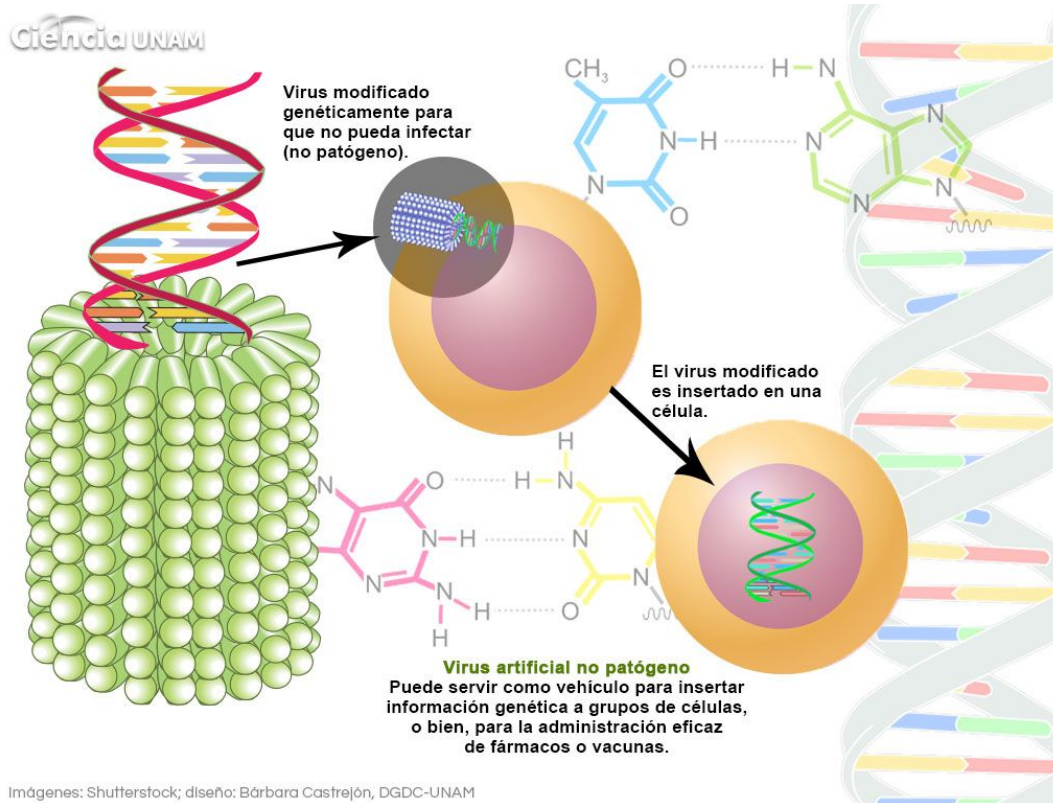


Is it possible to  
create a virus  
inside a  
laboratory?



Short answer is yes, but it isn't as we  
all may think.

# Artificial viruses: gene delivery



**Not pathogenic viruses**

**Manipulation of DNA and RNA**  
sequences. Nanotechnology

All viruses can **auto-assemble**

**Insert genetic material** to cells

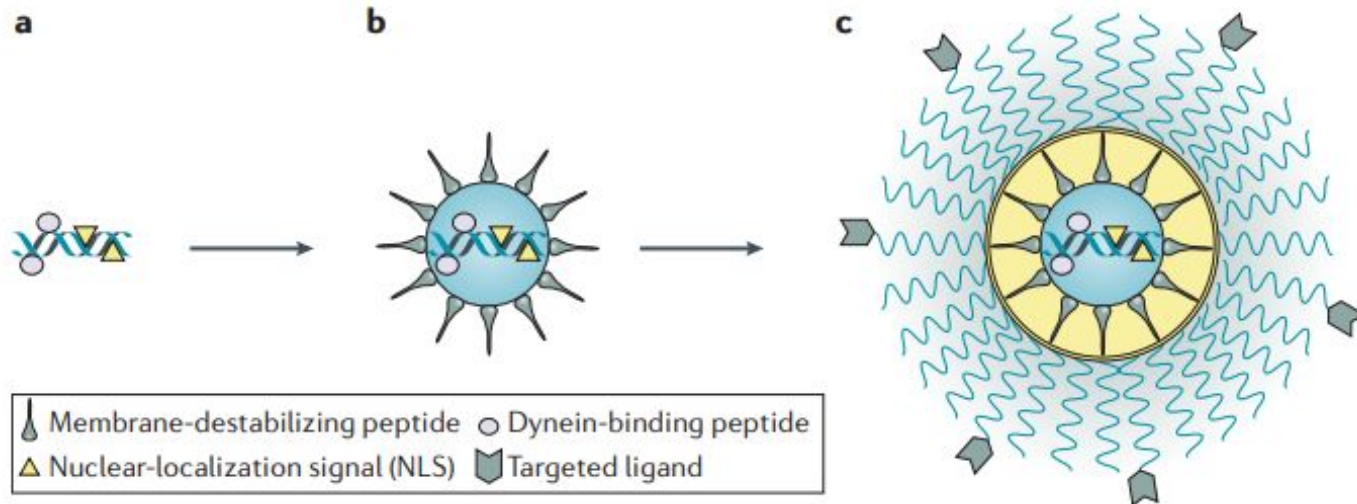
**Drugs and vaccines**  
administration

# Artificial viruses: conceptual model

a. Plasmid vector

b. Artificial virus core

c. Hydrophilic shell



A conceptual model of the assembly of a multi-layered artificial virus

# Artificial viruses: requisites

**1. Bio-compatible, bio-degradable and bio-invisible**

**4. Cytosolic trafficking**

**2. Cell binding and internalization**

**5. Nuclear import**

**3. Endosomal escape**

**6. Controllable and sustained transgene expression**

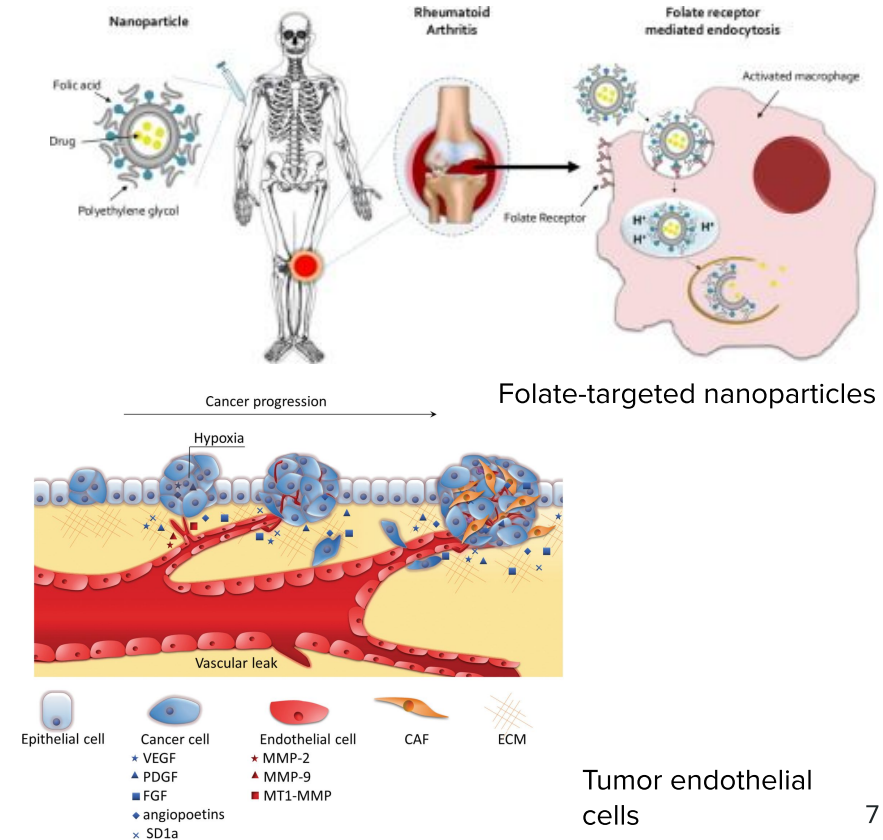
# Some artificial virus-like gene-delivery systems

**Folate-targeted nanoparticles** (France)

RGD-targeted reconstituted adenoviral envelopes around PEI complexed DNA (Germany)

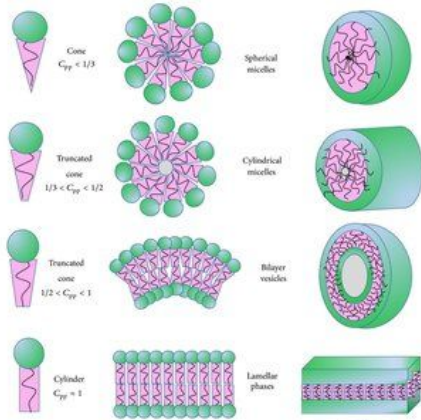
Polyplexes coated with lipids to which **monoclonal antibodies** as targeting ligands have been attached (Netherlands)

Polyethyl-enimine polyplexes coated with polyethylene glycol and targeted with RGD-peptide motifs towards **tumour endothelial cells** (USA)

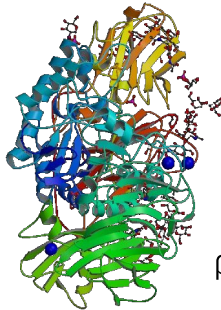




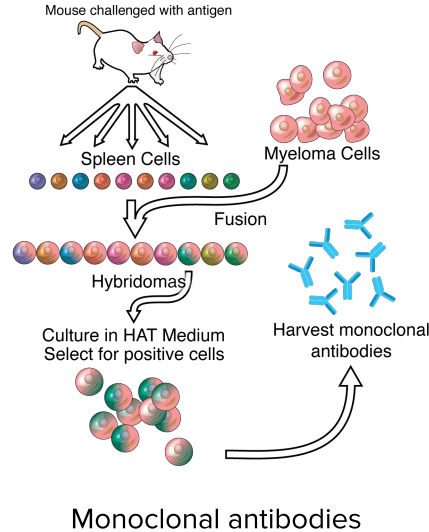
# Some artificial virus-like gene-delivery systems



Glyocluster amphiphiles



$\beta$ -galactosidase protein



Monoclonal antibodies

Reducible polypeptides containing **histidine and lysine residues** (UK)

Chimeric proteins:  **$\beta$ -galactosidase proteins** engineered to contain **RGD targeting motifs, NLS sequences and DNA condensing sequences** (Spain)

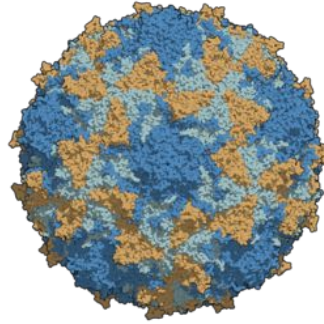
Poly(lysine) condensed DNA coated with PEG that is shed at low pH (Germany)

Neutral glyocluster nanoparticles made of pDNA complexed with **glyocluster amphiphiles** (Japan)



# Other viruses synthesized (created) by humans

**Poliovirus (USA)**



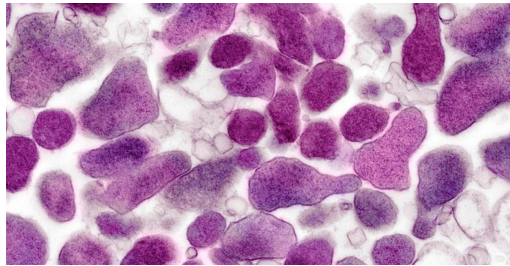
Poliovirus

**Bacteriophage virus (USA)**



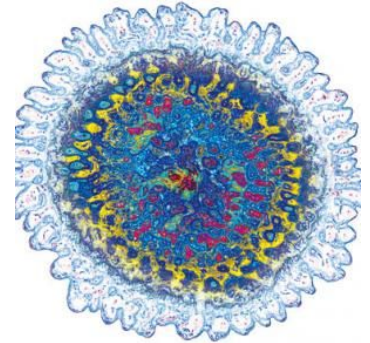
Bacteriophage virus

**Mycoplasma genitalium genome (USA)**



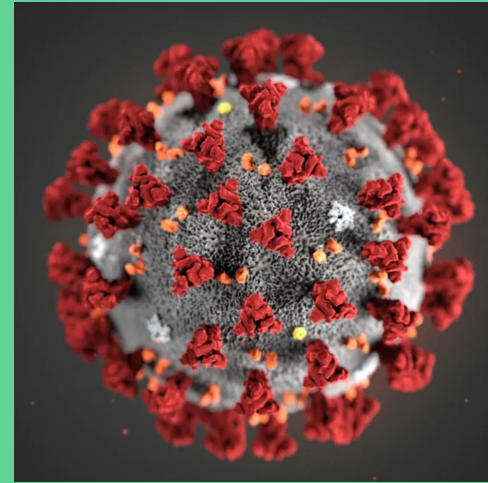
Mycoplasma  
genitalium

**H5N1 influenza virus (Netherlands)**



H5N1

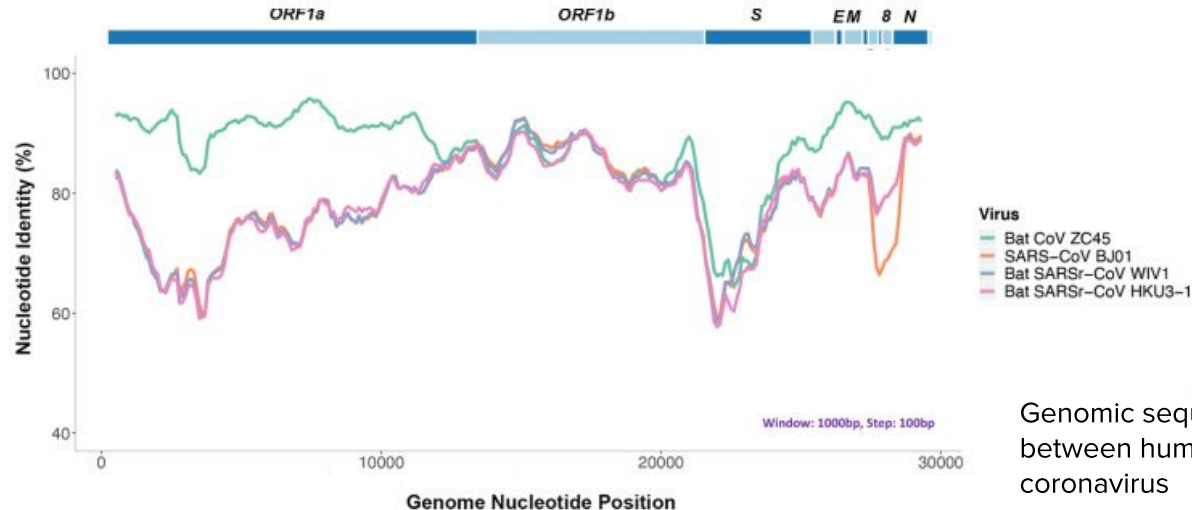
# Back to the Dr. Li-Meng Yan COVID-19 research



# COVID-19 controversy: hypothesis vs truths

**Hypothesis 1:** ZC45 virus, or a closely related bat coronavirus like ZXC21, should be the backbone used for the creation of SARS-CoV-2

**Truth:** If another coronavirus had been used as backbone, there would be certain traces in its sequence.

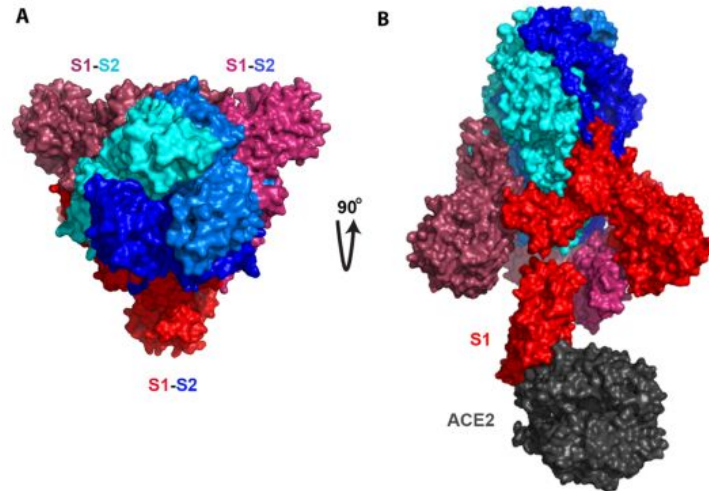


Genomic sequence analysis  
between human and bat  
coronavirus

# COVID-19 controversy: hypothesis vs truths

**Hypothesis 2:** The Spike protein of SARS CoV-2 resembles to the SARS-CoV-1 one from the 2003 epidemic in an 80%.

**Truth:** If only the Spike protein of SARS-CoV-1 had been entered in some amino acid of the ZC45 virus inside a laboratory, there won't be thousands of mutations, just some no more than ten.



Spike protein in the SARS-Cov-2

# COVID-19 controversy: hypothesis vs truths

**Hypothesis 3:** RaTG13 coronavirus (supposed to be artificial too) discovered in 2013 has a sequence homology of 96% with SARS-CoV-2 after performing an alignment between them.

**Truth:** 20% of difference from SARS-CoV-1 and 4% from RaTG13 express mutations throughout the genome in approximately 3 to 4 thousand amino acids. Natural selection is easier.

```

SARS_G202 |-----442-----472-----479-----487-----491-----|
MIV16     DATSTGNYNKYRSLRHGKLRPFERDISNVFSPDGKPCCT-PPAFNCYWPLNDYGFYITNGIGYQPYRVV
Rs4874     DATSTGNYNKYRSLRHGKLRPFERDISNVFSPDGKPCCT-PPAFNCYWPLNDYGFYITNGIGYQPYRVV
Rs4231     DSSTSGNYNLYRHVRRSKLNIPYERDLSNDIYSPGGQSCS-AIGPNCYNPLRPYGFFTAGVGHPYRVV
Rs3367     DATSTGNYNKYRSLRHGKLRPFERDISNVFSPDGKPCCT-PPAFNCYWPLNDYGFYITNGIGYQPYRVV
MIV1       DATSTGNYNKYRSLRHGKLRPFERDISNVFSPDGKPCCT-PPAFNCYWPLNDYGFYITNGIGYQPYRVV
Rs7327     DATSTGNYNKYRSLRHGKLRPFERDISNVFSPDGKPCCT-PPAFNCYWPLNDYGFYITNGIGYQPYRVV
Rs9401     DATSTGNYNKYRSLRHGKLRPFERDISNVFSPDGKPCCT-PPAFNCYWPLNDYGFYITNGIGYQPYRVV
RsSHC014   DSSTSGNYNLYRHVRRSKLNIPYERDLSNDIYSPGGQSCS-AVGPNCCYNPLRPYGFFTAGVGHPYRVV
Rs4084     DSSTSGNYNLYRHVRRSKLNIPYERDLSNDIYSPGGQSCS-AVGPNCCYNPLRPYGFFTAGVGHPYRVV
→ RaTG13   DAKEGGNFNLYRLFRKANLKPFERDISTEIQAGSKPCNGQTGLNCCYPLRYGFYPTDGVGHQPYRVV
Rs4081     DQGG-----YYRSSRKTCLKPFERDLSO-----E-NGVRTLSTYDFYPTVPIEQATRVV
Rs4255     DQGG-----YYRSSRKTCLKPFERDLSO-----E-NGVRTLSTYDFYPTVPIEQATRVV
Rs4237     DQGG-----YYRSSRKTCLKPFERDLSO-----E-NGVRTLSTYDFYPTVPIEQATRVV
Rs6526     DKGG-----YYRSSRKTCLKPFERDLSO-----E-NGVRTLSTYDFYPTVPIEQATRVV
Rs4247     DTGH-----YYRSHRKTCLKPFERDLSO-----DGNGVYTLSTYDFNPNVPVAYQATRVV
Rf4092     DVGS-----YFYRSHRSSKCLKPFERDLSO-----E-NGVRTLSTYDFNPNVPVAYQATRVV
Rs3369     DSSTSGNYNLYRHVRRSKLNIPYERDLSNDIYSPGGQSCS-AVGPNCCYNPLRPYGFFTAGVGHPYRVV
Rs4075     DVGS-----YFYRSHRSSKCLKPFERDLSO-----E-NGVRTLSTYDFNPNVPVAYQATRVV
Rs4085     DTGH-----YYRSHRKTCLKPFERDLSO-----DGNGVYTLSTYDFNPNVPVAYQATRVV
Rs4108     DQGG-----YYRSSRKTCLKPFERDLSO-----E-NGVRTLSTYDFYPTVPIEQATRVV
Consensus D.g.....Y.YR..R..KLKPFERDIS#.....Ngv.tLstYdf.ptvp..yQatRVV
```

Sequence alignment comparing the RBMs of SARS (top) and RaTG13 (red arrow) to the RBMs of bat coronaviruses

# COVID-19 controversy: hypothesis vs truths

**Hypothesis 4:** RaTG13 coronavirus sequence uploaded to GenBank was manufactured: it doesn't come from a biological sample and was fraudulently and randomly made by humans.

**Truth:** In the Institute of La Jolla, California, this virus sequence was re-analyzed to compare it with the original obtained in 2013. The data of which the dr. Yan talks is from 7 years ago.

**Hypothesis 5:** SARS-CoV-2 was made at the Third Military Medical University (Chongqing, China) and the Nanjing Command Medical Research Institute (Nanjing, China). Started working in 2003.

**Truth:** Nature has more time and possibility to create a new virus in contrast to laboratories in China that began operating just 17 years ago.

Thanks for your attention!



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