Evolution of viruses antiviral defense

K. Moelling,University of Zurich,Zurich,CH and Institute of Advanced Studies, Berlin,Dtl

EVOLUTION OF VIRUSES AND ANTIVIRAL DEFENCE

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Contemporary viruses can be organized in an evolutionay tree ranging from the RNA world to the DNA world, from ribozymes, via viroids, DNA-ribozymes, Influenza, retro-and para-retroviruses to DNA viruses – supporting a „virus-first" hypothesis. Retroviruses have shaped or may hav e even built the human genome, where up to 50% are retrovirus -related sequences to which increasing and decreasi ng complexities contributed. Rudimentary reverse transcription from RNA to DNA is still ongoing today in teleomeres during e mbryognesis and cancer(1). Sequence analysis of the human genome witnesses our past, indicating how long HIV-like viruses, reverse transcriptase and R NAses H have been around. Endogenization of retroviruses is actively ongoing in animal models and may allow a prediction on the f uture of HIV in people. Evolution of HIV takes place durin g antiretroviral therapies. An H IV suicide approach circumvents mutagenesis and escape mu tants(2,3). Co-evolution or crossing arms, also known from phage and bacteria, can be deduced from structural and functional similarities of retroviral replication and the siRNA-mediated antiviral defence machineries (4). An evolutionary relationship between siRNA and interferon can be construc ted by comparing their pathways. SiRNA involving dicer as well as interferon are active antiviral defence mechanisms in mammalian cells, tested by dicer and interferon knock-down analyses (5;6). The systems differ in strength and sequence specificities.

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Organization of presently known viruses according to a hypothetical appearance during evoluton (RNA to a DNA world).

From the RNA world to the DNA world

R —RT→ DD

Time, comlpexity, stability

Small interfering RNA is related to interferon as antiviral defence.

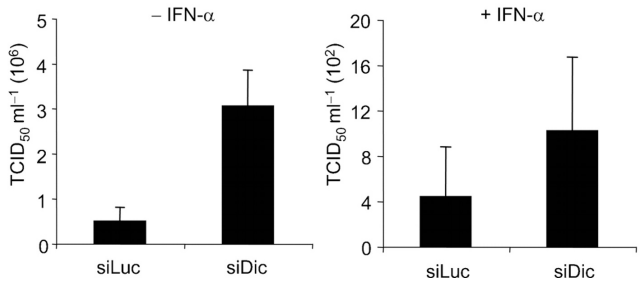
Relationship between Retroviruses and RISC

Retrovirus	siRNA
Reverse Transcriptase (RT)	PAZ
RNase H	PIWI
3'-OH, 5'-phosphate oligonucleotide	3'-OH, 5'-phosphate oligonucleotide
RT (primer-grip)	PAZ pocket
RT (RNA-dependent DNA polymerase/ DNA-dependent DNA polymerase)	RNA-dependent RNA polymerase
RT (DNA unwinding)	Helicase
Integrase (dinucleotides overhangs)	Dicer (dinucleotides overhangs)
Nucleocapsid (melting, RNA protection)	RNA Binding Proteins, TRBP, FMRP
TRBP	TRBP
Protease	?Caspases. PPARP

Todays viruses as witness of evolution

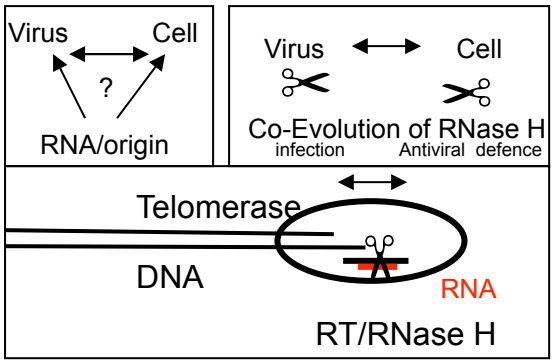
1.R-Rz --->2.R-RR--->3.R-RD-DD ---> 4.DD-R --->5.DD-DDR

1.RNA vioids, Ribozyme, catalytic, can open and close chemical bonds, bacterial viruses, plant viroids, Hepatitis Delta Virus
2.RNA Viruses, RNA in into double-stranded RNA, then progeny RNA,bacterial viruses, Influenza, Hanta, SARS,single or segmentedRNA
3. Retroviruses , RNA-DNA Hybrid intermediates, Double-stranded DNA proviruses, integrate, inheritable, stable for generations,transposons? Retroviruses (HIV, LV), und Retrotransposons, Telomerases(rudimentary RT with one RNA seq)
4.Para-Retorviruses**,** double-stranded DNA inside virions, single-stranded progenomic RNA, Hepatitis B, Caulimo Viruses, HBV developed Central Dogma and cellular nucleus
5.DNA into DNA via mRNA, all Organisms, Adeno, Papilloma, Herpes, Hepatitis C viruses,Transposons? Satellites of cellular origin?

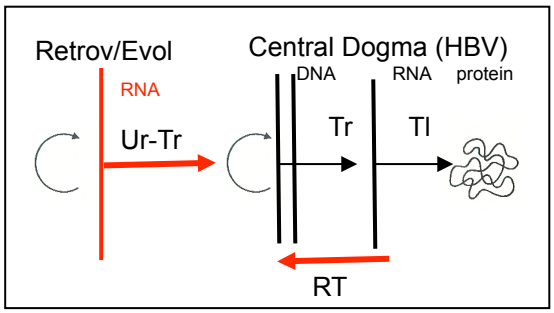


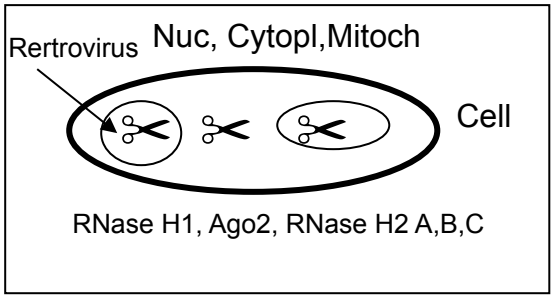
Structural/enzymatic relationship - evolutionary ?

AGO2	N-term	PAZ/PIWI
HIV	NC?	RT/RNaseH



Dicer protects aganst Influenza A





50% of human genome defective retroviruses, transposable elements, Junk? Benefit?

Evolution of viruses and antiviral defense

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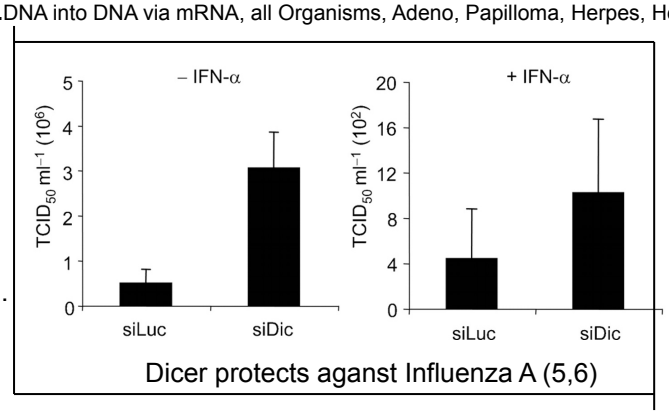
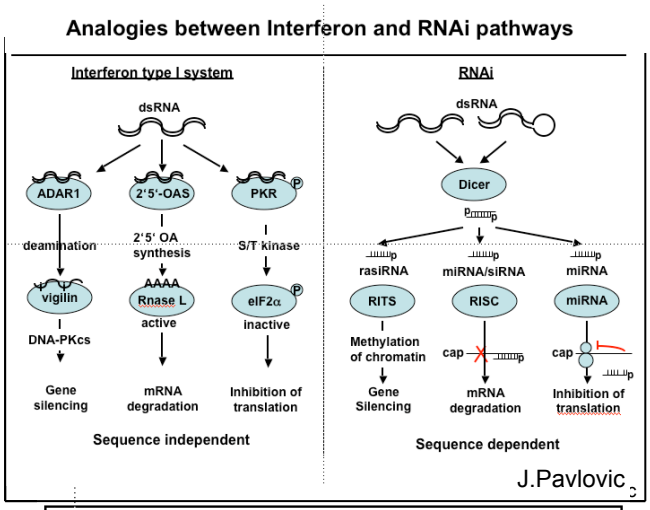
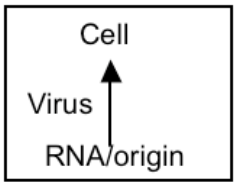
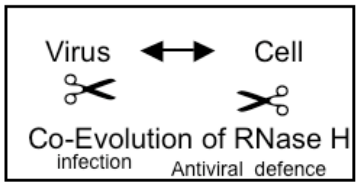


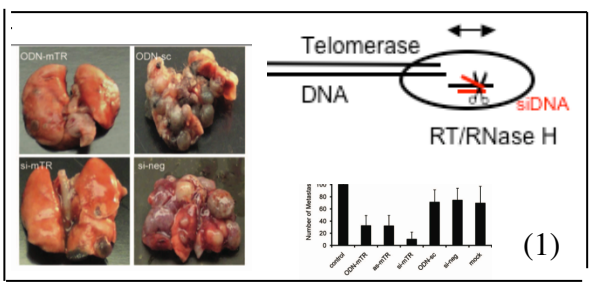
Dicer protects aganst Influenza A (5,6)

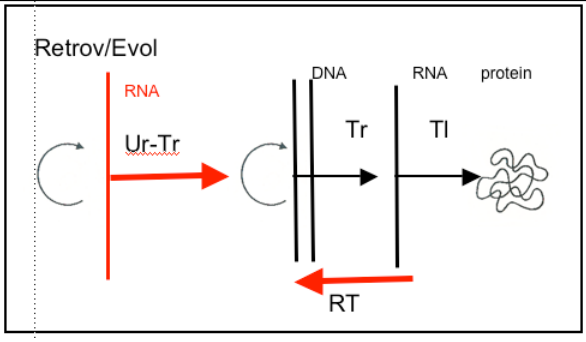
Small interfering RNA related to interferon antiviral











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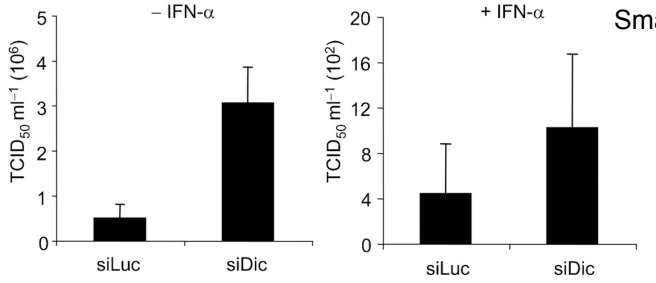

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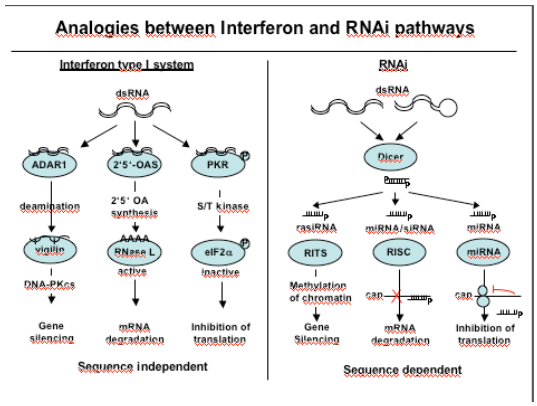

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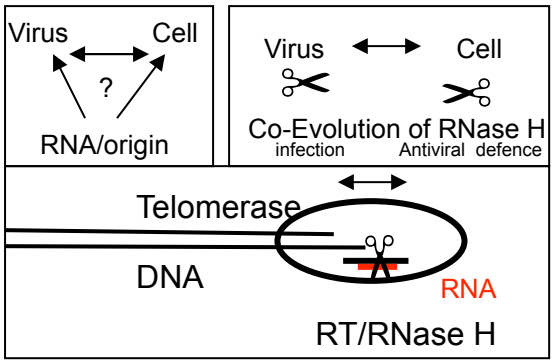

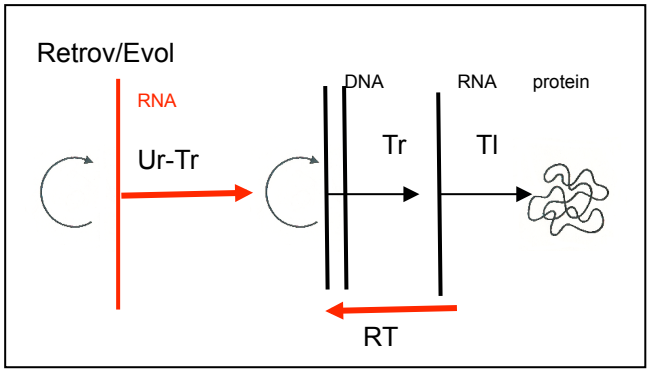

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