

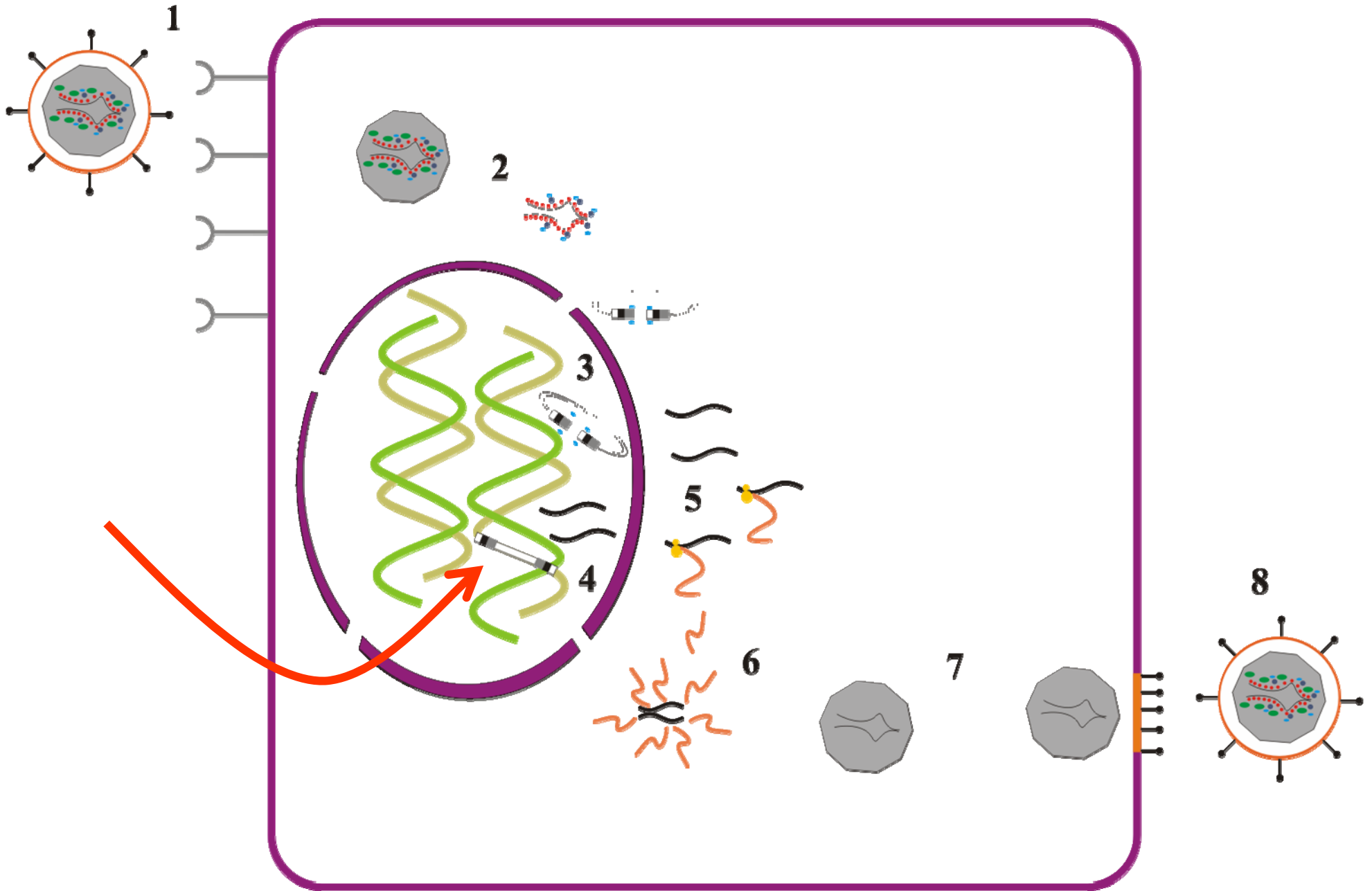


Isolation of an Infectious Endogenous Retrovirus in Live Attenuated Vaccines for Pets

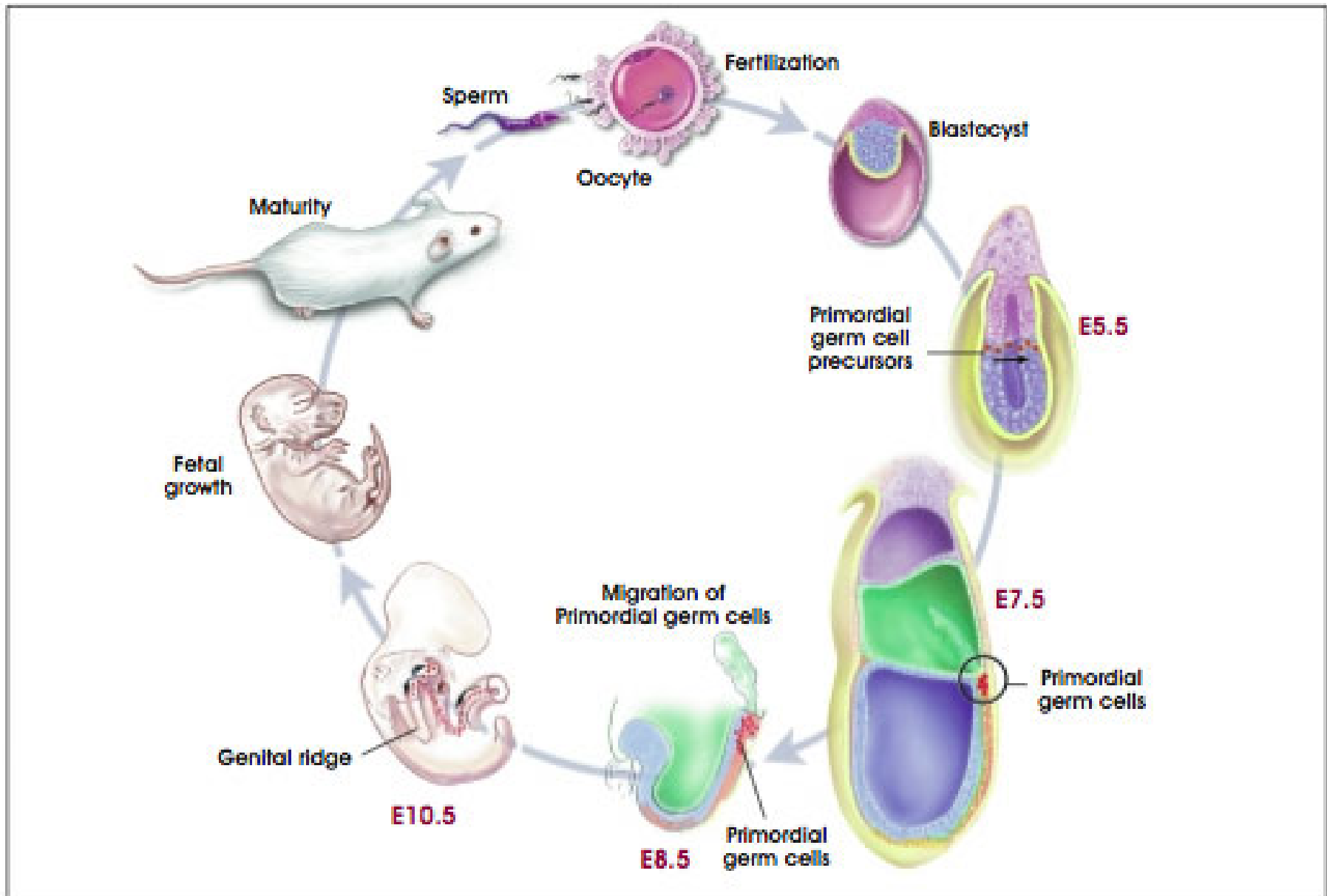
Massimo Palmarini



ociated with the infected cell



Integration of "endogenous" retroviruses in genome of the host



erent lifestyles.....



Exogenous" retroviruses: horizontally transmitted from infected to uninfected host like any other virus

Endogenous" retroviruses: vertically transmitted from mother to offspring like any other Mendelian genes

Endogenous retroviruses (ERVs)



Form a substantial part of the genome of every animal species (e.g. ~ 8% of the human genome)

50-100 ERV families in each species (several copies for each family)

Most ERVs are replication defective (during evolution they have acquired mutations/deletions that hamper their ability to replicate)

r genomes infectious ERVs



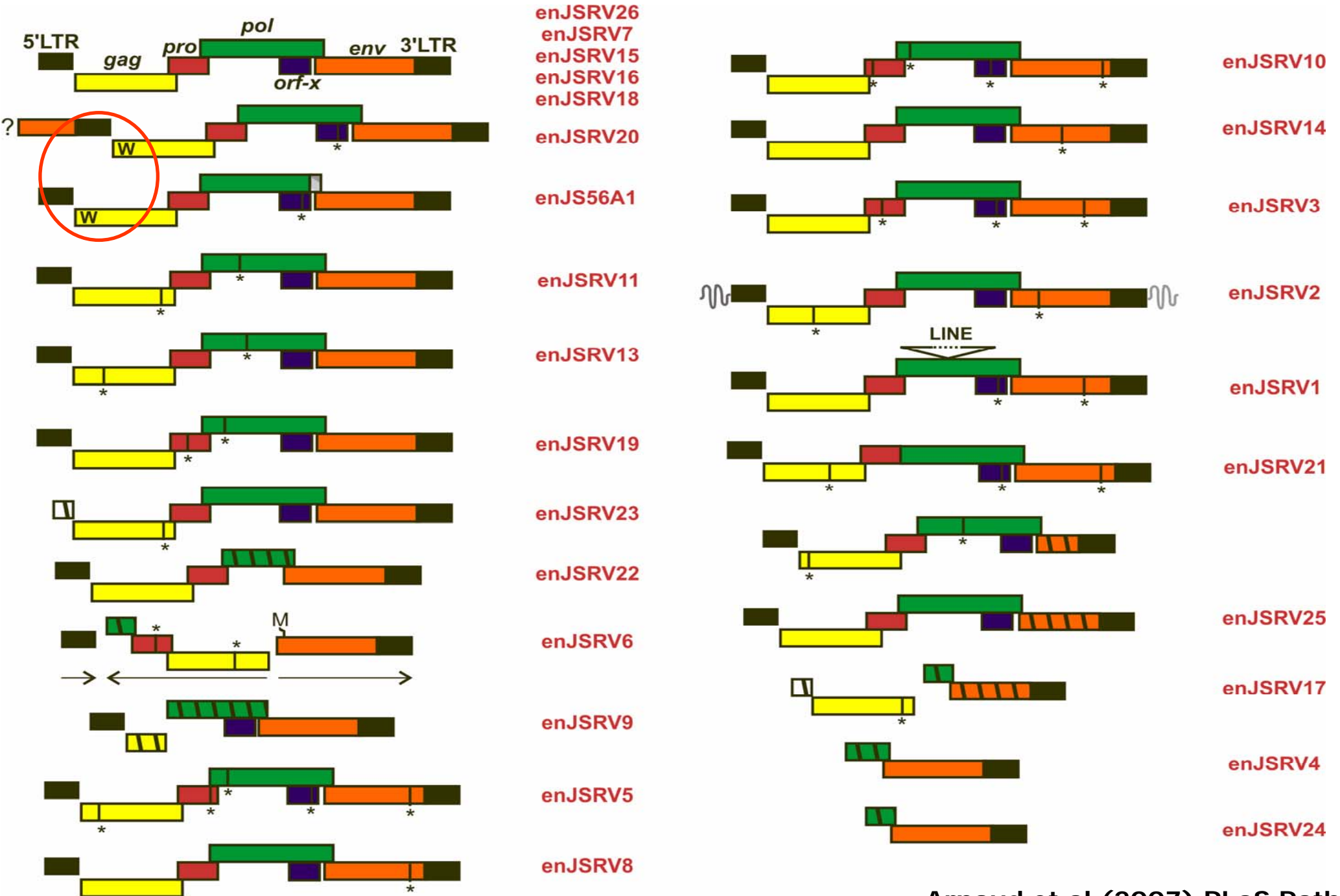
NO

YES

YES

NO

SRVs) in the sheep genome





ERVs fixed in the genome of any given primate species can be assumed to be non-pathogenic, otherwise they would not survive" evolution.

However, there are no differences between an exogenous pathogen such as HIV and ERVs with the exception that the latter have reached a evolutionary equilibrium with their host.

SRVs are...



Medical Research
University of
Centre for Virus

essential for reproductive biology of sheep (*Dunlap et al, PNAS 2006, 103:14390*)

interfere with the replication of exogenous
pathogenic retroviruses (*Mura et al, PNAS 2004, 101:11117*
Chaud et al PLoS Pathogens 2007, 3:e170)



- Replication competent ERV
of cats

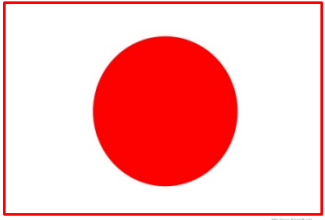
- Expressed in variable amount
by several cat cell lines incl
CRFK



- Could RD-114 be in vaccine
for pets? (Takayuki Miyazawa)

Experimental approach

an



Vaccines licensed in
Japan

RT-qPCR interference
assay

R

UK

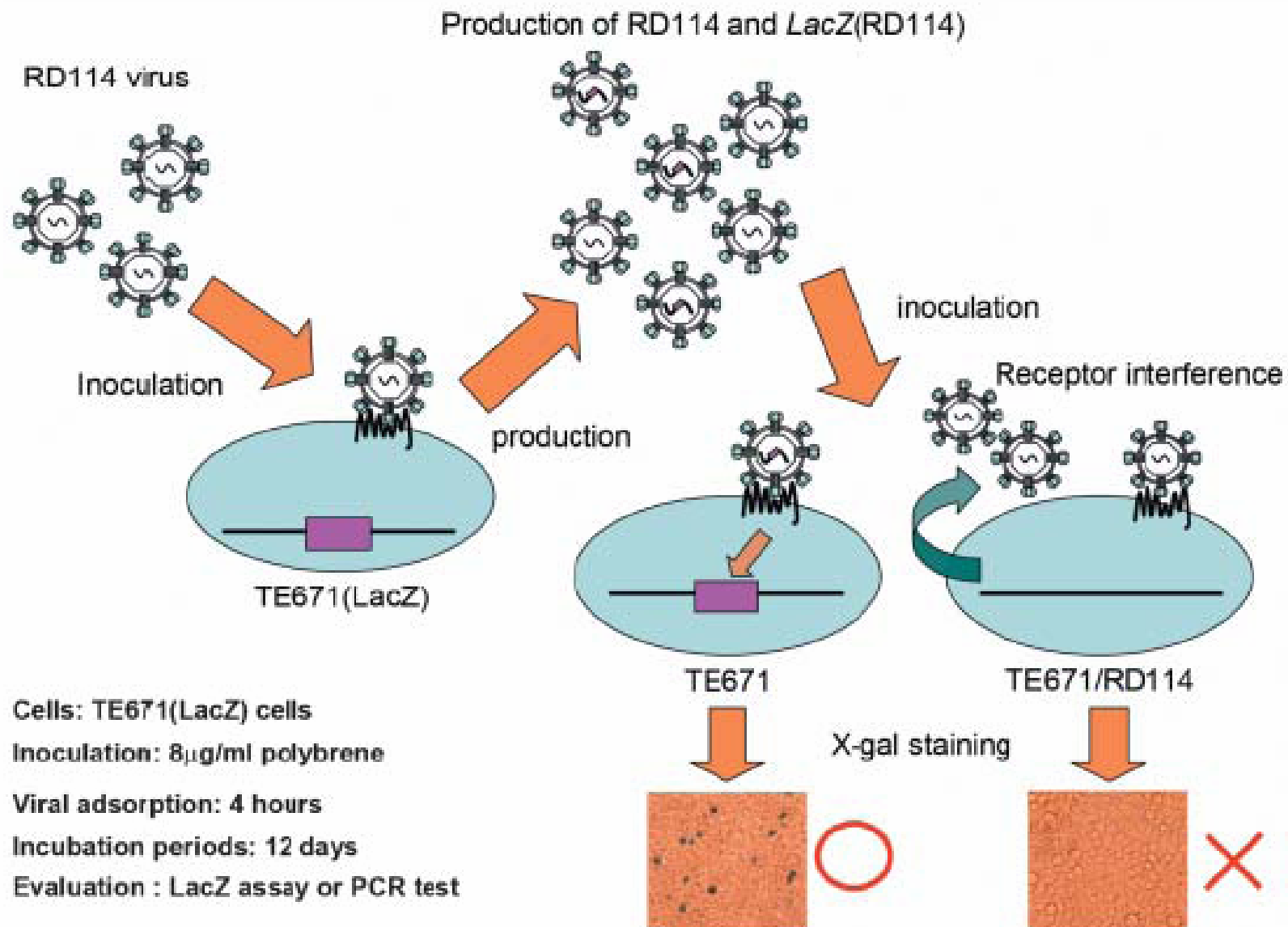


- Vaccines licensed in UK
- Virus isolation in TE670
- Western blotting
- RT-assay



Z Interference assay

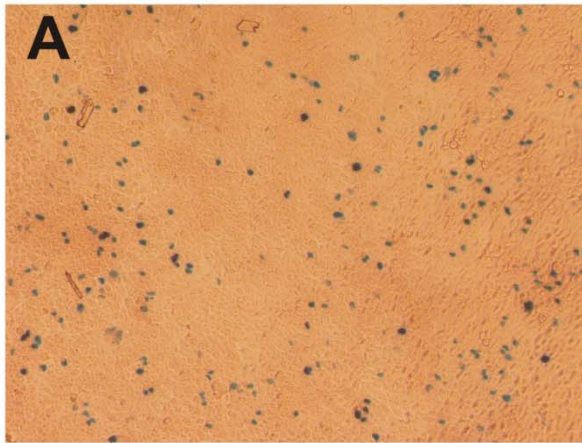
A



TE67

TE67(RD114Env)

JCd1



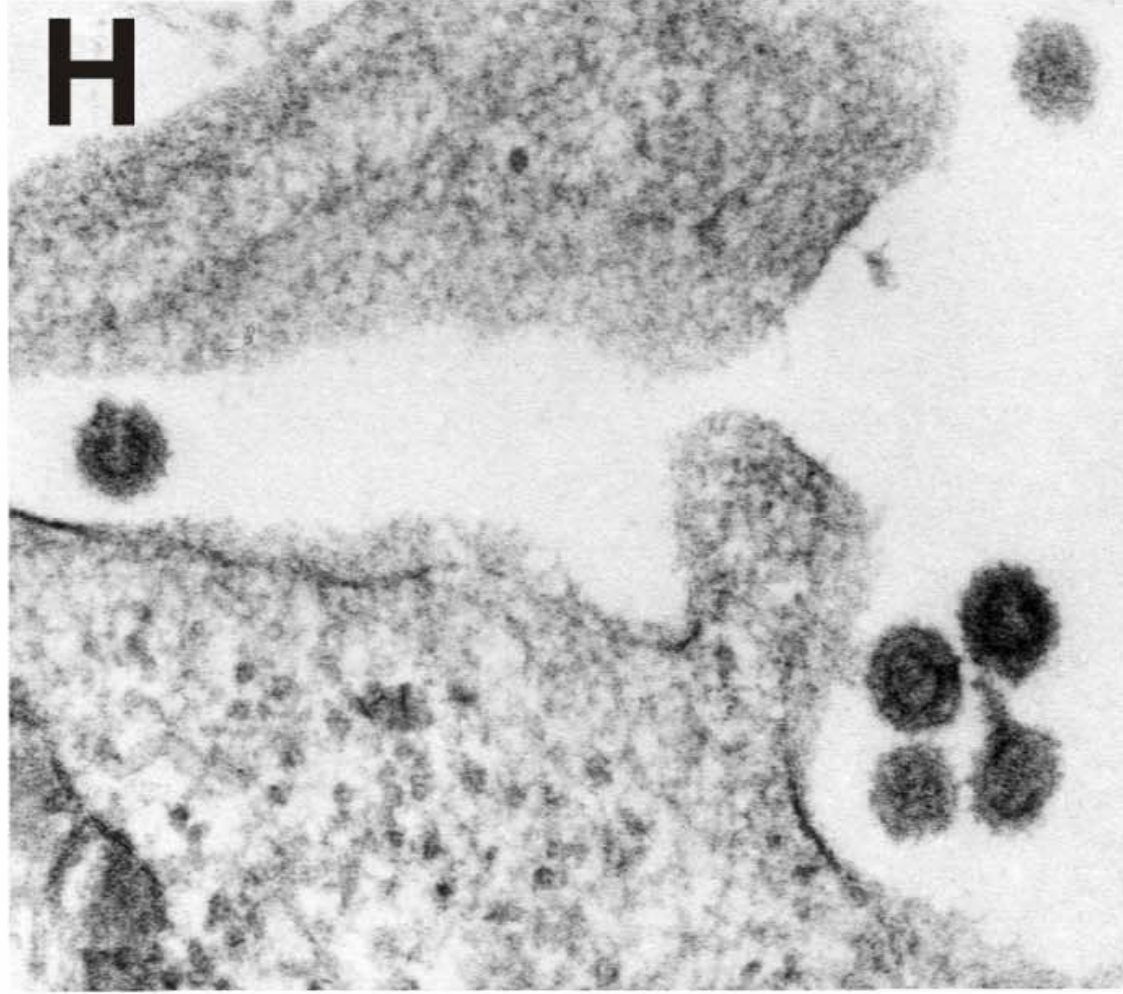
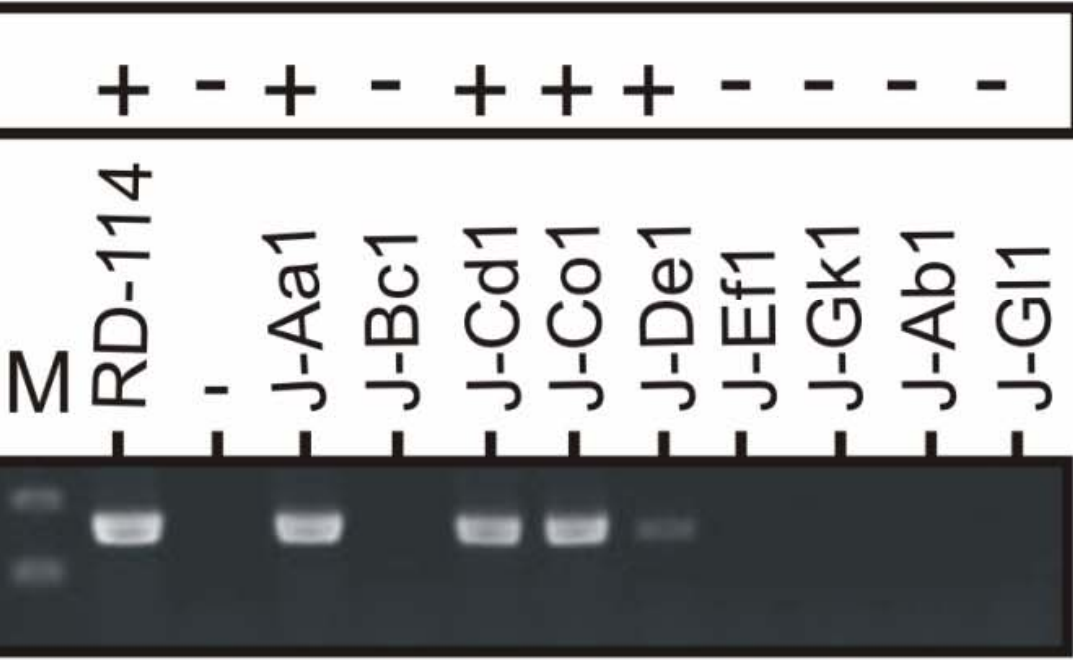
JCo1

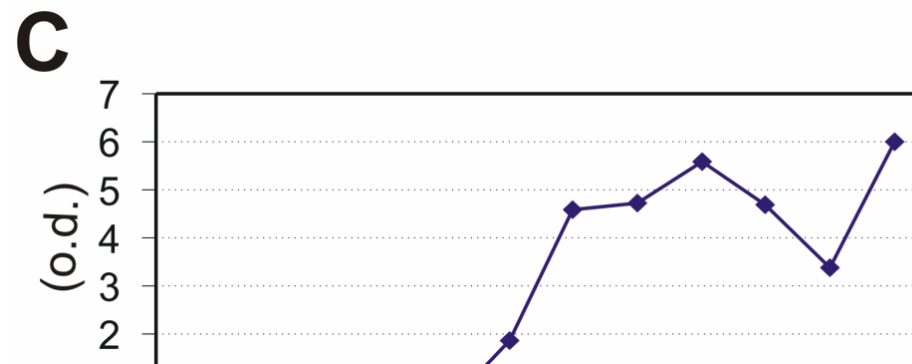
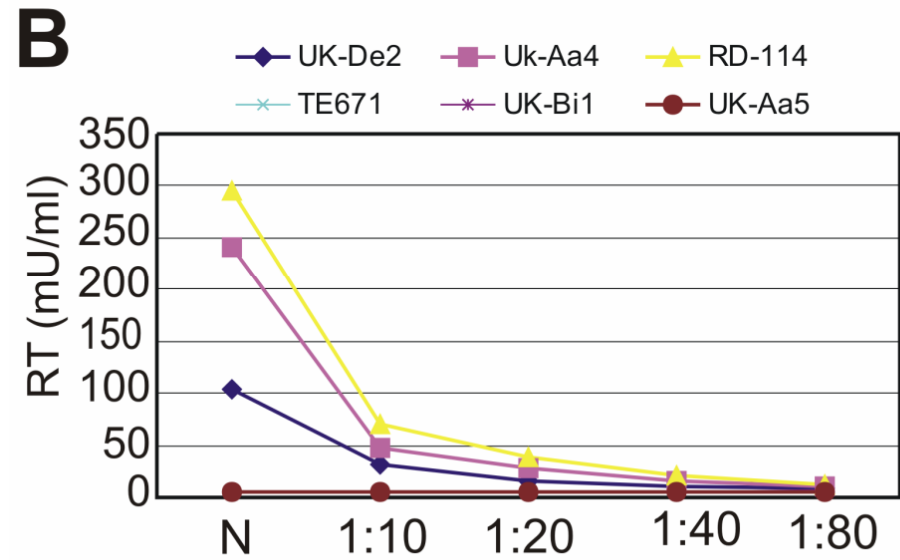
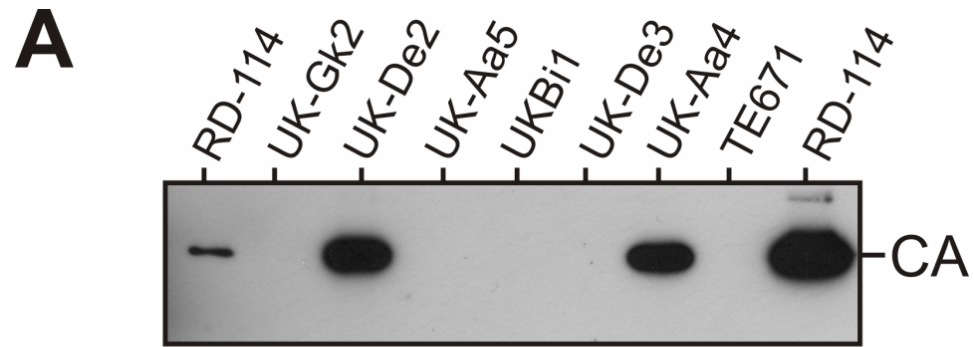


+



LacZ rescue assay







Vaccine code ^a	Target species ^b	No. of positive results/no. of vials tested by ^c :	
		LacZ or Western blotting LacZ ^d	PCR or RT activity-PCR ^e
J-Aa1	Cats	3/6	2/2
J-Aa2	Cats	1/1	1/1
J-Aa3	Cats	0/2	0/2
J-Bc1	Cats	0/3	0/3
J-Bc2	Cats	0/3	0/3
J-Cd1	Dogs	2/2	2/2
J-Co1	Dogs	1/1	1/1
J-Co2	Dogs	1/1	1/1
J-De1	Dogs	1/1	1/1
J-Ef1	Dogs	0/1	0/1
J-Gk1	Dogs	0/1	0/1
J-Ab1	Dogs	0/1	0/1
J-Gl1	Dogs	0/1	0/1
J-Em1	Cats	0/1	0/1
J-Hn1	Cats	0/3	0/1
		Western blotting ^f	RT ^g
UK-Aa4	Cats	3/4	2/3
UK-Aa5	Cats	0/2	0/2
UK-Bi1	Dogs	0/2	0/2
UK-De2	Dogs	2/2	2/2
UK-De3	Dogs	1/4	1/3
UK-Eg1	Dogs	0/1	nt
UK-Gk2	Dogs	0/2	0/2
UK-Eh1	Dogs	0/2	0/2
TE671	-	0/4	0/2

RD-114 was detected in live attenuated vaccines for cats and dogs

Detection of RD-114 was carried out in two different laboratories using different techniques and reagents

RD-114 levels in vaccines are very low. Virus was not detectable in every batch/vial of a "RD-114 +" vaccine

Methods to detect retroviruses in veterinary vaccines might not be adequate

Acknowledgements



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