UvA-DARE (Digital Academic Repository)

Endogenous retrovirus sequences and their usefulness to the host

van der Kuyl, A.C.

Publication date
1997

Published in
Trends in Microbiology

[Link to publication](#)

Citation for published version (APA):

van der Kuyl, A. C. (1997). Endogenous retrovirus sequences and their usefulness to the host. *Trends in Microbiology*, 5, 339.

General rights

It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: <https://uba.uva.nl/en/contact>, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

- 171, 954–960
- 13 Edlin, B.R. *et al.* (1992) *New Engl. J. Med.* 326, 1514–1521
- 14 Pearson, M.L. *et al.* (1992) *Ann. Intern. Med.* 117, 191–196
- 15 Kimberlin, D.W. and Whitley, R.J. (1996) *J. Antimicrob. Chemother.* 37, 403–421
- 16 Sacks, S.L. *et al.* (1989) *Ann. Intern. Med.* 111, 893–899
- 17 Ljungman, P. *et al.* (1990) *J. Infect. Dis.* 162, 244–248
- 18 Kost, R.G. *et al.* (1993) *New Engl. J. Med.* 329, 1777–1782
- 19 Safrin, S. *et al.* (1991) *Ann. Intern. Med.* 115, 19–21
- 20 Kyslik, P. *et al.* (1993) *Biotechnol. Bioeng.* 41, 325–329
- 21 Lee, S.W. and Edlin, G. (1985) *Gene* 39, 173–180
- 22 Lenski, R.E., Simpson, S.C. and Nguyen, T.T. (1994) *J. Bacteriol.* 176, 3140–3147
- 23 Godwin, D. and Slater, J.H. (1979) *J. Gen. Microbiol.* 111, 201–210
- 24 Bouma, J.E. and Lenski, R.E. (1988) *Nature* 335, 251–252

Letters

Endogenous retrovirus sequences and their usefulness to the host

Mammalian genomes contain an estimated 1–5% of retrovirus-related sequences, a figure that reaches 10–30% if all retrotranscribed sequences are included. Considering the millions of years in which virus and host have coexisted, it seems likely that the efficient integration and spread of these sequences in a host genome offers some benefits to the host, as well as to the virus.

Recent reviews by Garfinkel¹ and Best² in this journal have shed some light on the value of retrosequences in the host genome. Apart from the role of retroelements in repairing double-stranded breaks in genomic DNA (Ref. 1), the recruitment of endogenous *gag* and *env* sequences in the battle against new virus infections² might be important to the host, as superinfection and/or replication of retroviruses is prevented in cells where related *gag* or *env* genes are expressed. In the two cases described by Best *et al.*², a truncated retroviral genome is located near a strong cellular promoter. This might be a chance occurrence; however, for complete retroviruses a similar mechanism could be proposed. If a replicating retrovirus is present in a cell, superinfection of this cell by a related virus is prevented^{3,4}. It is possible that the *env* protein non-competitively binds to viral receptors on the cell surface.

Individuals that are able to prevent retrovirus infection of themselves and their offspring (where infection might be lethal), even if this is by means of the expression of endogenous retrovirus sequences, could have a selective advantage, especially in times of pathogenic retrovirus epidemics. This could explain why proviral genomes become fixed in a population, often in large numbers in many

species. Most of these integrations have ancient origins and are shared between all individuals of a species. Of course, deleterious integrations into important genes will quickly be selected against. The higher level of expression of retroviral sequences in placental tissue could also be explained by these protective effects.

To expand its lifespan, integration into a host germ line is a good and safe option for a virus. Consequently, targeting to oocytes or the early embryo is common for at least some types of retroviruses. Another protective effect of retroviral expression in the placenta could arise from the immunosuppressive effects of the peptides encoded by the *env* gene of many retroviruses⁵, which would contribute to the local suppression of the mother's immune system, which in turn inhibits foetus rejection.

Response from Stoye, Le Tissier and Best

We are in perfect agreement with Dr van der Kuyl concerning the potential ability of intact endogenous proviruses to restrict novel infection. Although both of our examples involve deletions of viral long terminal repeats (LTRs) and the use of cellular promoters for transcription, we did not state that such events were required and did not intend to imply that they might be. Indeed, the *Fv1* open reading frame is transcribed at very low levels: in fact, lower than one might expect from a retroviral LTR.

The immunosuppressive properties of a peptide derived from the transmembrane region of an exogenous retrovirus were first

In summary, some types of retroviruses and their host species have developed a symbiotic coexistence, with the virus finding shelter in the host genome, and the host using the viral sequences for defence against new infections.

Antoinette C. van der Kuyl
Dept of Human Retrovirology,
Academic Medical Centre,
Meibergdreef 15,
1105 AZ Amsterdam,
The Netherlands

References

- 1 Garfinkel, D.J. (1997) *Trends Microbiol.* 5, 173–175
- 2 Best, S., Le Tissier, P.R. and Stoye, J.P. (1997) *Trends Microbiol.* 5, 313–318
- 3 Steck, F.T. and Rubin, M. (1966) *Virology* 29, 642–653
- 4 Hart, A.R. and Cloyd, M.W. (1990) *Virology* 177, 1–10
- 5 Cianciolo, G.J. *et al.* (1985) *Science* 230, 453–455

described over ten years ago, and this potential property of endogenous proviruses has been invoked on many occasions. However, we are not aware of any experimental data showing a physiological role played by this region of an endogenous retrovirus. Experiments to address this issue in an incisive fashion, once and for all, would be very welcome.

Jonathan P. Stoye, Paul R. Le Tissier
National Institute for
Medical Research,
The Ridgeway, Mill Hill,
London, UK NW7 1AA;

Steve Best
The Wellcome Trust Centre for
Human Genetics,
Windmill Road,
Oxford, UK OX3 7BN