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Receptors for retroviruses, retroviral vectors, endogenous retroviruses, silencing of retroviruses

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Research topics

The main scientific interest of our group has been traditionally focused on the interactions of retroviruses with the host cells. Retroviruses enter their natural host cells via specific receptors, integrate into the host genome, and use the cell transcription machinery to express their structural or enzymatically active proteins. Specific binding of retroviral envelope proteins to host cell receptors is the prerequisite for cell permissiveness to the infection. Retroviruses broaden their host range by mutations of the *env* gene; host cells develop resistance to retrovirus by mutations of genes encoding the specific receptors. We have described such an interesting semi-resistant phenotype in chicken line M and explained it by mutation of the receptor *Tvb*. Another defence mechanism used by the host cells is the inactivation of integrated invaders at the level of transcription via DNA methylation and modifications of adjacent histones. This is, however, an obstacle in using retroviruses as vectors for gene transfer and transgenesis. We have improved ASLV-based retroviral vectors by insertion of the core element from a CpG island between the promoter and the enhancer, which increases their resistance to transcriptional silencing and ensures long-term expression of transduced genes. We have successfully used a retroviral vector for transduction of reporter genes in the chicken male germ line, which opens the way to efficient transgenesis in chicken. We have also characterized the CpG methylation status in latent proviruses of HIV-1 and suggested a two-step model of HIV-1 latency. Finally, we have identified two genomic copies of porcine endogenous retroviruses as a potential risk factor in xenotransplantation of pig organs and tissues.

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Selected recent papers

1. Reinišová M, Šenigl F, Yin X, Plachý J, Geryk J, Elleder D, Svoboda J, Federspiel MJ, Hejnar J. A single amino acid substitution in the Tvb^{S1} receptor results in the semi-resistant phenotype of an inbred chicken line to infection by subgroup B and D avian sarcoma and leukosis viruses. **J Virol.** 2008;82:2097-2105.
2. Šenigl F, Plachý J, Hejnar J. The core element of a CpG island protects avian sarcoma and leukosis virus-derived vectors from transcriptional silencing. **J Virol.** 2008;82:7818-7827.
3. Reinišová M, Pavlíček A, Divina P, Geryk J, Plachý J, Hejnar J. Target site preference of subgroup C Rous sarcoma virus integration into the chicken DNA. **Open Genomics J.** 2008;1:6-12.
4. Mucksová J, Brillard J-P, Hejnar J, Poplštejn M, Kalina J, Bakst M, Yan H, Trefil P. Identification of various testicular cell populations in pubertal and adult cockerels. Accepted to **Anim Reprod Sci.**

DNA methylation and modification of histones associated with HIV-1 long terminal repeats in a two-step model of HIV-1 latency. Below, the active state. Right, the reactivable latency in line H12 and locked state in the 2D12 cell line.