

FeLIX is a restriction factor against mammalian retrovirus infections

A research group led by Professor Kazuo Nishigaki at the Laboratory of Molecular Immunology and Infectious Disease (Joint Graduate School of Veterinary Medicine, Yamaguchi University) recently identified a secreted protein that blocks various retrovirus infections, including those caused by the feline leukemia virus (FeLV), in domestic cats. The results of this study can facilitate the development of new prevention and treatment methods for infectious diseases.

FeLV is a retrovirus that causes anemia and hematopoietic diseases, such as lymphoma and leukemia, in domestic cats (*Felis catus*). This virus infects animals by binding to the entry receptor on the cell surface. Notably, different FeLV subgroups use different entry receptors. For example, the entry receptor for FeLV-A is THTR1, a vitamin B1 transporter, whereas that for FeLV-B is Pit, a phosphate transporter.

FeLV-A is transmitted among domestic cats. Interestingly, FeLV-A infection leads to viral gene recombination in domestic cats, resulting in the emergence of a new virus, FeLV-B. Unlike FeLV-A, FeLV-B is not transmitted among domestic cats. In this study, we investigated the mechanism responsible for this difference in the transmission of different viruses. Genomes analysis revealed that the secreted protein, FeLIX, blocked the transmission of FeLV-B among domestic cats.

FeLIX is encoded by an endogenous retrovirus, known as the ancient virus (footnote 1), and derived from its envelope gene. Genetic analysis revealed that FeLIX was derived from the ancient virus infecting the domestic cat ancestors approximately 700,000 years ago. In addition to domestic cats, FeLIX has been detected in the European wild cats (*F. silvestris*). Our findings revealed that FeLIX prevented FeLV-B infection by masking its entry receptor. FeLIX is a secreted protein released by lymphocytes that circulates in the blood of domestic cats and inhibits the cellular entry of viruses. Additionally, we observed retroviruses similar to FeLV-B in several animal species, including gibbons, bats, and koalas. Notably, FeLIX also inhibited the infections caused by these viruses. These findings suggest that FeLIX protects domestic cats against various retroviruses by acting as a restriction factor. The results of this study were published on March 05, 2024 in the Journal of Virology, American Society for Microbiology.

Footnote 1. Endogenous retroviruses. Genome retains the sequences of all retroviruses that previously infected the host. Endogenous retroviral sequences account for approximately 8% of the human genome.

【Information on published papers】

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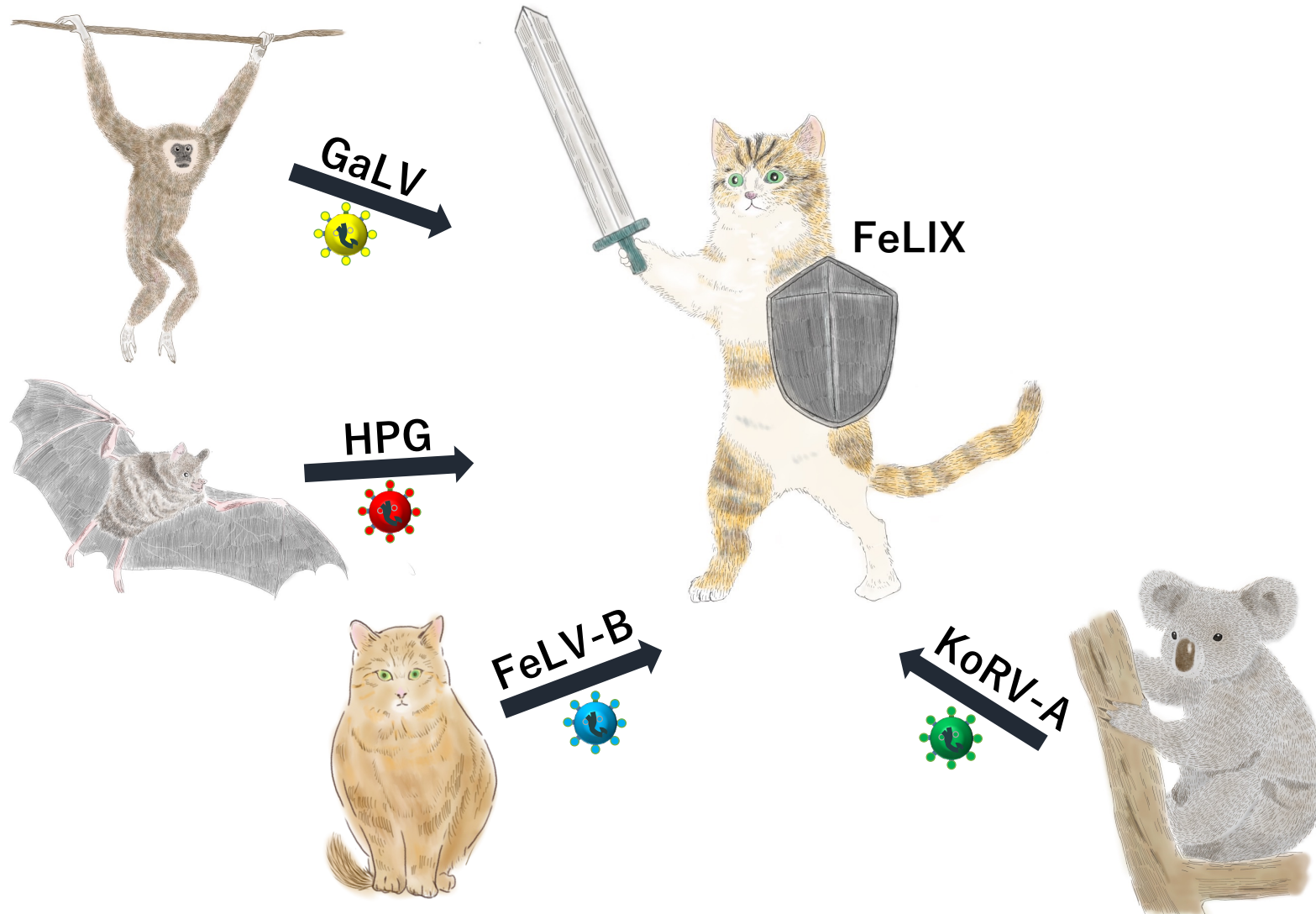


Figure Description: The domestic cat has a secreted protein, FeLIX, derived from endogenous retroviruses, which is suggested to block the spread of retroviruses (GaLV, HPG, KoRV-A, FeLV-B) in various animals. (Pictures were designed by Miyu Tanaka, a veterinarian; graduated from the Joint Faculty of Veterinary Medicine, Yamaguchi University in March 2023)