

Prof. Didier Trono

EPFL, School of Life Sciences, Laboratory of Virology and Genetics

Epigenetic control of retroelements

More than forty percent of the mammalian genome is derived from retroelements, about a quarter of which are endogenous retroviruses (ERVs). ERVs are transcriptionally silenced during early embryogenesis through histone and DNA methylation, although the initiators of this process, which is essential to protect genome integrity, remain largely unknown. Through a combination of genetic, functional and biochemical studies, we now demonstrate that KRAB zinc finger proteins and their universal cofactor KAP1 are key to the epigenetic control of ERVs. Our results provide a mechanism for the signs of strong positive selection exhibited by KRAB ZFP genes. Furthermore, considering that epigenetic silencing marks can spread from repetitive elements to neighboring genes, these data open new perspectives to explore retrotransposon-mediated control of cellular genes in development and in adult tissues. Furthermore, they suggest that KRAB/KAP1-mediated repression may partake in the establishment of HIV latency.