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Poster presentation

The epigenetic control of HERV loci encoding for fusogenic envelope glycoproteins in trophoblast

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Background

Up to 8% of the human genome is of retroviral origin, comprising numerous human endogenous retroviruses (HERVs), remnants of germ line transmission of exogenous retroviruses during primate and human evolution. Some endogenous retroviruses within the human genome remain intact open reading frames with translational potential. Gag and Env genes are often expressed in various human tissues and provide superantigens or restriction factors interfering with exogenous infections. Several Env products display fusogenic properties and it is temting to implicite them in various human pathologies like cancer, multiple sclerosis, and muscular dystrophies. Of particular importace are the fusogenic Env proteins expressed in placenta, *syncytin-1* and *2*, encoded by ERVWE1 and ERV-FRD proviral loci, respectively. These fusogenic Envs contribute to the differentiation of multinucleated syncytiotrophoblast in placental chorionic villi. In non-placental tissues, however, expression of these fusogenic proteins has to be suppressed because of high risk for tissue integrity and cancer development. We have previously shown that the 5' long terminal repeat, the regulatory region of *syncytin-1* is epigenetically suppressed by DNA methylation in non-placental tissues.

Results

We extend our previous analysis to *syncytin-2*, which shows the same pattern of heavy methylation in the testes and skin fibroblast in contrast to hypomethylated copies in placenta or choriocarcinoma cells. Chromatin immunoprecipitation analysis showed trimethylated H3K9 and H3K27 associated with U3 regions of both ERVWE1 and ERV-FRD in non-placental *in vitro* cultured cells. In contrast, U3 regions of ERVWE1 and ERV-FRD are associated wit hypomethylated but acetylated chromatin, a hallmark of transcriptionally active genes. *Syncytin-1* and *syncytin 2* are transcribed at a low level in testes and in this case, the expression of fusogenic protein product is prevented by the absence of retroviral splicing. The absence of splicing is particularly striking in the case of exogenous expression of syncytins in HeLa cells.

Conclusion

We have shown the epigenetic mechanisms suppressing expression of *syncytin-1* and *syncytin-2* in non-placental cells. Both loci are transcriptionally inactivated by DNA methylation and histone H3 trimethylation. We also suggest that the control of splicing might be important during the placental development and the occurrence of spliced transcript of *syncytins* might start the differentiation of syncytiotrophoblast from cytotrophoblast.

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