Département femme-mère-enfant

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HERV-W-Env protein expression in pediatric type 1 diabetes patients

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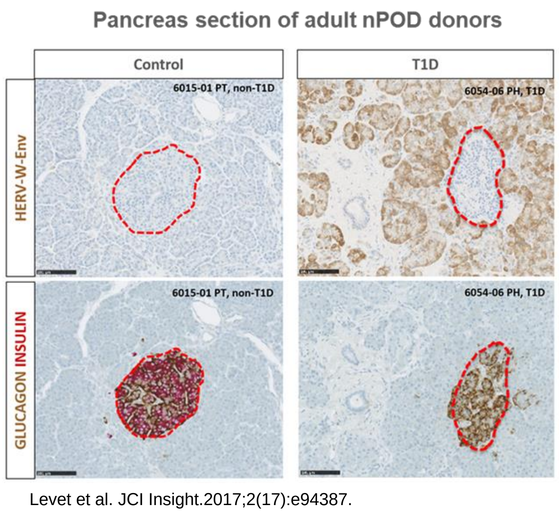
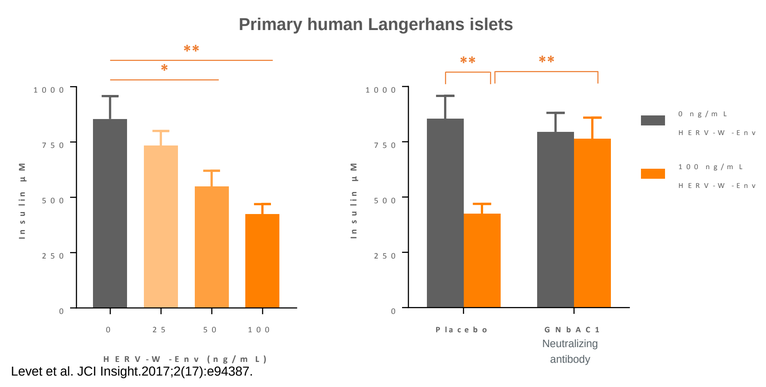
Introduction

- Envelope protein of Human Endogenous Retrovirus type W (HERV-W-Env) is associated with type 1 diabetes (T1D) pathogenesis in adults[1]. This protein is expressed in the pancreas of T1D patients and seems to correlate with macrophage infiltration.



Levet et al. JCI Insight.2017;2(17):e94387.

- *In vitro* and *in vivo* studies have demonstrated that HERV-W-Env inhibits insulin secretion and promotes hyperglycemia.



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- HERV-W-Env could be implicated in other auto-immune diseases.

Objectives

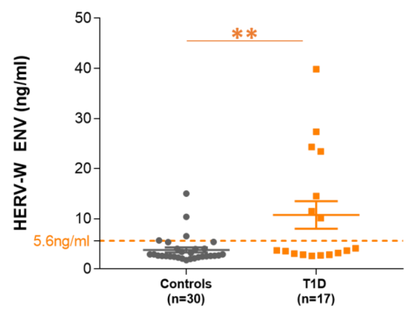
- To assess the prevalence of HERV-W-Env protein and its corresponding RNA in pediatric T1D patients.
- To identify a targeted immunotherapy in this cohort of T1D.

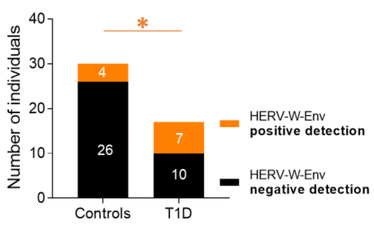
Patients

	Serum cohort		PBMC cohort	
	Controls	T1D	Controls	T1D
n	30	17	14	19
Age (Years) [Mean ± SD]	38.5 (± 13.7)	14.5 (± 2.4)	37.3 (± 11.9)	13.66 (± 3.6)
Female [n (%)]	13 (43.3%)	8 (47.1%)	6 (42.9%)	9 (47.4%)
Male [n (%)]	17 (56.7 %)	9 (52.9%)	8 (57.1%)	10 (52.6%)
Disease duration [Mean ± SD]	NA	6.4 (± 3.5)	NA	6.6 (± 3.5)
BMI SDS (n, %)				
≤-2.0	NA	0 (0%)	NA	0 (0%)
-1.99 to -1.01		0 (0%)		0 (0%)
1.0 to -1.0		8 (47%)		9 (47%)
1.01 to 1.99		6 (35%)		6 (32%)
≥2.0		3 (18%)		4 (21%)

Results

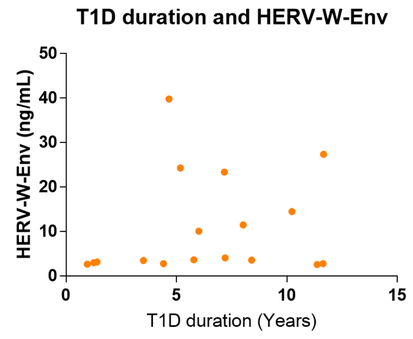
A: HERV-W-Env protein in serum of pediatric T1D patients



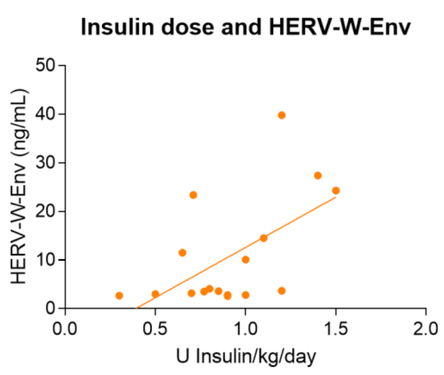


% HERV-W-Env positive individuals	Controls	T1D
	13%	41%

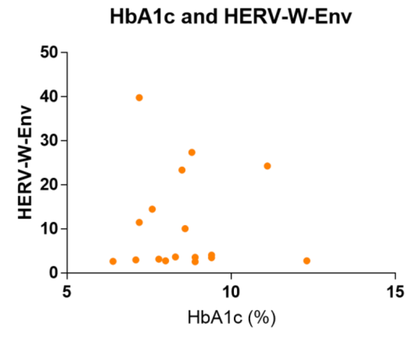
HERV-W-Env is significantly higher in T1D patients compared to control individuals (P < 0.01)



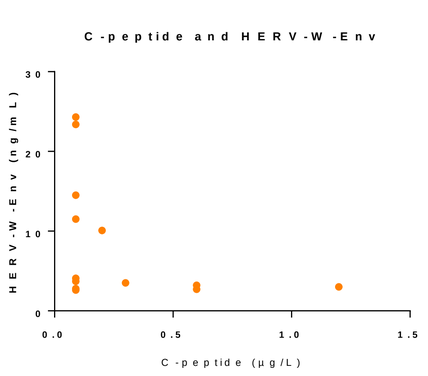
Daily insulin doses were positively correlated with HERV-W-Env expression (P < 0.05)



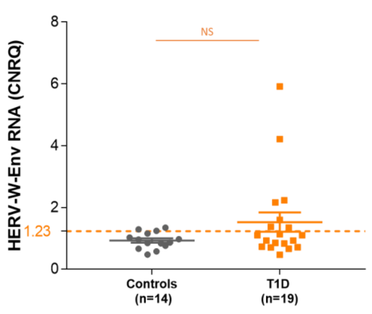
HERV-W-Env expression is not related to age, age at onset of diabetes, HbA1c or diabetes duration.

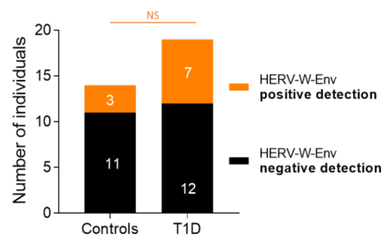


All T1D pediatric patients who expressed HERV-W-Env had low C-peptide levels



B: *HERV-W-env* mRNA in PBMC of pediatric T1D patients

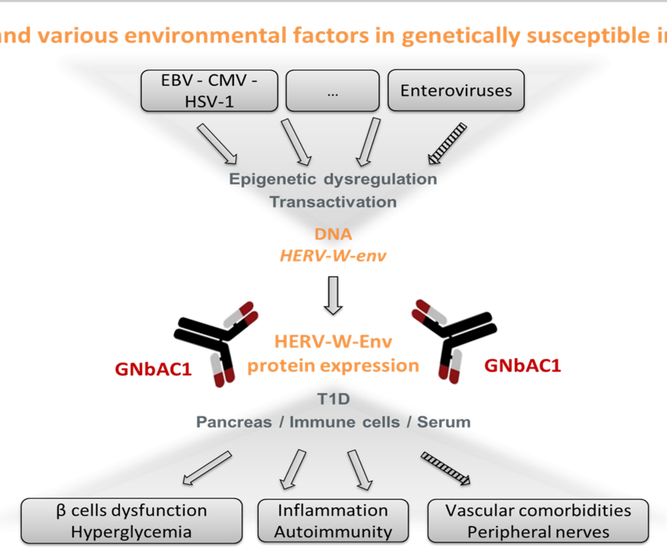




% HERV-W-Env positive individuals	Controls	T1D
	21%	37%

Discussion

- HERV-W-Env was detected in about 40% of pediatric T1D patients.
- Levels of HERV-W-Env were positively correlated with daily insulin doses, suggesting that HERV-W-Env may be associated with more severe β-cell destruction.
- As HERV-W could be implicated in other auto-immune diseases and affect endothelial and Schwann cells, a close monitoring of comorbidities in HERV-W-Env positive-patients seems essential.
- Overall, our results suggest that a specific subgroup of pediatric T1D patients might benefit from an anti-HERV-W-Env therapy with GNbAC1, a monoclonal antibody, potentially neutralizing the MSRV-Env protein expression.



References

1. Levet S, Medina J, Joanou J, et al. An ancestral retroviral protein identified as a therapeutic target in type-1 diabetes. JCI Insight. 2017;2(17).

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57ESPE 83--P1

Diabetes and insulin

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Poster presented at: 57th ESPE 2018 Meeting ATHENS GREECE 27-29 September 2018

PosterSessionOnline.com