Activación de retrovirus endógenos y su relación con los síntomas en FM, SFC y COVID persistente

Grupo de investigación UCV “Expresión génica e inmunidad”
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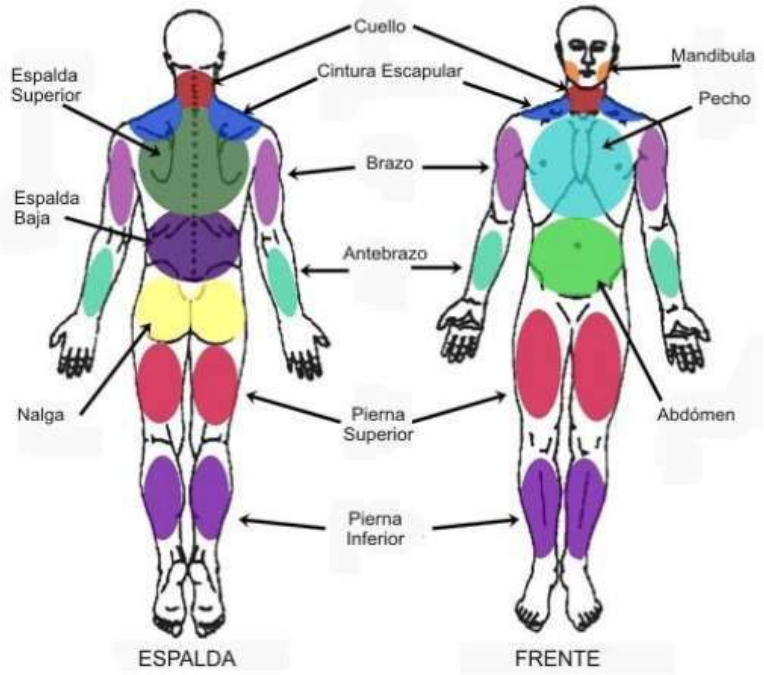
La palabra **fibromialgia (FM)** significa **dolor en los músculos** y en el tejido fibroso (ligamentos y tendones). La fibromialgia se caracteriza por **dolor musculoesquelético generalizado** y sensación dolorosa a la presión en unos puntos específicos (puntos dolorosos). Este dolor se parece al originado en las articulaciones, pero no es una enfermedad articular.

La fibromialgia es frecuente, la padece entre **el 2% al 6%** de la población, sobre todo mujeres.

Índice de Dolor Generalizado – Widespread Pain Index (WPI)



código **M79.7** Clasificación Internacional de Enfermedades (CIE-10)

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La **encefalomielitis miálgica / síndrome de fatiga crónica (EM/SFC)** es una enfermedad de largo plazo que **afecta a muchos sistemas del cuerpo**. Las personas con esta enfermedad no son capaces de realizar sus actividades cotidianas. A menudo, pueden ser confinadas a una cama. La afección también se puede llamar enfermedad de **intolerancia al esfuerzo sistémico** (EIES).

Es más común en quienes tienen entre 40 y 60 años. Las **mujeres** adultas lo presentan con mayor frecuencia.

Código **R53.82** o **G93. 3, si post-viral**
Clasificación Internacional de Enfermedades (CIE-10)

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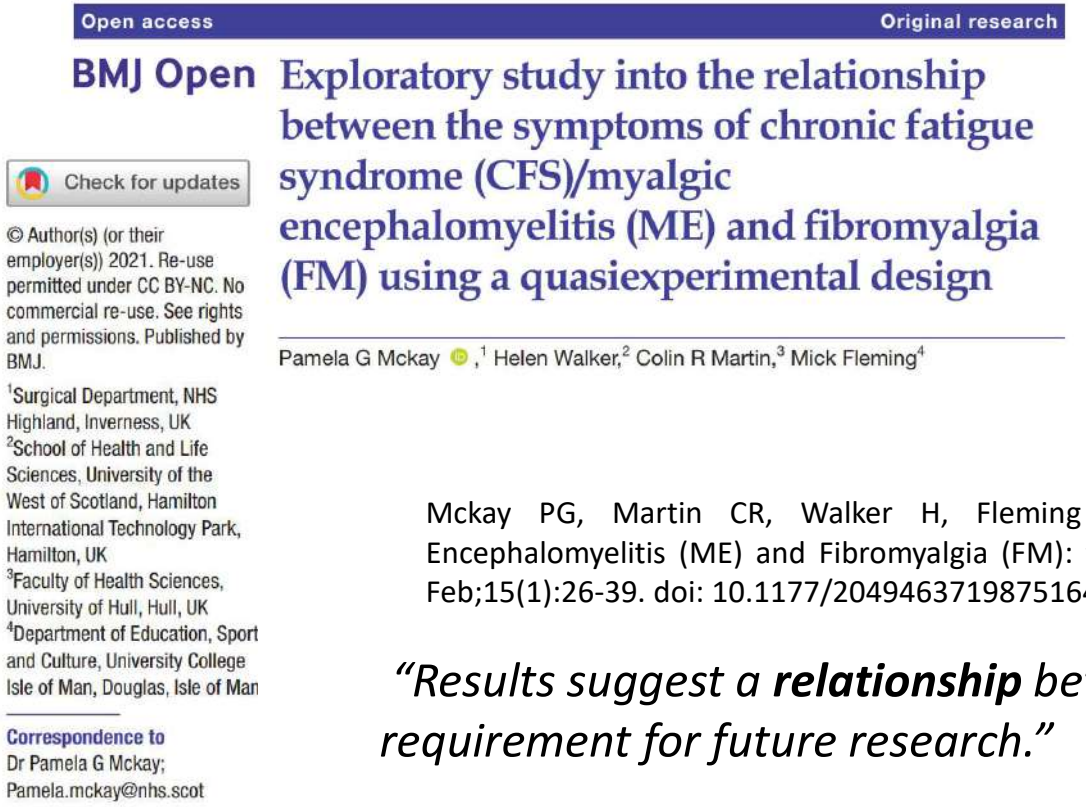
Meeus M, Ickmans K, Struyf F, Kos D, Lambrecht L, Willekens B, Cras P, Nijs J. What is in a name? Comparing diagnostic criteria for chronic fatigue syndrome with or without fibromyalgia. Clin Rheumatol. 2016 Jan;35(1):191-203. doi: 10.1007/s10067-014-2793-x.



Open access Original research

BMJ Open

Exploratory study into the relationship between the symptoms of chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME) and fibromyalgia (FM) using a quasiexperimental design

Check for updates

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*"diagnosis of comorbid FM selected symptomatically worse and **more disabled** patients."*

Mckay PG, Martin CR, Walker H, Fleming M. Chronic fatigue syndrome (CFS)/Myalgic Encephalomyelitis (ME) and Fibromyalgia (FM): the foundation of a relationship. Br J Pain. 2021 Feb;15(1):26-39. doi: 10.1177/2049463719875164.

*"Results suggest a **relationship** between CFS/ME and FM, indicating the requirement for future research."*

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2 Cuestionarios específicos y 7 genéricos

101 CFS/ME and 107 FM

Conclusion Participants responded in a similar manner to the questionnaire, confirming the same symptom experience. It is important to consider this in context with differing criteria and management guidelines, as this may influence diagnosis and the trajectory of patient's management. With the biomedical cause currently unclear, it is the symptom experience and the impact on quality of life that is important. These findings are meaningful for patients, clinicians and policy development and support the requirement for future research.

Table 1 Description of questionnaires used for data collection

Symptom	Questionnaire	Purpose	Reliability	Validity	Author
	Specific questionnaire/ criteria				
Diagnostic Criteria for CFS/ME	American Centers for Disease Control and Prevention Diagnostic Criteria (CDC) for CFS/ ME. Symptom inventory.	Diagnostic criteria. In addition, measures, frequency, intensity and duration of eight symptoms.	Good. Cronbach's alpha (α) ranging from 0.82 to 0.91 r >0.77.[33 52 53]	Good. Significant correlations r=0.54–0.54 (p<0.001).[53 63]	Fukuda et al Wagner et al[15 32]
Diagnostic criteria for FM	American College of Rheumatology Diagnostic Criteria for FM	Diagnostic criteria for FM.	n/a	n/a	Wolfe et al[4]
Symptom experience of FM	The Fibromyalgia Impact Questionnaire	Comprises 20 items to assess the impact of symptoms of FM on patients' daily lives and their response to any management/treatment offered. Questions address patient's function, pain level, fatigue, sleep disturbance and psychological distress.	Good α=0.72–0.93 r=0.58–0.83.[34 54]	Good. Significant correlations with the Arthritis Impact Scale (p<0.0001).[55]	Burkhardt et al[54]
	Generic questionnaire				
Pain	McGill Pain Questionnaire	Measures frequency and intensity of pain, namely: affective, evaluative, sensory and miscellaneous. There is a body diagram to indicate areas of pain, 72 descriptor words to assess pain and pain rating intensity scale. Each section is scored based on the guidelines.	Good. α>0.9. r≥0.89 (p≤0.001).[28 56]	Good. Coefficient ranging between 0.3 and 0.4.[28]	Melzack[28]
Fatigue	Multidimensional Fatigue Inventory	Measures 20 items on five dimensions: general, physical, mental, reduced motivation and reduced activity. Each dimension contains four items: two items relating to fatigue and two items that are contraindicative of fatigue.	Good. α>0.80 with average of 0.84. Stability r ≥ 0.72.[28 57]	Good. p<0.001 High scores 0.77 general fatigue, 0.7 physical fatigue, 0.61 reduced activity, 0.56 reduced motivation mental fatigue 0.23 (p<0.01).[28 57]	Smets et al[28]
Sleep quality	The Pittsburgh Sleep Quality Index	Measures sleep over the period of 1 month. Comprising 19 items, generating seven component scores measuring: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, the use of sleeping medication and day-time dysfunction.	Good. α>0.83. Mean component scores r=0.56. Individual items α>0.83. r≥0.85 (p<0.0001).[27 58 59]	Good r=0.33 (p<0.001).[27 58]	Buysse et al[27]
Quality of life	The SF-36 V2 Questionnaire (SF-36 V2)	Comprises 36 questions within eight domains of health namely: pain general health, vitality, physical functioning, social functioning, role limitations through physical problems, role limitations due to emotional problems and mental health including anxiety, depression, loss of behavioural/emotional control and physiological well-being. Results in two summary components of health physical and mental well-being of the patient. Aims to identify the positive and negative aspects of health that are most important to patients.	Good. α>0.7 in all aspects except emotional role α>0.6.[60 62]	Good. Construct validity measuring >0.7.[61]	Ware and Sherbourne[29]
Anxiety and depression	Hospital Anxiety and Depression Scale (HADS)	Measures anxiety and depression in non-psychiatric populations. Comprises 14 questions. Seven questions for anxiety (HADS-A) and seven questions for depression (HADS-D).	Good. α=0.93–0.98, t=0.93–0.97.[30 63 64]	Good. Range 0.5–0.8.[30 63 64]	Zigmond and Snaith[30]
Ability to approach illness	Multidimensional Health Locus of Control Form C	Measures self-related beliefs, comprised four scales namely: internal, chance, doctors and other people. Internal and chance scales comprise six questions, and doctors and other people comprise three questions. A total of 18 questions.	Good. α=0.60–0.75. Internal consistency measures 0.71–0.87 t >0.80.[31 65]	Good. r=0.39–0.65 (p<0.001).[11 65]	Wallston et al Michielsen et al[31 65]
Self-esteem	The Rosenberg Self-Esteem Scale	Measures 10 items related to self-esteem. Includes feelings of self-worth and self-acceptance with five positive worded questions and five negatively worded questions. The negative items have their scores reversed prior to analysis.	Good. α=0.78–0.89 t=0.63–0.92. Internal consistence 0.77.[66 67]	Good. r=0.57–0.79 (p<0.01).[67 68]	Rosenberg[32]

Adapted from McKay et al.[28]
CFS/ME, chronic fatigue syndrome/myalgic encephalomyelitis; FM, fibromyalgia; SF, Short Form.

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RMD Open
Rheumatic & Musculoskeletal Diseases

ORIGINAL RESEARCH

Fibromyalgia: a new facet of the post-COVID-19 syndrome spectrum? Results from a web-based survey

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ABSTRACT

Objective Postacute COVID-19 syndrome (PACS) is an emerging entity characterised by a large array of manifestations, including musculoskeletal complaints, fatigue and cognitive or sleep disturbances. Since similar symptoms are present also in patients with fibromyalgia (FM), we decided to perform a web-based cross-sectional survey aimed at investigating the prevalence and predictors of FM in patients who recovered from COVID-19.

Methods Data were anonymously collected between 5 and 18 April 2021. The collection form consisted of 28 questions gathering demographic information, features and duration of acute COVID-19, comorbid diseases, and other individual's attributes such as height and weight. The American College of Rheumatology (ACR) Survey Criteria and the Italian version of the Fibromyalgia Impact Questionnaire completed the survey.

Results A final sample of 616 individuals (77.4% women) filled the form 6±3 months after the COVID-19 diagnosis. Of these, 189 (30.7%) satisfied the ACR survey criteria for FM (56.6% women). A multivariate logistic regression model including demographic and clinical

Key messages

What is already known about this subject?

- Postacute COVID-19 syndrome (PACS) is emerging as a complex condition with a wide range of clinical manifestations.
- Clinical features of PACS include musculoskeletal pain, fatigue, cognitive impairment and sleep disturbances.

What does this study add?

- Our study suggests that up to 30% of patients with PACS may satisfy criteria for fibromyalgia (FM).
- Obesity and male gender represent the strongest risk factors for post-COVID-19 FM.

How might this impact on clinical practice or further developments?

- It is reasonable to expect that rheumatologists will soon face up with a sharp rise of cases of this new entity that we defined 'FibroCOVID'.

frontiers in Medicine

OPINION
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Will COVID-19 Lead to Myalgic Encephalomyelitis/Chronic Fatigue Syndrome?

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Keywords: COVID-19, SARS-CoV-2, post-infectious fatigue syndrome, post-viral fatigue syndrome, myalgic encephalomyelitis/chronic fatigue syndrome

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INTRODUCTION

"Recovering" from COVID-19 does not guarantee a return to a person's usual state of health. For one thing, some people with multi-system injury—particularly to the brain, heart and kidneys—may develop permanent dysfunction of those organs.

In addition, a more subtle form of chronic illness may develop. For some people with COVID-19, even those who are only mildly affected at first, the ensuing weeks and months of "recovery" bring a surprise and a betrayal: they do not return to full health. Although nucleic acid tests no longer detect the virus, people still suffer from ongoing symptoms. They call themselves "long haulers," and the condition is being called "long COVID."

HOW COMMON IS A LINGERING POST-COVID-19 ILLNESS?

The Centers for Disease Control and Prevention (CDC) followed nearly 300 people who were PCR-positive for SARS-CoV-2 for several weeks. Three weeks after the positive test, nearly half of the patients still had symptoms, such as fatigue and cough—particularly people who were older

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¿Podrían ser la fibromyalgia y la encefalomielitis miálgica síndromes post-virales?

¿Cuál podría ser el mecanismo desencadenante en ausencia de infección?

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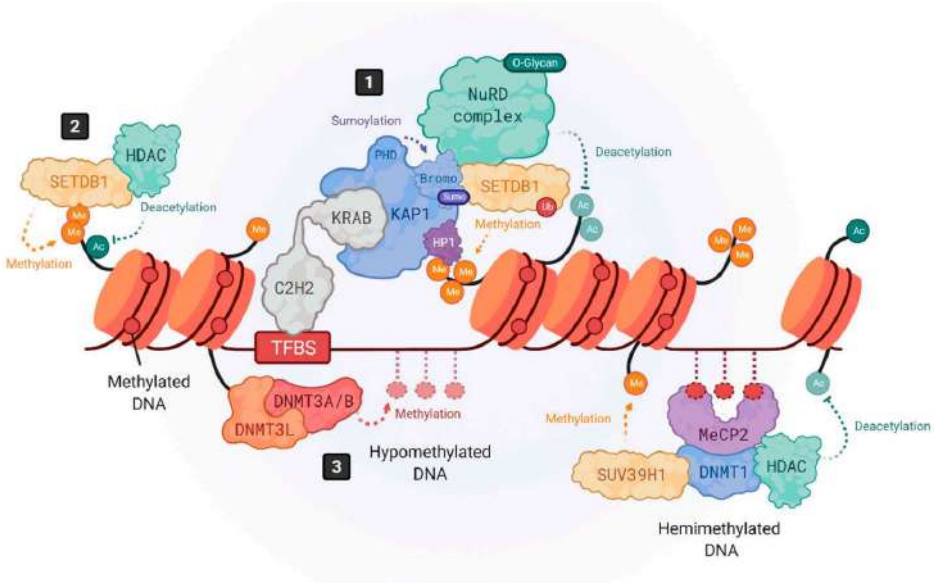
- Los retrovirus endógenos o **HERVs** son **secuencias virales** que se integraron **en el genoma humano** durante la evolución >450 M
- Corresponden al **8%** del genoma humano
- Junto a otras secuencias repetitivas se le denominó “DNA basura” porque se les estimaba “inútiles” su papel se decía era espaciar los genes realmente “útiles” en nuestro organismo
- Se estimaba hasta no hace mucho que los HERVs estaban silenciados, reprimidos, es decir, no expresados



Giménez-Orenga K, Oltra E. Human Endogenous Retrovirus as Therapeutic Targets in Neurologic Disease. Pharmaceuticals (Basel). 2021 May 24;14(6):495. doi: 10.3390/ph14060495.

- Los mecanismos **epigenéticos** que mantienen los **HERVs** silenciados, bajo control, no siempre funcionan.
- Tanto las infecciones virales, como otros factores ambientales (estilo de vida, tóxicos, estados emocionales, etc), es decir el **EXPOSOMA** del individuo, pueden alterar el **EPIGENOMA,** y en consecuencia activar los HERVs.
- Una vez activados **los HERVs pueden comportarse como virus exógenos**, desencadenar respuesta del sistema inmune e inducir síntomas similares a infecciones virales.

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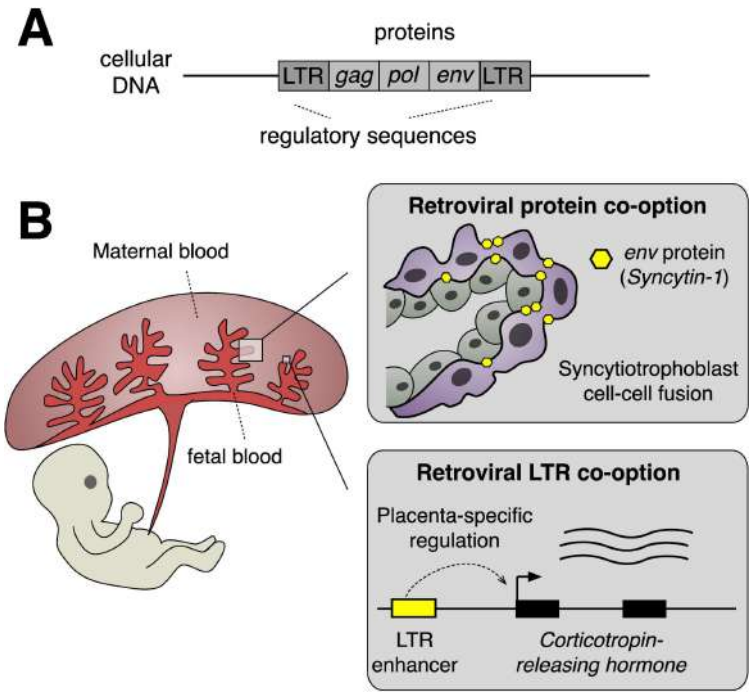
¿Es la activación de retrovirus endógenos siempre un problema?



Chuong EB. ThChuong EB. The placenta goes viral: Retroviruses control gene expression in pregnancy. PLoS Biol. 2018 Oct 9;16(10):e3000028. doi: 10.1371/journal.pbio.3000028.e

Table 1. RefSeq transcripts beginning within a previously unrecognized TE[a]

Gene	Full name	Functional role (disease)[b]	Probable TE involvement in human[c]	TE in mouse[d]	Human expression[e]	Mouse expression[f]
CYP19	Aromatase	Estrogen synthesis (reproduction abnormality)	**LTR** is one of at least six promoters	No	LTR drives very high placental expression	No placental expression
TMPRSS3	Transmembrane protease, serine 3	Serine protease (deafness)	**LTR** and **Alu**[g] as an alternative promoter	No	TE form is expressed primarily in PBLs; other forms are widespread	Inner ear, kidney, stomach, testis
HYAL-4	Hyaluronidase 4	Hyaluronan catabolism	Antisense **L1 and Alu**[g] as only known promoter	No	Primarily placenta	Primarily skin
ENTPD1 (CD39)	Ectonucleoside triphosphate diphospho-hydrolase 1	Lymphoid cell activation antigen	**LTR** as one of two promoters and results in HERV-derived N-terminus	No	LTR drives expression in placenta and melanoma; overall expression is widespread	Widespread
CASPR4	Contactin associated protein-like 4	Brain cell adhesion	LTR as one of three promoters and results in HERV-derived N-terminus	No	LTR form is expressed in brain, testis, tumors; overall expression is high in brain and spinal cord	Brain
MKKS	McKusick-Kaufman syndrome gene	Chaperonin (Mckusick-Kaufman syndrome)	**LTR and L2**[g] as an alternative promoter	No	TE form is expressed in testis and fetal tissues; overall expression widespread	Widespread
CA1	Carbonic anhydrase 1	Carbon metabolism	**LTR** as one of two major promoters	Yes	LTR drives erythroid expression	LTR drives erythroid expression
SPAM1 (PH20)	Sperm adhesion molecule 1	Sperm-egg adhesion	Antisense ERV as only known promoter	Yes	Primarily testis	Primarily testis
KLK11	Kallikrein 11	Serine protease	**MIR** as one of three promoters and leads to an altered N-terminus	Yes	Widespread	Brain and prostate
MSLN (MPF)	Mesothelin	Megakaryocyte potentiating factor	**LTR** as one of two promoters and part of 5′ UTR of other transcript form;	Yes (both)	Widespread	Widespread but not from LTR or MIR

van de Lagemaat LN, Landry JR, Mager DL, Medstrand P. Transposable elements in mammals promote regulatory variation and diversification of genes with specialized functions. Trends Genet. 2003 Oct;19(10):530-6.

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¿Cuándo es la activación de retrovirus endógenos un problema?

Table 1. HERVs associated with neurological diseases.

Disease	Retrotransposon	Elevated Cytokines	Ref.
Multiple Sclerosis	HERV-W ENV, *POL* HERV-H ENV	IFN-γ, IL-6, TNF-α, IL-17, IL-22, IL-12, IL-1	[26–29]
Schizophrenia	HERV-W ENV, GAG	IL-6, IL-1β, IL-2, sIL-2R, IL-8, IL-1, IL-1RA, TNF-α, IFN-γ, IL-4, TGF-β, IL-18, IL-10	[30–34]
Bipolar disorder (BD)	HERV-W *ENV* HERV-H *ENV*	IL-6, TNF-α, IL-10, sIL-2R, IL-1β, IL-1RA	[34–36]
Autism spectrum disorder (ASD)	HERV-K *ENV* HERV-W *ENV*	IFN-γ, IL-1β, IL-6, TNF-α, IL-10	[37]
Attention deficit hyperactivity disorder (ADHD)	HERV-H *ENV*	IL-6, TNF-β, IFN-γ, IL-2, IL-10, IL-13, IL-16	[38–40]
Sporadic amyotrophic lateral sclerosis (sALS)	HERV-K *GAG, POL, ENV*	TNF-α, IFN-γ, IL-6, IL-8, IL-1β, IL1RA, IL-2, IL-4, IL-5, IL-7, IL-9, IL-10, IL-12p70, IL-13, IL-15, IL-17, IL-18, IL-21	[41,42]
Fibromyalgia (FM)	HERV-W *POL* HERV-K *ENV* HERV-H *GAG*	INF-β, INF-γ, IL-1RA, IL-6, IL-17A,	[43,44]
Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/MS)	HERV-K *POL*	IFN-γ, IFN-α, IL-4, IL-5, IL-7, IL-13, IL-6, IL-1β, IL-2, IL-12	[45,46]

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HERVs y otros elementos repetitivos activados por infecciones víricas

Number of DE subfamilies

	Virus	Cell type	Group	GEO study	ERV		LINE		SINE		DNA		tRNA		other		total DE genes	total DE repeats
					Up	Down	Up	Down	Up	Down	Up	Down	Up	Down	Up	Down		
dsDNA	HSV-1	HFF-1	dsDNA	GSE100576	558	0	170	0	58	0	283	0	33	0	56	0	4458	1158
dsDNA	EBV	CD19+ B cells	dsDNA	GSE126379	3	450	1	152	0	56	1	241	1	3	1	37	10372	946
dsDNA	HCMV	MRC5	dsDNA	GSE120890	274	32	129	2	41	3	178	13	0	0	23	14	3876	709
dsDNA	VZV	MeWo	dsDNA	GSE85493	25	16	16	4	5	0	4	3	0	0	2	0	3119	75
dsDNA	HPV	HFK	dsDNA	GSE92496	0	6	0	1	0	4	0	11	5	0	3	6	3001	36
dsDNA	ORFV	HFF-1	dsDNA	GSE93226	24	1	4	0	0	0	4	1	0	0	1	0	2757	35
dsDNA	KSHV	MC116	dsDNA	GSE119608	3	0	0	0	0	0	0	0	1	0	1	3	1240	8
dsDNA	KSHV	HUVEC	dsDNA	GSE119608	0	0	0	0	0	0	0	0	2	0	0	0	55	2
retrovirus (+) ssRNA	DFV	huh-7.5	(+) ssRNA	GSE110512	64	24	29	6	13	1	60	5	0	2	10	5	4139	219
retrovirus (+) ssRNA	HCV	huh-7.5	(+) ssRNA	GSE103730	16	85	3	28	0	2	6	11	0	0	2	7	7651	160
retrovirus (+) ssRNA	SINV	HEK293	(+) ssRNA	GSE125182	69	6	10	1	1	1	12	10	0	0	7	2	392	119
retrovirus (+) ssRNA	ZIKV	MDM	(+) ssRNA	GSE118305	25	1	2	0	0	0	2	1	2	0	4	1	2022	38
retrovirus (+) ssRNA	HIV	activated CD4+ T cells	(+) ssRNA	GSE122735	30	9	0	0	1	0	3	3	1	0	3	3	4030	53
retrovirus (+) ssRNA	HIV	resting CD4+ T cells	(+) ssRNA	GSE122735	6	1	0	1	1	0	0	0	0	0	1	1	3588	11
(-) ssRNA	RVFV	HSAEC	(-) ssRNA	GSE102481	518	1	163	1	58	0	265	0	27	0	49	1	8001	1083
(-) ssRNA	SeV	Namalwa B cells	(-) ssRNA	GSE115266	332	68	127	12	42	0	208	19	24	2	32	10	10704	876
(-) ssRNA	IAV	A549	(-) ssRNA	GSE82232	215	0	54	0	51	0	44	0	41	0	30	1	3964	436
(-) ssRNA	HRSV	A549	(-) ssRNA	GSE99298	27	52	0	26	3	0	8	18	2	7	1	10	6542	154
(-) ssRNA	EBOV	ARPE-19	(-) ssRNA	GSE105414	80	16	3	2	0	0	11	1	5	0	6	3	6847	127
(-) ssRNA	MeV	glioma cells	(-) ssRNA	GSE111247	47	11	6	1	1	0	21	4	2	0	4	1	1138	98
(-) ssRNA	EBOV	MDM	(-) ssRNA	GSE84188	10	14	3	1	2	0	2	1	0	0	1	2	2796	36
(-) ssRNA	EBOV	CD4+ T cells	(-) ssRNA	GSE99389	3	0	0	0	2	0	0	0	1	0	0	1	719	7
(-) ssRNA	RESTV	MDM	(-) ssRNA	GSE84188	4	0	0	0	0	0	0	0	0	0	1	0	384	5

Macchietto MG, Langlois RA, Shen SS. Virus-induced transposable element expression up-regulation in human and mouse host cells. Life Sci Alliance. 2020 Jan 21;3(2). pii: e201900536. doi: 10.26508/lsa.201900536

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International Journal of *Molecular Sciences*

MDPI

Article

Activation of Transposable Elements in Immune Cells of Fibromyalgia Patients

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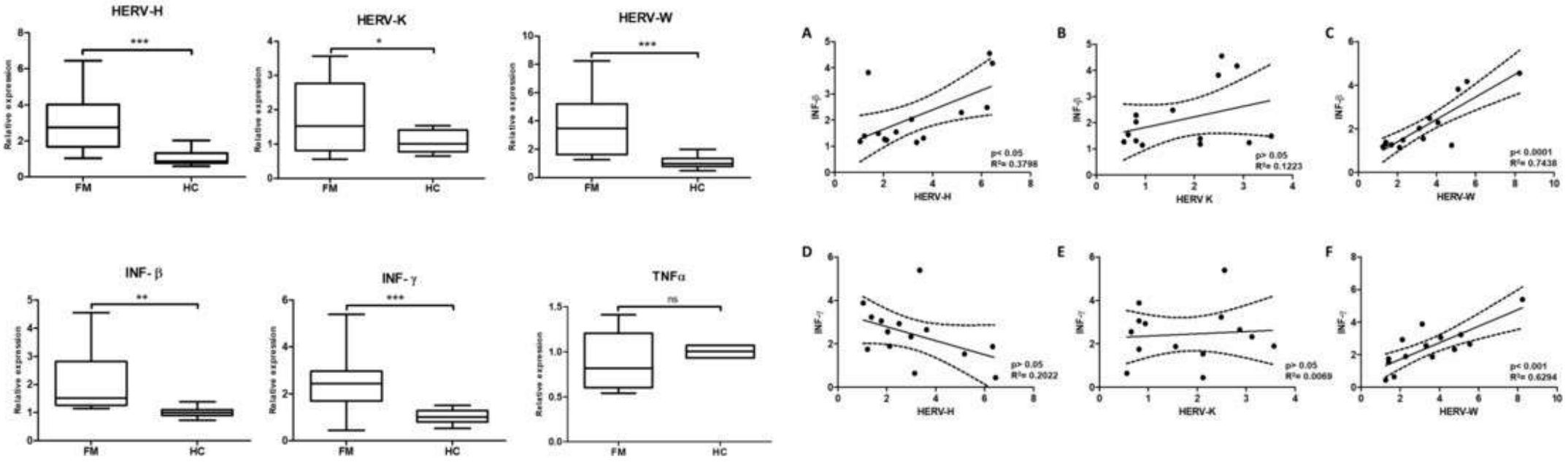
Algunos retrovirus endógenos parecen estar activos en células del sistema inmune de pacientes con Fibromialgia y SFC



Ovejero T, Sadones O, Sánchez-Fito T, Almenar-Pérez E, Espejo JA, Martín-Martínez E, Nathanson L, Oltra E. Activation of Transposable Elements in Immune Cells of Fibromyalgia Patients. Int J Mol Sci. 2020 Feb 18;21(4). pii:E1366. doi: 10.3390/ijms21041366.

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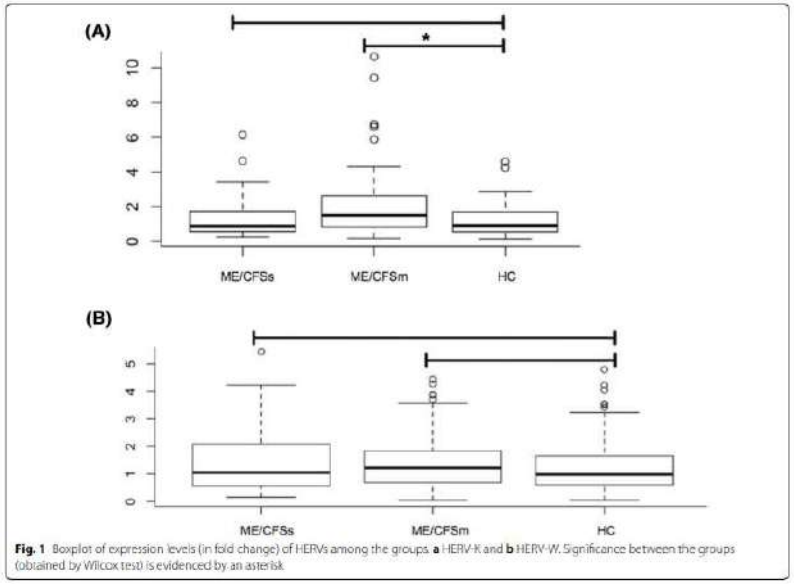

Fig. 1 Boxplot of expression levels (in fold change) of HERVs among the groups. **a** HERV-K and **b** HERV-W. Significance between the groups (obtained by Wilcox test) is evidenced by an asterisk.

Table 1 Primers used in real-time PCR assays

Oligo	Sense	Antisense
HERV-W	CCAATGCATCAGGTGGGTAAC	GAGGTACCACAGACAAAAAATATTCCT
HERV-K	TCCCCTTGGAATACTCCTGTTTT	CATTCCTTGTGGTAAAACTTTCCA
GAPDH	ACCCACTCCTCCACCTTTGAC	TGTTGCTGTAGCCAAATTCGTT

Rodrigues *et al. Autoimmun Highlights* (2019) 10:12
https://doi.org/10.1186/s13317-019-0122-8

Autoimmunity Highlights

ORIGINAL RESEARCH **Open Access**

HERV-K and HERV-W transcriptional activity in myalgic encephalomyelitis/chronic fatigue syndrome

Lucas S. Rodrigues[1†], Luiz H. da Silva Nali[1,2†], Cibele O. D. Leal[1], Ester C. Sabino[1,3], Eliana M. Lacerda[4], Caroline C. Kingdon[4], Luis Nacul[4] and Camila M. Romano[1,5*]

Abstract

Background: Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/MS) is an incapacitating chronic disease that dramatically compromise the life quality. The CFS/ME pathogenesis is multifactorial, and it is believed that immunological, metabolic and environmental factors play a role. It is well documented an increased activity of Human endogenous retroviruses (HERVs) from different families in autoimmune and neurological diseases, making these elements good candidates for biomarkers or even triggers for such diseases.

Methods: Here the expression of Endogenous retroviruses K and W (HERV-K and HERV-W) was determined in blood from moderately and severely affected ME/CFS patients through real time PCR.

Results: HERV-K was overexpressed only in moderately affected individuals but HERV-W showed no difference.

Conclusions: This is the first report about HERV-K differential expression in moderate ME/CFS. Although the relationship between HERVs and ME/CFS has yet to be proven, the observation of this phenomenon deserves further attention.

Keywords: Endogenous retroviruses, HERV-W, HERV-K, Myalgic encephalomyelitis, Chronic fatigue

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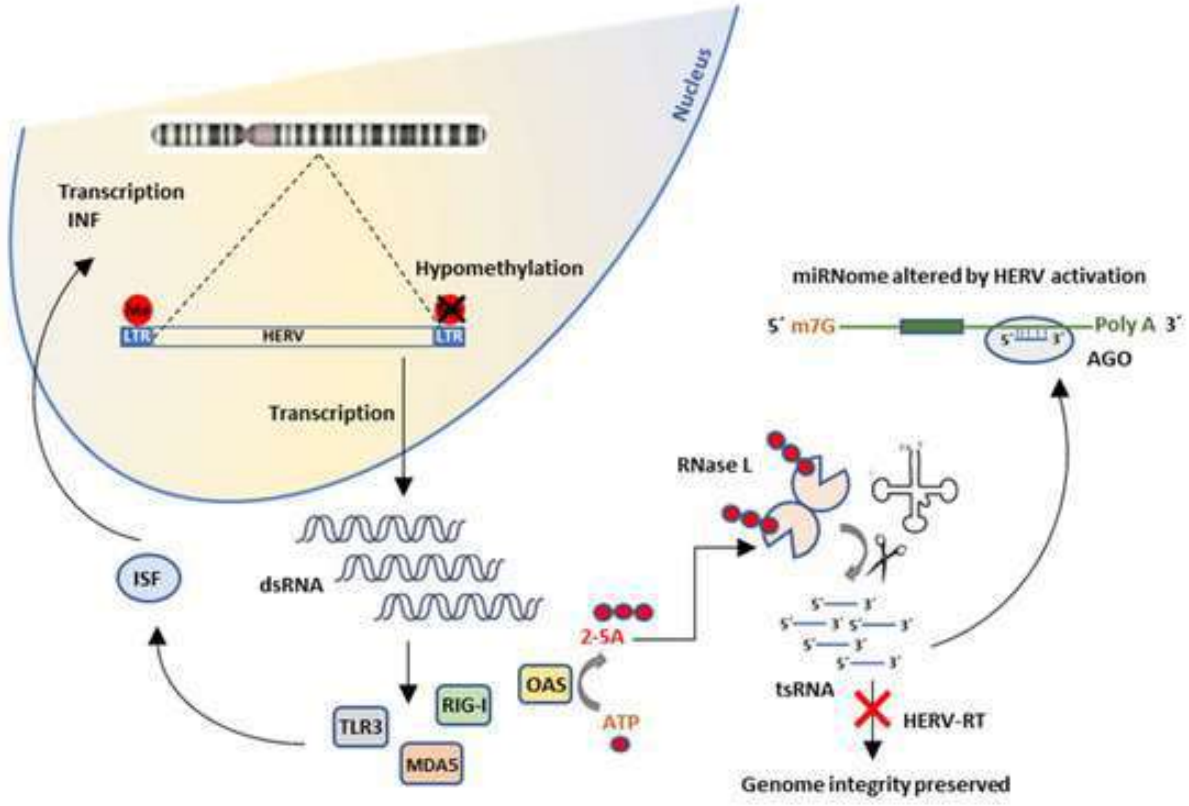
San Vicente Mártir

Modelo que propone la activación de los HERVs como agentes causantes de los síntomas metabólicos e inmunológicos de FM y SFC



Ovejero T, Sadones O, Sánchez-Fito T, Almenar-Pérez E, Espejo JA, Martín-Martínez E, Nathanson L, Oltra E. Activation of Transposable Elements in Immune Cells of Fibromyalgia Patients. Int J Mol Sci. 2020 Feb 18;21(4). pii:E1366. doi: 10.3390/ijms21041366.

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San Vicente Mártir

"Leads to different course of symptoms and **severity** of the COVID-19 infection"

El **patrón de HERVs** activados debe informar de los síntomas y **grado de severidad** de la Fibromialgia y del Síndrome de Fatiga Crónica/Encefalomielitis Miálgica

ISSN 0095-4527, Cytology and Genetics, 2020, Vol. 54, No. 6, pp. 588–604. © Allerton Press, Inc., 2020.

Genomic Study of COVID-19 Corona Virus Excludes Its Origin from Recombination or Characterized Biological Sources and Suggests a Role for HERVS in Its Wide Range Symptoms

Ahmed M. El-Shehawi[a, b, *], Saqer S. Alotaibi[a], and Mona M. Elseehy[b]

[a] *Department of Biotechnology, College of Science, Taif University, P.O. Box 11099, Taif, 21944 Saudi Arabia*

[b] *Department of Genetics, Faculty of Agriculture, University of Alexandria, Alexandria, 21527 Egypt*

**e-mail: elshehawi@hotmail.com*

Received July 7, 2019; revised July 12, 2019; accepted November 18, 2020

Abstract—The COVID-19 corona virus has become a world pandemic which started in December 2019 in Wuhan, China with no confirmed biological source. Various countries reported the genomic sequence of different isolates obtained from infected patients. This allowed us to obtain a number of 38 isolates of full genomic sequences. Alignment of nucleotide (nt) sequence was carried out using Clustal Omega multiple alignment service at the EBI website. Alignment of nt sequence and phylogenetic relationship revealed that the COVID-19 is a new viral strain and its biological source has not been yet detected. The expected orf pattern was different among isolates obtained from the same country or different countries as well as from SARS-CoV isolates or bats CoV suggesting different virus human interaction possibilities during infection and severity. All isolates had the main five orfs (1ab, S, M, N, E), whereas they differed in the expected accessory orfs. Being with the biological source of COVID-19 undetected, the role of human endogenous retrovirus (HERVs) in the regulation of the host cell gene expression or the encoding for products that could modulate COVID-19 infection and the spectrum of its symptoms is discussed.

Keywords: COVID-19, genome, nucleotide sequence alignment, Human endogenous retroviruses (HERVs)

DOI: 10.3103/S0095452720060031

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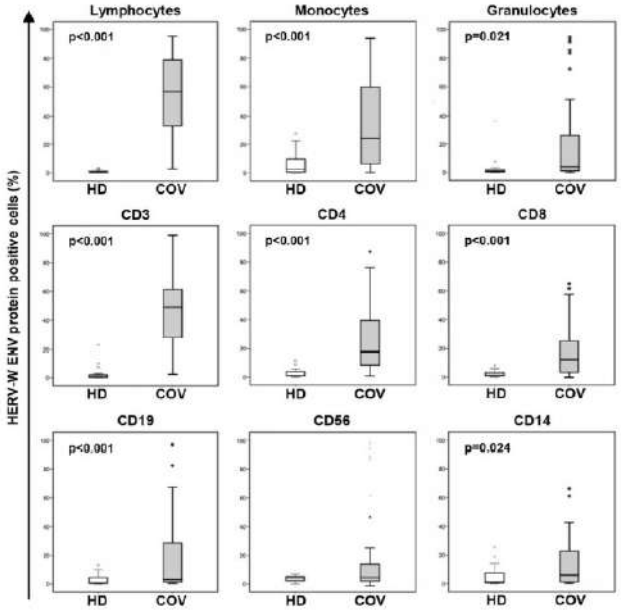

COVID-19 patients N=30
HD (healthy donors) N=17

EBioMedicine 66 (2021) 103341

Contents lists available at ScienceDirect

EBioMedicine

journal homepage: www.elsevier.com/locate/ebiom

Research paper

Evidence of the pathogenic HERV-W envelope expression in T lymphocytes in association with the respiratory outcome of COVID-19 patients

Emanuela Balestrieri[a,i], Antonella Minutolo[a,i], Vita Petrone[a], Marialaura Fanelli[a], Marco Iannetta[b,c], Vincenzo Malagnino[b,c], Marta Zordan[b,c], Pietro Vitale[c], Benjamin Charvet[d,e], Branka Horvat[d], Sergio Bernardini[a], Enrico Garaci[f], Paolo di Francesco[a], Paola Sinibaldi Vallebona[a,g], Loredana Sarmati[b,c], Sandro Grelli[a,h], Massimo Andreoni[b,c], Hervé Perron[e,i], Claudia Matteucci[a,*]

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[c] Infectious Diseases Clinic, Policlinic of Tor Vergata, Rome 00133, Italy
[d] International Center for Infectiology Research (CIRI), INSERM U1111, CNRS UMR5308, Ecole Normale Supérieure de Lyon, University of Lyon, Lyon, France
[e] Geneuro – Innovation, Lyon 69008, France
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Cytokine storm
COVID-19
HERV-W, human endogenous retroviruses
Inflammation
Respiratory outcome
T-cell exhaustion

ABSTRACT

Background: Despite an impressive effort in clinical research, no standard therapeutic approach for coronavirus disease 2019 (COVID-19) patients has been established, highlighting the need to identify early biomarkers for predicting disease progression and new therapeutic interventions for patient management. The present study aimed to evaluate the involvement of the human endogenous retrovirus -W envelope (HERV-W ENV) in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection considering recent findings that HERVs are activated in response to infectious agents and lead to various immunopathological effects. We analysed HERV-W ENV expression in blood cells of COVID-19 patients in correlation with clinical characteristics and have discussed its potential role in the outcome of the disease.
Methods: We analysed HERV-W ENV expression in blood samples of COVID-19 patients and healthy donors by flow cytometry and quantitative reverse transcriptase PCR analysis, and evaluated its correlation with clinical signs, inflammatory markers, cytokine expression, and disease progression.
Findings: HERV-W ENV was highly expressed in the leukocytes of COVID-19 patients but not in those of healthy donors. Its expression correlated with the markers of T-cell differentiation and exhaustion and blood cytokine levels. The percentage of HERV-W ENV-positive lymphocytes correlated with inflammatory markers and pneumonia severity in COVID-19 patients. Notably, HERV-W ENV expression reflects the respiratory outcome of patients during hospitalization.

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¿Se **vuelven a silenciar** las secuencias de HERV después de que desaparece la infección por COVID?

¿O **permanecen activos** en pacientes con **COVID persistente** ?

Si es así, ¿**los HERV activos de LONG COVID son iguales o diferentes** a los activos en ME / CFS o FM?

¿Se correlaciona la expresión de HERVs con los **síntomas y la cronicidad en FM y EM / SFC o COVID persistente**?

¿Se puede establecer **causa-efecto** para los HERVs en estas enfermedades?

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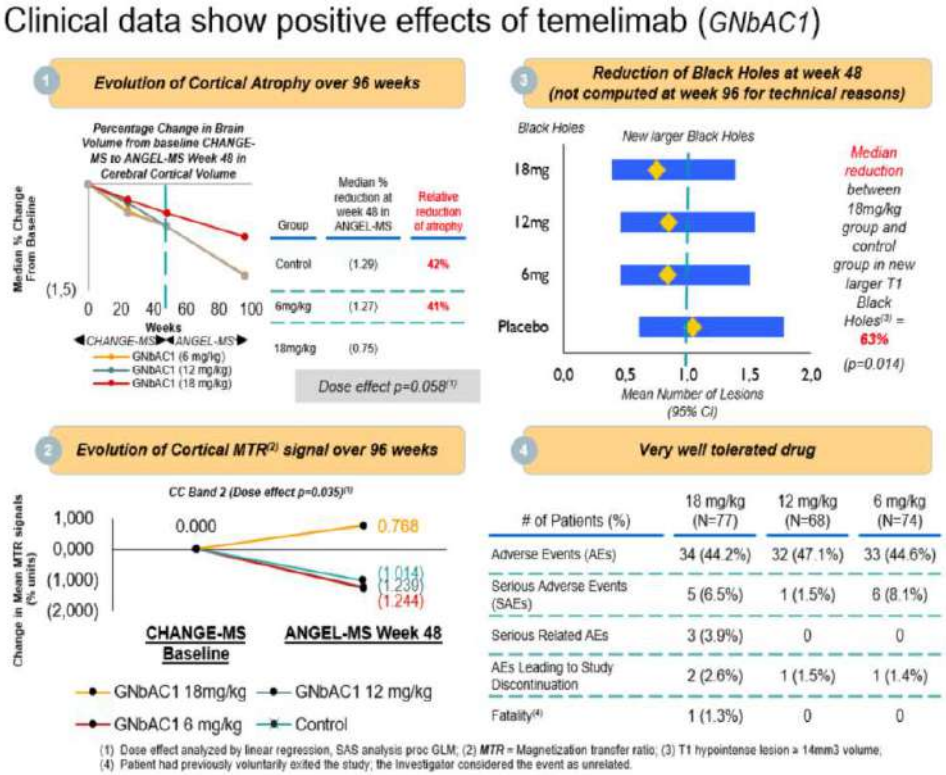
La detección y la focalización de HERV abren **nuevas vías diagnósticas** y **terapéuticas**, quizás no solo para la EM, la ELA y la Diabetes Tipo 1

¿Puede ser de ayuda la trayectoria trazada por **GeNeuro**?



Clinical Trials Phase II

http://www.geneuro.com/en/clinicaltrials/english

EBioMedicine 67 (2021) 103363

Contents lists available at ScienceDirect

EBioMedicine

journal homepage: www.elsevier.com/locate/ebiom

Commentary

HERV-W envelope expression in blood leukocytes as a marker of disease severity of COVID-19

Marta Garcia-Montojo, Avindra Nath*

Section of Infections of the Nervous System, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, USA

"A humanized IgG4 monoclonal antibody to HERV-W envelope, GNbAC1, has already been developed and clinical studies have been conducted in patients with multiple sclerosis and type 1 diabetes.

Hence the **safety profile is known** at least in the context of these phase 1 and 2 studies where the antibody seemed remarkably safe [10].

This might represent **an excellent opportunity to conduct a randomized controlled clinical study in patients with COVID-19** to determine if it may provide any benefit to hospitalized patients who are severely ill."

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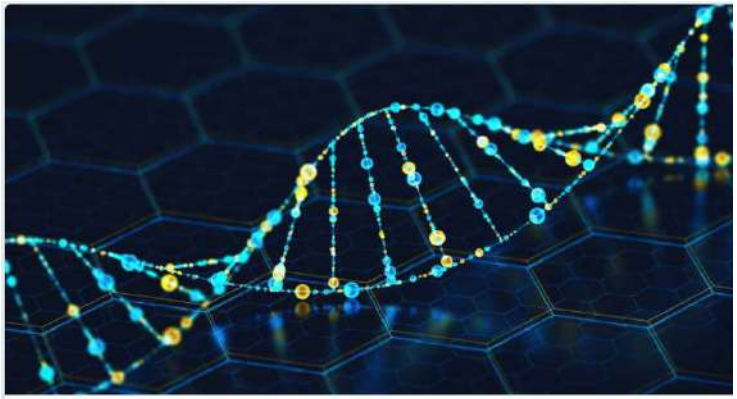
San Vicente Mártir



The effect of activated HERVs and the associated immune response in severe ME/CFS

Principal investigator

Prof. Elisa Oltra

Institution

Catholic University of Valencia, Valencia, Spain

Start date

December 2020

"Prof. Oltra's hypothesis is that **epigenetic** changes cause activation of HERVs, which then leads to an **innate immune response** and the resulting flu-like symptoms and autoimmune problems that are characteristic of ME/CFS."

"Prof. Oltra's hope is that these HERV 'fingerprints' could be used in the diagnosis of ME/CFS, or for patient subtyping. But her findings will also help establish whether activation of HERVs might be at the root of the disease. Furthermore, the **cell model** she is developing could be a valuable tool in the future for assessing **potential treatments for ME/CFS**".

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Expresión génica e inmunidad

Universidad Católica de Valencia San Vicente Mártir

ME RESEARCH UK

Eva Martín-Martínez

UNIVERSITY OF OXFORD

Karl Morten

Lubov Nathanson

NSU NOVA SOUTHEASTERN UNIVERSITY

Universidad Católica de Valencia San Vicente Mártir

Los **HERVs** codifican y regulan a su vez los **microRNAs** (otro componente epigenético de control de la expresión genética)

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nature research

OPEN

Assessing diagnostic value of microRNAs from peripheral blood mononuclear cells and extracellular vesicles in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome

Eloy Almenar-Pérez[1], Leonor Sarria[2], Lubov Nathanson[2] & Elisa Oltra[2,3]*

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a debilitating multisystemic disease of unknown etiology, affecting thousands of individuals worldwide. Its diagnosis still relies on ruling out medical problems leading to unexplained fatigue due to a complete lack of disease-specific biomarkers. Our group and others have explored the potential value of microRNA profiles (miRNomes) as diagnostic tools for this disease. However, heterogeneity of participants, low numbers, the variety of samples assayed, and other pre-analytical variables, have hampered the identification of disease-associated miRNomes. In this study, our team has evaluated, for the first time, ME/CFS miRNomes in peripheral blood mononuclear cells (PBMCs) and extracellular vesicles (EVs) from severely ill patients recruited at the monographic UK ME biobank to assess, using standard operating procedures (SOPs), blood fractions with optimal diagnostic power for a rapid translation of a miR-based diagnostic method into the clinic. Our results show that routine creatine kinase (CK) blood values, plasma EVs physical characteristics (including counts, size and zeta-potential), and a limited number of differentially expressed PBMC and EV miRNAs appear significantly associated with severe ME/CFS ($p < 0.05$). Gene enrichment analysis points to epigenetic and neuroimmune dysregulated pathways, in agreement with previous reports. Population validation by a cost-effective approach limited to these few potentially discriminating variables is granted.

PLOS ONE

RESEARCH ARTICLE

Identification of Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome-associated DNA methylation patterns

Malav S. Trivedi[1], Elisa Oltra[2], Leonor Sarria[3], Natasha Rose[1], Vladimir Beljanski[4], Mary Ann Fletcher[3,5], Nancy G. Klimas[3,5], Lubov Nathanson[3]*

1 College of Pharmacy, Nova Southeastern University, Fort Lauderdale, United States of America, 2 School of Medicine and Dentistry, Catholic University of Valencia, Valencia, Spain, 3 Institute for Neuro Immune Medicine, Dr. Kiran C. Patel College of Osteopathic Medicine, Nova Southeastern University, Fort Lauderdale, United States of America, 4 Cell Therapy Institute, Dr. Kiran C. Patel College of Allopathic Medicine, Nova Southeastern University, Fort Lauderdale, United States of America, 5 Miami VAMC, Miami Florida, United States of America

* lnathanson@nova.edu

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Epigenetic Components of Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome Uncover Potential Transposable Element Activation

Eloy Almenar-Pérez, MSc[1]; Tamara Ovejero, PhD[2]; Teresa Sánchez-Fito, MSc[1]; José A. Espejo, BSc[3]; Lubov Nathanson, PhD[4,5]; and Elisa Oltra, PhD[2,6]

[1]Escuela de Doctorado, Universidad Católica de Valencia San Vicente Mártir, Valencia, Spain; [2]School of Medicine, Universidad Católica de Valencia San Vicente Mártir, Valencia, Spain; [3]School of Experimental Sciences, Universidad Católica de Valencia San Vicente Mártir, Valencia, Spain; [4]Kiran C. Patel College of Osteopathic Medicine, Nova Southeastern University, Fort Lauderdale, Florida, USA; [5]Institute for Neuro Immune Medicine, Nova Southeastern University, Fort Lauderdale, Florida, USA; and [6]Unidad Mixta CIPF-UCV, Centro de Investigación Príncipe Felipe, Valencia, Spain

pharmaceutics MDPI

Communication

Impact of Polypharmacy on Candidate Biomarker miRNomes for the Diagnosis of Fibromyalgia and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Striking Back on Treatments

Eloy Almenar-Pérez [1], Teresa Sánchez-Fito [1], Tamara Ovejero [2], Lubov Nathanson [3,4] and Elisa Oltra [2,5,*]

1 Escuela de Doctorado, Universidad Católica de Valencia San Vicente Mártir, 46001 Valencia, Spain; eloy.almenar@ucv.es (E.A.-P.); mt.sanchez@ucv.es (T.S.-F.)
2 School of Medicine, Universidad Católica de Valencia San Vicente Mártir, 46001 Valencia, Spain; tamara.ovejero@ucv.es
3 Kiran C Patel College of Osteopathic Medicine, Nova Southeastern University, Ft Lauderdale, FL 33314, USA; lnathanson@nova.edu
4 Institute for Neuro Immune Medicine, Nova Southeastern University, Ft Lauderdale, FL 33314, USA
5 Unidad Mixta CIPF-UCV, Centro de Investigación Príncipe Felipe, 46012 Valencia, Spain
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Journal of Cellular and Molecular Medicine Open Access

ORIGINAL ARTICLE | Open Access

Unravelling myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS): Gender-specific changes in the microRNA expression profiling in ME/CFS

Amanpreet K. Cheema, Leonor Sarria, Mina Bekheit, Fanny Collado, Eloy Almenar-Pérez, Eva Martín-Martínez, Jose Alegre, Jesus Castro-Marrero, Mary A. Fletcher, Nancy G. Klimas ... See all authors

First published: 14 April 2020 | https://doi.org/10.1111/jcmm.15260 | Citations: 1

Funding information:

This study was supported by NIH awards 1R15NS087604-01A1, 1R21AI124187-01 and Presidential Faculty Research and Development Grant from Nova Southeastern University (all awarded to LN). We are grateful to all the participants who took part in the studies. The study used PBMC samples collected under CDMRP award W81XWH-09-2-0071 (PI: NK), NIH awards 5R01NS090200-02 (PI: MAF) and 5R01AR057853-04 (PI: NK), UCV-2019-270-001 (PI: EO) and Catalonia Association for Fibromyalgia, Chronic Fatigue Syndrome/Myalgic Encephalomyelitis and Environmental Sensitivities/Multiple Chemical Sensitivity (ACAF, www.fibromialgia.cat). The sponsors had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript. Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by either by the Department of Defense or National Institute of Health.

EXP.	INVESTIGADOR PRINCIPAL	ENTIDAD
AICO/2020/254	OLTRA GARCÍA, ELISA	UNIVERSIDAD CATÓLICA DE VALENCIA SAN VICENTE MÁRTIR

ANEXO I

Resolución de concesión de las subvenciones para grupos de investigación consolidables. AICO/2020

GENERALITAT VALENCIANA

SOL·LICITUD DE SUBVENCIONS PER A GRUPS D'INVESTIGACIÓ CONSOLIDABLES AICO/2020
SOLICITUD DE SUBVENCIONES PARA GRUPOS DE INVESTIGACIÓN CONSOLIDABLES AICO/2020

A **DADES DE L'INVESTIGADOR RESPONSABLE/ *DATOS DEL INVESTIGADOR RESPONSABLE* (*)**

1r COGNOM/*1º APELLIDO*	2n COGNOM/*2º APELLIDO*	NOM/*NOMBRE*	DNI / NIF / NIE
OLTRA	**GARCÍA**	**ELISA**	**22551940A**

B **MEMÒRIA CIENTIFICO-TÈCNICA/ *MEMORIA CIENTÍFICO-TÉCNICA***

Validation of blood biomarkers discriminating power for the differential diagnosis of fibromyalgia and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)

Memòria cientifico-tècnica de les activitats que es desenrotllaran i pressupost del projecte d'investigació per a tota la duració del projecte, distribuït per anualitats.
Memoria científico-técnica de las actividades que se desarrollarán y presupuesto del proyecto de investigación para toda la duración del proyecto, distribuido por anualidades.

Universidad Católica de Valencia San Vicente Mártir

GENERALITAT VALENCIANA

Fundació Fisabio

DICTAMEN DEL COMITÉ ÉTICO DE INVESTIGACIÓN DE LA DIRECCIÓN GENERAL DE SALUD PÚBLICA
Y CENTRO SUPERIOR DE INVESTIGACIÓN EN SALUD PÚBLICA
Referencia: 20210604/04/01

Current projects

- The effect of activated HERVs and the associated immune response in severe ME/CFS
  Prof. Elisa Oltra, Catholic University of Valencia

ME RESEARCH UK

Red Valenciana de Biobancos

RVB Red Valenciana de Biobancos

¿Qué es el Biobanco IBSP-CV?

ibsp
INVESTIGACIÓN BIOMÉDICA Y SALUD PÚBLICA
BIOBANCO

El Biobanco para la Investigación Biomédica y en Salud Pública de la Comunidad Valenciana (IBSP-CV), se constituye como un servicio de apoyo a la investigación de excelencia cuya finalidad es gestionar colecciones de muestras biológicas humanas de alta calidad e información asociada a las mismas que permitan a los grupos de investigación el abordaje de proyectos de interés biomédico y en materia de salud pública, priorizándose todos aquellas propuestas que se enmarquen dentro de los objetivos estratégicos de la Conselleria de Sanitat.

Además, el Biobanco IBSP actúa como coordinador de la **Red Valenciana de Biobancos (RVB)** y se define como un servicio de almacenamiento de muestras biológicas humanas dirigido a comunidad científica para la realización de estudios de genómica a gran escala, proteómica e identificación de nuevas dianas terapéuticas.

"This work is supported by ME Research UK (SCIO charity number SCO36942)".

¿Cuál es la importancia de los **hallazgos del grupo del Dr. Andersson**?

RESEARCH ARTICLE

Passive transfer of fibromyalgia symptoms from patients to mice

Andreas Goebel,[1,2] Emerson Krock,[3] Clive Gentry,[4] Mathilde R. Israel,[4] Alexandra Jurczak,[3] Carlos Morado Urbina,[3] Katalin Sandor,[3] Nisha Vastani,[4] Margot Maurer,[4] Ulku Cuhadar,[4] Serena Sensi,[2] Yuki Nomura,[3] Joana Menezes,[3] Azar Baharpoor,[3] Louisa Brieskorn,[3] Angelica Sandström,[5] Jeanette Tour,[5] Diana Kadetoff,[5,6] Lisbet Haglund,[7] Eva Kosek,[5,8] Stuart Bevan,[4] Camilla I. Svensson,[3] and David A. Andersson[4]

[1]Walton Centre NHS Foundation Trust, Liverpool, United Kingdom. [2]Pain Research Institute, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, United Kingdom. [3]Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden. [4]King's College London, Wolfson CARD, Institute of Psychiatry, Psychology & Neuroscience, Guy's Campus, London, United Kingdom. [5]Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden. [6]Stockholm Spine Center, Upplands Väsby, Sweden. [7]Department of Surgery, Division of Orthopaedic Surgery, McGill University, Montreal, Quebec, Canada. [8]Department of Surgical Sciences, Uppsala University, Uppsala, Sweden.

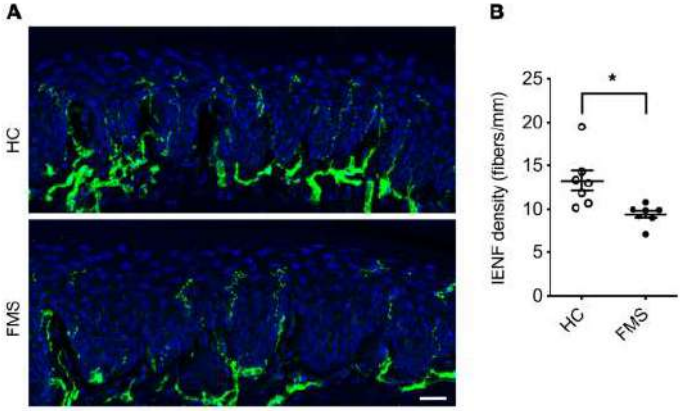

Figure 10. FMS IgG transfer decreases intraepidermal nerve fiber density. Intraepidermal nerve fibers (IENFs) were identified in the glabrous hind-paw skin with an anti–PGP 9.5 antibody (**A**). The number of IENFs crossing from the dermis to the epidermis was decreased following transfer of FMS IgG compared with HC IgG 14 days after the first injection (**B**) (pooled, 8 mg per day for 4 consecutive days). Scale bar: 20 μm. Data points are mean ± SEM ($n = 7$). *$P < 0.05$ by unpaired t test.

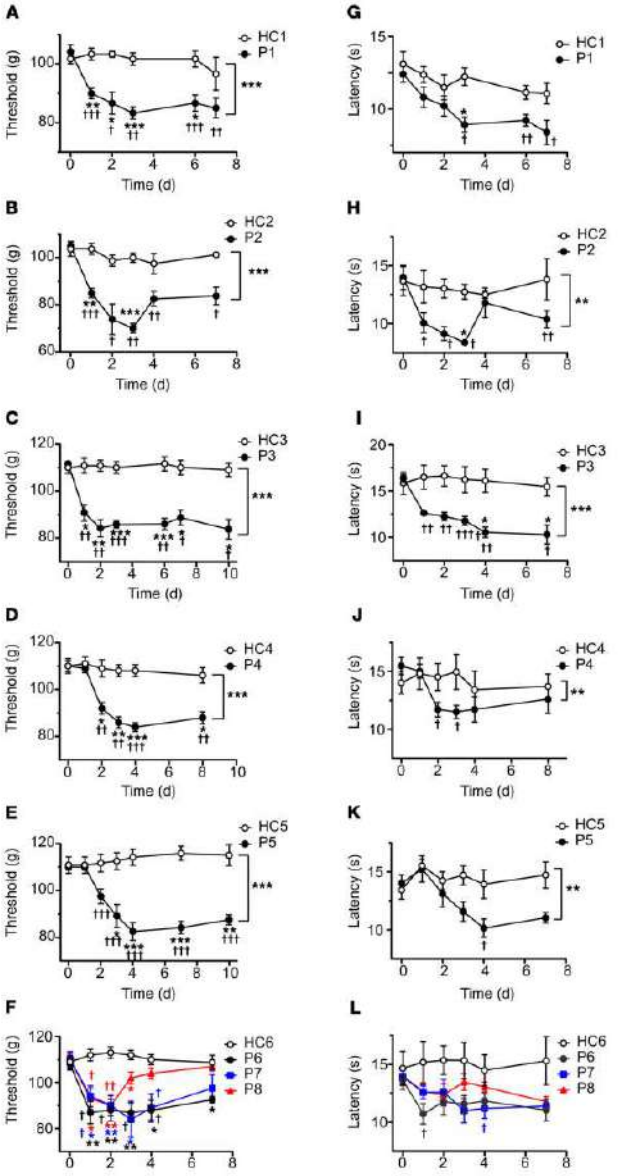

Figure 1. Passive transfer of hypersensitivities from fibromyalgia patients to mice. Administration of IgG (8 mg on 4 consecutive days) from each of 8 different FMS patients (P1–P8) significantly reduced the withdrawal threshold in the paw-pressure test (**A**–**F**) compared with IgG from healthy control subjects (HC1–HC6). The paw withdrawal latency in the cold-plate test was reduced by IgG from 7 of 8 patients (**G**–**L**). Data points are mean ± SEM of $n = 6$ mice in **A**, **C**, **E**, **G**, **I**, and **K**; $n = 5$ in **D**, **F**, **J**, and **L**; and $n = 4$ in **B** and **H**. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, FMS IgG compared with HC IgG; 2-way repeated measure ANOVA followed by Sidak's correction. †$P < 0.05$, ††$P < 0.01$, †††$P < 0.001$, compared with the naive preinjection value at time zero; 2-way repeated measure ANOVA followed by Dunnett's test.

Universidad Católica de Valencia San Vicente Mártir

ACCEPTED MANUSCRIPT

Research Recommendations Following the Discovery of Pain Sensitising IgG Autoantibodies in Fibromyalgia Syndrome

Andreas Goebel ✉, David Andersson, Chris Barker, Neil Basu, Craig Bullock, Stuart Bevan, Rachael J M Bashford-Rogers, Ernest Choy, David Clauw, Debra Dulake ...
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Pain Medicine, pnab338, https://doi.org/10.1093/pm/pnab338
Published: 26 November 2021

UCVnews

Sábado, 11 de Diciembre de 2021

Investigación

David A. Andersson imparte un seminario sobre el tratamiento de la fibromialgia

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Volver

Noticia publicada el
viernes, 5 de noviembre de 2021

Etiquetas
OTRI, observatorio para la libertad de enseñanza, oficina de relaciones internacionales, elisa oltra, Vicerrectorado de Investigación, CITSAM, David A. Andersson

Visitas
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El Vicerrectorado de Investigación, La Oficina de Transferencia de Resultados de la Investigación (OTRI), el Centro de Investigación Traslacional San Alberto Magno (CISAM-UCV), y el Grupo de Investigación *Expresión Génica e Inmunidad* han organizado un seminario sobre investigación en fibromialgia, impartido por David A. Andersson, del King´s College of London del Reino Unido.

En la sesión, Andersson ha expuesto su línea de trabajo, que se centra en el estudio de los mecanismos de transducción de neuronas sensoriales y en estudios traslacionales de las condiciones de dolor en humanos.

Así, el ponente ha mostrado los resultados de su último trabajo, publicado el pasado mes de julio en el Journal of Clinical Investigation, en el que muestra que las inmunoglobulinas (IgG) de pacientes con Fibromialgia (FM) producen hipersensibilidad sensorial en ratón al sensibilizar sus neuronas nociceptivas.

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¿Cuál es la importancia de los descubrimientos de nuestro grupo en **desbalances de microARNs**?

¿Cuál es la importancia de las **alteraciones en la expresión de HERVs** asociadas a la enfermedad?

IMPLICACIONES EN DIAGNÓSTICO Y EN EL DESARROLLO DE TRATAMIENTOS

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