Relevance of mobile genetic elements (MGE) on biology and evolution: from first hominids to modern humans – Review

Gabriel Dorado [1], Fernando Luque [2], Francisco José Esteban [3], Plácido Pascual [4], Inmaculada Jiménez [5], Francisco Javier S. Sánchez-Cañete [6], Patricia Raya [7], Teresa E. Rosales [8], Víctor F. Vásquez [9], Pilar Hernández [10]

[1] Author for correspondence, Dep. Bioquímica y Biología Molecular, Campus Rabanales C6-1-E17, Campus de Excelencia Internacional Agroalimentario (ceiA3), Universidad de Córdoba, 14071 Córdoba (Spain), eMail: <bb1dopeg@uco.es>; [2] Laboratorio de Producción y Sanidad Animal de Córdoba, Ctra. Madrid-Cádiz km 395, 14071 Córdoba; [3] Servicio de Informática, Edificio Ramón y Cajal, Campus Rabanales, Universidad de Córdoba, 14071 Córdoba; [4] Laboratorio Agroalimentario de Córdoba, Consejería de Agricultura y Pesca, Junta de Andalucía, 14004 Córdoba; [5] IES Puertas del Campo, Avda. San Juan de Dios 1, 51001 Ceuta; [6] EE.PP. Sagrada Familia de Baena, Avda. Padre Villoslada 22, 14850 Baena (Córdoba); [7] Dep. Radiología y Medicina Física, Unidad de Física Médica, Facultad de Medicina, Avda. Menéndez Pidal s/n, Universidad de Córdoba, 14071 Córdoba; [8] Laboratorio de Arqueobiología, Avda. Juan Pablo II s/n, Universidad Nacional de Trujillo, 13011 Trujillo (Peru); [9] Centro de Investigaciones Arqueobiológicas y Paleoecológicas Andinas Arqueobios, C/. Martínez de Compañón 430-Bajo 100, Urbanización San Andrés, 13008 Trujillo (Peru); [10] Instituto de Agricultura Sostenible (IAS), Consejo Superior de Investigaciones Científicas (CSIC), Alameda del Obispo s/n, 14080 Córdoba.

ABSTRACT

The more we discover about ancient biology, the more fascinated we are. An example of that is what made us human. Besides the three previously reviewed surprises (*NOTCH2NL* genes, spurious transcription and nucleic-acid methylation), mobile genetic elements (MGE) were also involved in the evolution from first hominids to modern humans. The most relevant MGE are transposable elements (TE) or transposons. They are parasites that can cause pathologies and even death, so we fight them. But that is a difficult task, since they hide inside our genome, becoming part of us. Surprisingly, some of them become beneficial eventually. That way, the placenta was generated and our immune system was enhanced. Even more relevant is their implication in making us human. Yet, their deregulation may be involved in diseases, including neurodegenerative ones and cancer. They are so powerful that are being used to build a genome engineering toolbox in applied biology, which should allow to treat diseases like cancer.

Key words: Retrotransposons, retroviruses, addictions, stress, diet, epigenetics, adaptation, evolution.

RESUMEN

Cuanto más descubrimos sobre la biología antigua, más nos fascina. Un ejemplo de ello es lo que nos hizo humanos. Además de las tres sorpresas reseñadas anteriormente (genes NOTCH2NL, transcripción espuria y metilación de ácidos nucleicos), los elementos genéticos móviles (EGM) también intervinieron en la evolución desde los primeros homínidos hasta los humanos modernos. Los EGM más relevantes son los elementos transponibles (ET) o transposones. Son parásitos que pueden causar patologías e incluso la muerte, por lo que luchamos contra ellos. Pero es una tarea difícil, ya que se esconden dentro de nuestro genoma, formando parte de nosotros. Sorprendentemente, algunos de ellos acaban siendo beneficiosos. Así se generó la placenta y se mejoró nuestro sistema inmunitario. Aún más relevante es su implicación en hacernos humanos. Sin embargo, su desregulación puede estar implicada en enfermedades, incluidas las neurodegenerativas y el cáncer. Son tan potentes que se están utilizando para construir una caja de herramientas de ingeniería genómica en biología aplicada, que debería permitir tratar enfermedades como el cáncer.

Palabras clave: Retrotransposones retrovirus adicciones estrés dieta epigenética adaptación evolución.

1. Introduction

Human evolution is a fascinating topic. It was exciting when archaeology was considered a social discipline. And it is even more provocative now that it is also a science topic. That has been accomplished thanks to the marriage between classical archaeology and modern molecular biology, as we have previously described (Dorado et al, 2007-2023). Such interaction has allowed to decipher previously intractable topics (Dorado et al, 2007). One of them is the molecular basis of the transition from first hominids to modern humans. In other words, what made us human. Interestingly, and perhaps as expected, there was not a single biological factor, but several, involved in such formidable evolution. They include the ones that we have previously reviewed as: i) duplication, repair and conversion of Notch Homolog 2 (*NOTCH2*) genes into Notch Homolog 2 N-terminal-Like (*NOTCH2NL*) ones (Dorado et al, 2018); ii) pervasive or spurious transcription into non-coding RNA, that later on acquired functionality (Dorado et al, 2020); and iii) nucleic-acid methylation (Dorado et al, 2022). Likewise, iv) mobile genetic elements (MGE), as reviewed in this work. Among other changes, they generated an increase in brain volume in general, and its cortex in particular, allowing the development of human-specific features that set us apart from other (irrational) animals.

Mobile genetic elements include different types, like transposable elements (TE) or transposons. They were discovered by Barbara McClintock in maize (*Zea mays*) in 1948 (Fig. 1). They are extremely abundant in eukaryotes, mainly in animals and plants. Thus, retrotransposons account for 45% to 48% of mammalian genomes, as well as 48% to 85% of plant genomes. As a consequence, they increase the intrinsic background “noise” of eukaryotic genomes (Palazzo and Koonin, 2020). Additionally, MGE carry out significant genetic horizontal transfers in the gut microbiome (Sheahan et al, 2024). That can be accomplished by conjugation or phage transduction. Such genetic interchanges may have opposite consequences: i) enhance our health with new metabolic capabilities; or ii) cause negative effects. Significant examples of them are bile-salt detoxification by commensal microbes, as well as antibiotic resistance of pathogenic ones, respectively (Jiang et al, 2019).

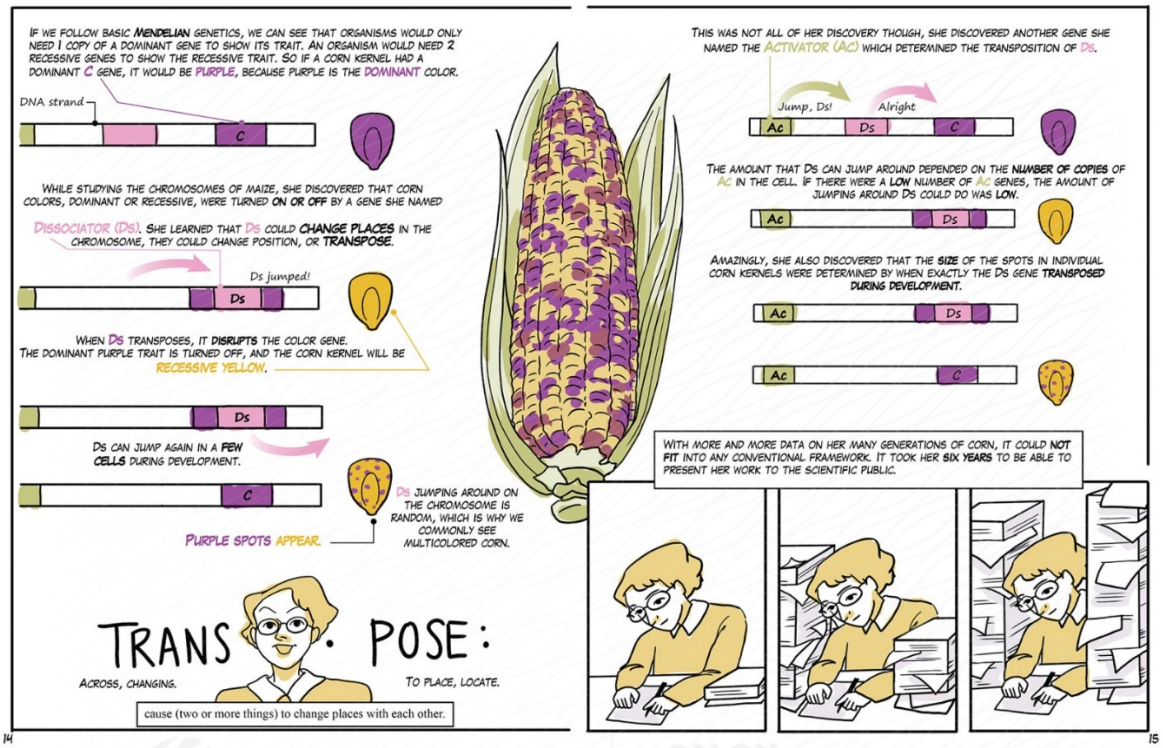

Figure 1. Discovery of transposons. Genetic mobile elements were discovered by Barbara McClintock in maize. © 2020 Association of Medical Illustrators. The Life of Barbara McClintock and Her Jumping Gene <https://meetingarchive.ami.org/2020/project/the-life-of-barbara-mcclintock-and-her-jumping-gene>.

2. Classification of mobile genetic elements

Ancestral mobile genetic elements have generated an amazing variety. They include plasmids, transposons, Clustered Regularly-Interspaced Short Palindromic Repeats (CRISPR; Dorado et al, 2017), Genomic Islands (GEI or GI), integrons, introns, Insertion Sequences (IS) with introns (IStrons), viral agents and inteins. The most relevant are transposable elements. They are extremely diverse, due to their high mutation rate, abundance and different replication mechanisms. Besides, there are hybrid TE, which can be complex. TE are classified taking into account their transposition mechanisms, sequence similarities and structural relationships. There are two main classes based on the nature of its nucleic acid: Class 1 (retrotransposons, which transpose via an RNA intermediate) and Class 2 (DNA transposons). Interestingly, bacterial TE are mainly IS, corresponding to class 2, Both phylogenetic and bioinformatics tools have been used to classify and display them in 2D and 3D graphs (Wicker et al, 2007; Arkhipova, 2017, Pappalardo et al, 2021; Camargo et al,

2024), as shown below (Fig. 2). Databases of repetitive DNA have also been published, like Repbase <https://www.girinst.org/repbase> (Kapitonov and Jurka (2008).

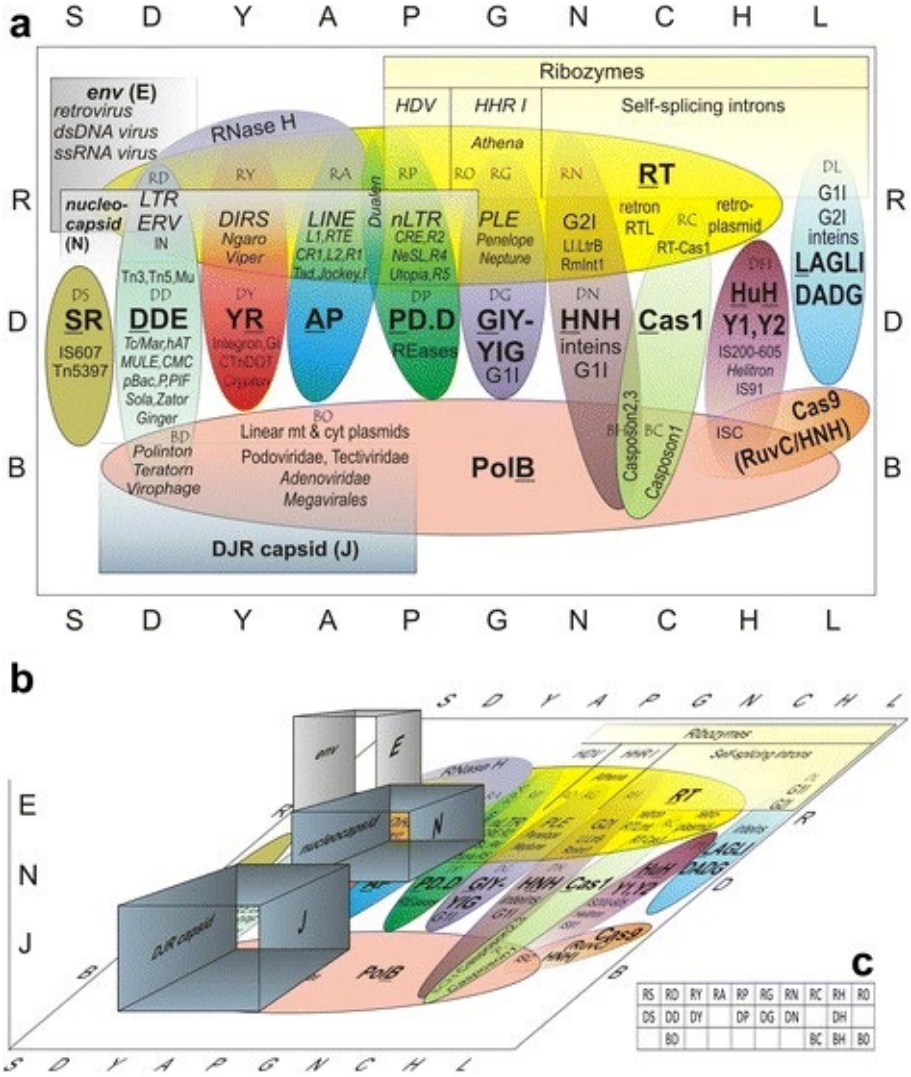

Figure 2. Transposable elements. 2D **(a and c)** and 3D **(b)** representations of TE. Such classification is based on their replication, integration and structural components. © The author, in BioMed Central (Arkhipova, 2017).

3. Mobile genetic elements arise as parasites: arms race with hosts

Mobile genetic elements originally arose as molecular parasites, eliciting defense mechanisms from hosts. That can be graphically represented, taking into account mobility and selfishness (Koonin et al, 2020), as shown below (Fig. 3).

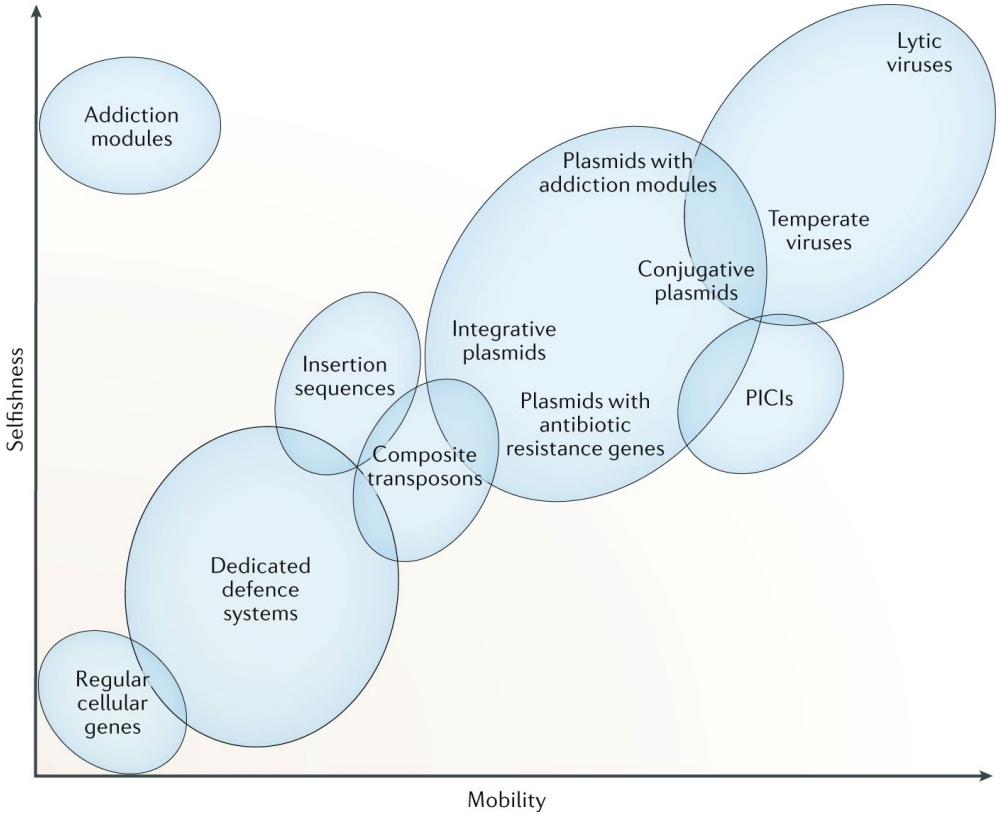

Figure 3. Mobile genetic elements and defense systems. The diagram shows the inextricable and interesting connection between MGE and host anti-MGE systems. © 2020 Springer Nature Switzerland (Koonin et al, 2020).

Indeed, the human genome contains remnants of ancient retroviruses, proof of the war that we fought (and continue to fight) against them. As an interesting example, it has been found that some ancient retroviral infections are responsible for pathogenic burdens linked to addictions. It is thought that only one of them is still replicating: HERV-K HML2 (HK2), showing different variants in different humans. The rationale explaining such effect is that one of such variants is integrated near a gene related to brain dopaminergic activity. Curiously, such variant is more frequent in drug addicts, being associated with such addictions (Karamitros et al, 2018). Likewise, MGE can produce mutations and may be involved in pathologies like cancer, autoimmune disorders and infectious diseases (Ferrari et al, 2021).

4. Some mobile genetic elements may have positive effects eventually

Some parasites are strict and always remain like that. Yet, that is not the best evolutionary approach. Indeed, lethal or too-aggressive parasites may kill hosts, which

may eventually lead to the parasite extinction. That is why such behavior may evolve into less-aggressive or non-lethal parasitism; with the possibility to further evolving even into symbiosis. That represents an Evolutionarily Stable Strategy (ESS), as previously described (Smith, 1972). Indeed, some MGE evolve that way, contributing to reshape genomes and the evolution of their hosts. This way, they may generate useful features and capabilities for the latter.

In these scenarios, it is interesting to note that mammals are classified as: i) monotremes (echidnas and platypus), which lay eggs; ii) marsupials (like kangaroos); and iii) placentals (like humans), which have developed placenta. That has significant implications. In the absence of placenta, the embryo must be protected with an eggshell. Otherwise, it would be destroyed by the immune system of the mother, since its proteins would be recognized as being from a different organism, much as happens with infections. But in such situation, the embryo growth is limited by the nutrients inside such container. Species laying eggs can be nidicolous (remaining in the nest to complete development) or nidifugous (leaving the nest shortly after hatching). A further evolution in mammals involves giving birth to offsprings at a very early stage of development. In such a case, they must attach to a teat (which in some species is inside a pouch called marsupium) to nourish from its milk. A much more elaborated system in mammals is the development of the placenta (Fig. 4).

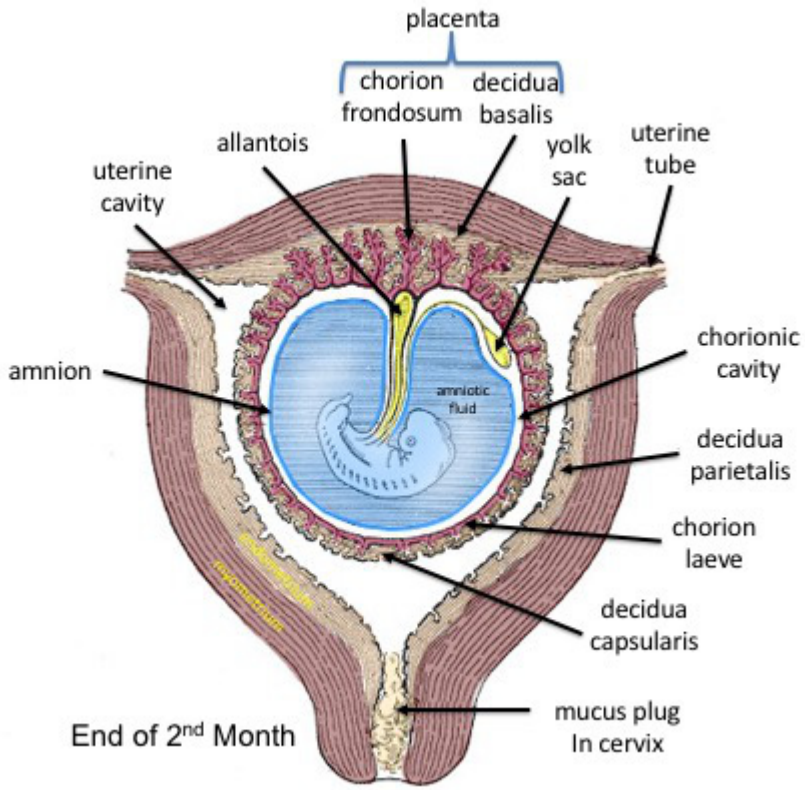

Figure 4. Human placenta. Fetus at week eight of development, showing the placenta and other structures from the embryo and mother. © 2019 Dennis M DePace, Wikimedia Commons <http://commons.wikimedia.org> and Creative Commons <http://creativecommons.org>.

The placenta attaches to the uterus of the mother, protecting the embryo. That way, it can remain inside and nourish from the mother for a much longer period. That allows to give birth much more developed offsprings, increasing their survival odds. Indeed, the placenta is a tissue like no other, working as an amazing gatekeeper. Thus, it must: i) protect the embryo from the immune system of the mother (that otherwise would kill it); ii) allow oxygen, antibodies and nutrients from the mother to pass through; and iii) allow carbon dioxide and waste from the embryo to get out. That may seem impossible, but surprisingly enough, such feat was accomplished by an infection of an ancient retrovirus.

Retroviruses have genomes made of RNA, which encode reverse transcriptase or retrotranscriptase enzymes. After invading the host cell, such enzymes retrotranscribe the virus RNA into DNA. Then, they use integrase enzymes to integrate into the genome (DNA) of the host cell. The virus is then considered a provirus, being

camouflaged as part of the host genome. One of such viruses is the human immunodeficiency virus (HIV).

And now is when the story of the origin of the mammalian placenta becomes surprising. One of such viruses infected an egg-laying vertebrate female ~200 million years ago. By chance, such virus infected an egg cell, which luckily was fertilized by a spermatozoon. Therefore, the offspring generated had copies of such virus in all its cells. Fortunately, such infection did not kill the offspring or the mother then.

A this point, it is interesting to note that viruses usually fuse with molecules to infect cells. In this fascinating story, the virus produced a protein (syncytin) that allowed the embryo to fuse cells, generating a syncytium or symplasm. It mediates the placental cytotrophoblast fusion, and thus allows the placental morphogenesis. Thus, the fetus makes a sac filled with amniotic fluid, which becomes thick on one side (the placenta) and attaches to the womb. The outermost layer of the placenta is a layer of cells that have fused together, as previously described, forming a special housekeeper wall that prevents the blood streams of mother and offspring to mix (syncytiotrophoblast), being in contact with the uterus. That is a remarkable accomplishment, since the placenta can do what no other tissue is capable: i) connects the mother with the offspring for some functions required for the fetus growth; but at the same time ii) keeps them as two independent and separate immune systems, so that they do not destroy each other (Mi et al, 2000, Mitra, 2020).

Additionally, MGE may also enhanced the immune system of their hosts, as shown in the example below for protection against HIV infections (Fig. 5). That involves: a) expression of human Endogenous-RetroViruses (hERV) mRNA, which can hybridize with HIV RNA. Such double-stranded RNA (dsRNA) cannot be translated into proteins. Besides, they are identified as pathogen-associated molecular patterns (PAMP), triggering cellular defenses; b) interaction of hERV proteins with the ones of HIV, interfering their assembly and release; and c) binding of hERV proteins to HIV cellular receptors, preventing external HIV binding and entry. Interestingly, HIV infections can trigger hERV upregulation, further maintaining and enhancing such protective effects of the host immune system (Grandi and Tramontano, 2018).

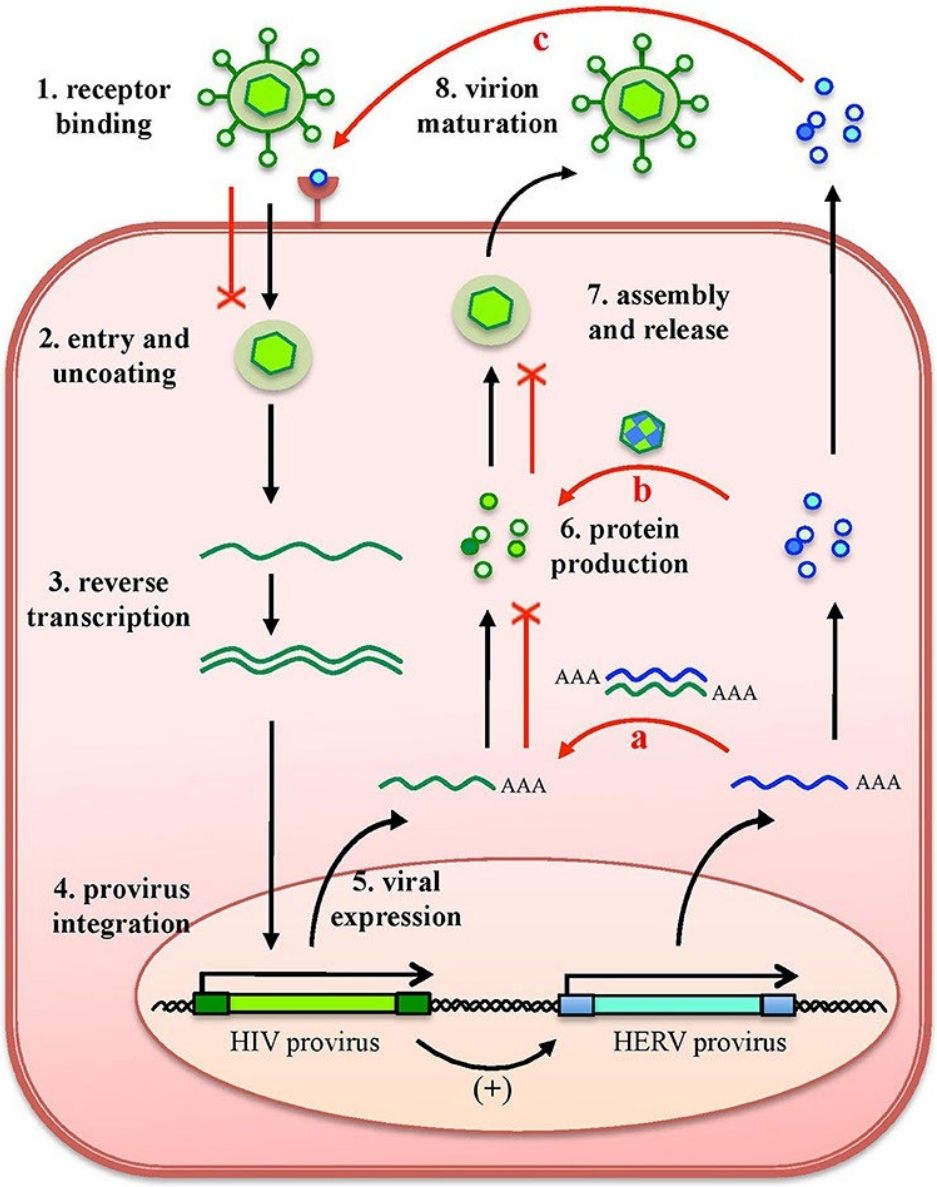

Figure 5. Enhancements of immune system by ancient human endogenous-retroviruses. The protective effects of hERV (red lines) are shown by the impairment of HIV infection. **a)** generation of dsRNA; **b)** interaction with HIV proteins; and **c)** binding to HIV cellular receptors. © The authors, in Frontiers Media (Grandi and Tramontano, 2018).

Most significantly, MGE participated in the development of the mammalian nervous system in general, and primate brain in particular (Fig. 6), contributing to making us humans. That includes: i) non-coding RNA derived from TE; ii) proteins generated from retrotransposons; iii) RNA-regulatory sites produced by exonization of TE, modulating mRNA stability and translation; iv) enhancers originating from RE, providing Tissue Factor (TF) binding sites, further modifying transcription of brain genes; and v) 3D genome organizers, modulating expression of brain-specific genes (Ferrari et al, 2021).

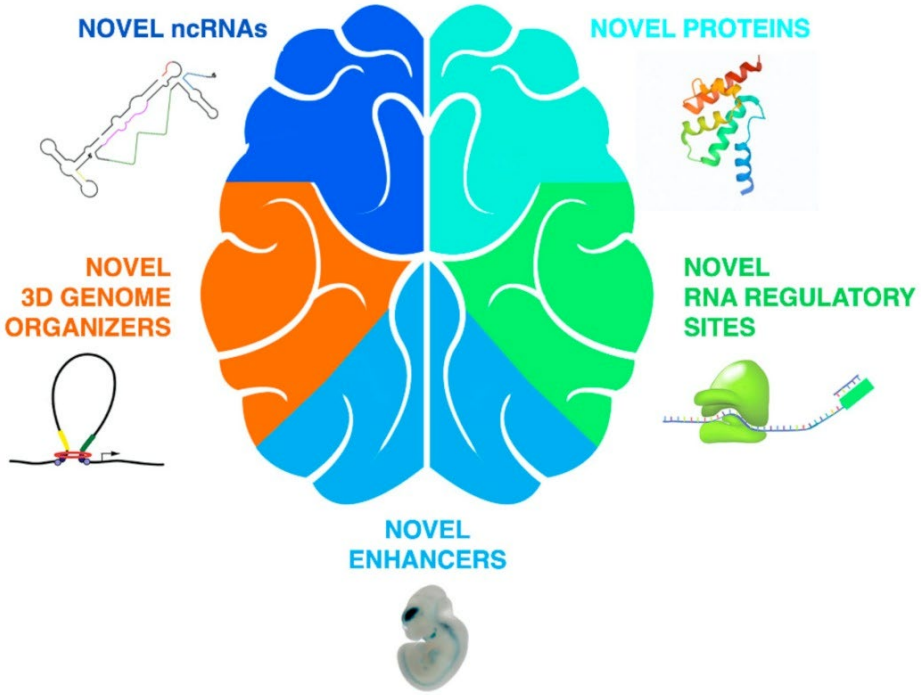

Figure 6. Retrotransposon involvement in brain evolution. Five types of regulatory element (RE) exaptation are shown (clockwise, from top left side): i) non-coding RNA generated from TE; ii) retrotransposon proteins; iii) exonization of TE, generating RNA-regulatory sites; iv) enhancers produced from RE; and v) 3D genome organizers. © The authors, in MDPI (Ferrari et al, 2021).

5. Concluding remarks and future prospects

MGE are involved in transcriptional and posttranscriptional control of gene expression, including chromatin organization. Thus, they modulate genome dynamics, interaction with the environment, adaptation and evolution. Not surprisingly, there is a correlation between their activity and environmental factors like stress and diet. That may be accomplished by epigenetic changes, including histone modifications, nucleic-acid methylations (Dorado et al, 2022) and transcription of non-coding RNA (Dorado et al, 2020). That way, TE may remain active by transposition and propagation into different genome places, thus evading silencing mechanisms by the host. Such activity is initially pathogenic, generating higher mutation rate and diseases in the host. But the higher genetic diversity produced may become beneficial in some instances, including regulatory innovations, allowing natural selection to act on it (Pappalardo et al, 2021).

In summary, we were and are at war with MGE. At the beginning of the infection, they are detrimental and even kill us, but some of them remain in our genomes and, although

originally they are harmful, eventually some of them became advantageous. So, in some way, we domesticated some MGE, but such MEG also domesticated us. Part of us became MGE, and part of MGE became human, both behaving as symbionts. While the arms race between hosts and TE continue as a never-ending fight with some MGE, they have been proposed to build a genome engineering toolbox, to empower applied biology, and treat diseases like cancer. That way, we can take even more advantage of them (Zhang et al, 2024).

***Acknowledgements*.** Supported by “Ministerio de Economía y Competitividad” (MINECO grant BIO2015-64737-R) and “Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria” (MINECO and INIA RF2012-00002-C02-02); “Consejería de Agricultura y Pesca” (041/C/2007, 75/C/2009 and 56/C/2010), “Consejería de Economía, Innovación y Ciencia” (P11-AGR-7322) and “Grupo PAI” (AGR-248) of “Junta de Andalucía”; and “Universidad de Córdoba” (“Ayuda a Grupos”), Spain.

6. References

Arkhipova IR (2017): Using bioinformatic and phylogenetic approaches to classify transposable elements and understand their complex evolutionary histories. Mobile DNA 8: 19 (14 pp).

Camargo AP, Roux S, Schulz F, Babinski M, Xu Y, Hu B, Chain PSG, Nayfach S, Kyrpides NC (2024): Identification of mobile genetic elements with geNomad. Nature Biotechnology 42: 1303-1312.

Dorado G, Gálvez S, Rosales TE, Vásquez VF, Hernández P (2021a): Analyzing modern biomolecules: the revolution of nucleic-acid sequencing – Review. Biomolecules (section Molecular Genetics) 11: 1111 (18 pp).

Dorado G, Jiménez I, Rey I, Sánchez-Cañete FJS, Luque F, Morales A, Gálvez M, Sáiz J, Sánchez A, Rosales TE, Vásquez VF, Hernández P (2013): Genomics and proteomics in bioarchaeology - Review. Archaeobios 7: 47-63.

Dorado G, Luque F, Esteban FJ, Pascual P, Jiménez I, Sánchez-Cañete FJS, Raya P, Sáiz J, Sánchez A, Rosales TE, Vásquez VF, Hernández P (2021b): Molecular biology to infer phenotypes of forensic and ancient remains in bioarchaeology – Review. Archaeobios 15: 49-64.

Dorado G, Luque F, Esteban FJ, Pascual P, Jiménez I, Sánchez-Cañete FJS, Raya P, Rosales TE, Vásquez VF, Hernández P (2023): Archaeology and phylogeny to ascertain the evolution of amniotic egg and viviparity – Review. Archaeobios 18: 103-112.

Dorado G, Luque F, Esteban FJ, Pascual P, Jiménez I, Sánchez-Cañete FJS, Raya P, Sáiz J, Sánchez A, Rosales TE, Vásquez VF, Hernández P (2022): Involvement of nucleic-acid methylation on biology and evolution: from first hominids to modern humans – Review. Archaeobios 17: 104-116.

Dorado G, Luque F, Pascual P, Jiménez I, Sánchez-Cañete FJS, Pérez-Jiménez M, Raya P, Gálvez M, Sáiz J, Sánchez A, Rosales TE, Vásquez VF, Hernández P (2015): Second-generation nucleic-acid sequencing and bioarchaeology - Review. Archaeobios 9: 216-230.

Dorado G, Luque F, Pascual P, Jiménez I, Sánchez-Cañete FJS, Pérez-Jiménez M, Raya P, Sáiz J, Sánchez A, Martín J, Rosales TE, Vásquez VF, Hernández P (2016): Sequencing ancient RNA in bioarchaeology - Review. Archaeobios 10: 103-111.

Dorado G, Luque F, Pascual P, Jiménez I, Sánchez-Cañete FJS, Raya P, Sáiz J, Sánchez A, Rosales TE, Vásquez VF (2017): Clustered Regularly-Interspaced

Short-Palindromic Repeats (CRISPR) in bioarchaeology - Review. Archaeobios 11: 179-188.

Dorado G, Luque F, Pascual P, Jiménez I, Sánchez-Cañete FJS, Raya P, Sáiz J, Sánchez A, Rosales TE, Vásquez VF, Hernández P (2018): Evolution from first hominids to modern humans: philosophy, bioarchaeology and biology - Review. Archaeobios 12: 69-82

Dorado G, Luque F, Pascual P, Jiménez I, Sánchez-Cañete FJS, Raya P, Sáiz J, Sánchez A, Rosales TE, Vásquez VF, Hernández P (2019): Bioarchaeology to bring back scents from extinct plants - Review. Archaeobios 13: 66-75.

Dorado G, Luque F, Pascual P, Jiménez I, Sánchez-Cañete FJS, Raya P, Sáiz J, Sánchez A, Rosales TE, Vásquez VF, Hernández P (2020): Implications of non-coding RNA on biology and evolution: from first hominids to modern humans - Review. Archaeobios 14: 107-118.

Dorado G, Rey I, Rosales TE, Sánchez-Cañete FJS, Luque F, Jiménez I, Gálvez M, Sáiz J, Sánchez A, Vásquez VF (2009): Ancient DNA to decipher the domestication of dog (REVIEW). Archaeobios 3: 127-132.

Dorado G, Rey I, Rosales TE, Sánchez-Cañete FJS, Luque F, Jiménez I, Morales A, Gálvez M, Sáiz J, Sánchez A, Hernández P, Vásquez VF (2010): Biological mass extinctions on planet Earth (REVIEW). Archaeobios 4: 53-64.

Dorado G, Rosales TE, Luque F, Sánchez-Cañete FJS, Rey I, Jiménez I, Morales A, Gálvez M, Sáiz J, Sánchez A, Vásquez VF, Hernández P (2011): Ancient nucleic acids from maize - A review. Archaeobios 5: 21-28.

Dorado G, Rosales TE, Luque F, Sánchez-Cañete FJS, Rey I, Jiménez I, Morales A, Gálvez M, Sáiz J, Sánchez A, Vásquez VF, Hernández P (2012): Isotopes in bioarchaeology - Review. Archaeobios 6: 79-91.

Dorado G, Sánchez-Cañete FJS, Pascual P, Jiménez I, Luque F, Pérez-Jiménez M, Raya P, Gálvez M, Sáiz J, Sánchez A, Rosales TE, Vásquez VF, Hernández P (2014): Starch genomics and bioarchaeology - Review. Archaeobios 8: 41-50.

Dorado G, Vásquez V, Rey I, Luque F, Jiménez I, Morales A, Gálvez M, Sáiz J, Sánchez A, Hernández P (2008): Sequencing ancient and modern genomes (REVIEW). Archaeobios 2: 75-80.

Dorado G, Vásquez V, Rey I, Vega JL (2007): Archaeology meets Molecular Biology (REVIEW). Archaeobios 1: 1-2.

Ferrari R, Grandi N, Tramontano E, Dieci G (2021): Retrotransposons as Drivers of Mammalian Brain Evolution. Life 11: 376 (29 pp).

Grandi N, Tramontano E (2018): Human endogenous retroviruses are ancient acquired elements still shaping innate immune responses. Frontiers in Immunology 9: 2039 (16 pp).

Jiang X, Hall AB, Xavier RJ, Alm EJ (2019): Comprehensive analysis of chromosomal mobile genetic elements in the gut microbiome reveals phylum-level niche-adaptive gene pools. PLoS One 14: e0223680 (22 pp).

Kapitonov VV, Jurka J (2008): A universal classification of eukaryotic transposable elements implemented in Repbase. Nature Reviews Genetics 9: 411-412.

Karamitros T, Hurst T, Marchi E, Karamichali E, Georgopoulou U, Mentis A, Riepsaame J, Lin A, Paraskevis D, Hatzakis A, McLauchlan J, Katzourakis A, Magiorkinis G (2018): Human Endogenous Retrovirus-K HML-2 integration within RASGRF2 is associated with intravenous drug abuse and modulates transcription in a cell-line model. Proceedings of the National Academy of Sciences 115: 10434-10439.

Koonin EV, Makarova KS, Wolf YI, Krupovic M (2020): Evolutionary entanglement of mobile genetic elements and host defence systems: guns for hire. Nature Reviews Genetics 21: 119-131.

Mi S, Lee X, Li X, Veldman GM, Finnerty H, Racie L, LaVallie E, Tang XY, Edouard P, Howes S, Keith JC Jr, McCoy JM (2000): Syncytin is a captive retroviral envelope protein involved in human placental morphogenesis. Nature 403: 785-789.

Mitra A (2020): How the placenta evolved from an ancient virus. Web text <https://whyy.org/segments/the-placenta-went-viral-and-protomammals-were-born> and audio <https://whyy-od.streamguys1.com/news/0131PLACENTAweb.mp3>.

Palazzo AF, Koonin EV (2020): Functional long non-coding RNAs evolve from junk transcripts. Cell 183: 1151-1161.

Pappalardo AM, Ferrito V, Biscotti MA, Canapa A, Capriglione T (2021): Transposable elements and stress in vertebrates: an overview. International Journal of Molecular Sciences 22: 1970 (16 pp).

Sheahan ML, Coyne MJ, Flores K, Garcia-Bayona L, Chatzidaki-Livanis M, Sundararajan A, Holst AQ, Barquera B, Comstock LE (2024): A ubiquitous mobile genetic element disarms a bacterial antagonist of the gut microbiota. Science 386: 414–420.

Smith, JM (1972). "Game Theory and The Evolution of Fighting". On Evolution. Edinburgh University Press, Edinburgh.

Wicker T, Sabot F, Hua-Van A, Bennetzen JL, Capy P, Chalhoub B, Flavell A, Leroy P, Morgante M, Panaud O, Paux E, SanMiguel P, Schulman AH (2007): A unified classification system for eukaryotic transposable elements. Nature Reviews Genetics 8: 973-982.

Zhang T, Tan S, Tang N, Li Y, Zhang C, Sun J, Guo Y, Gao H, Cai Y, Sun W, Wang C, Fu L, Ma H, Wu Y, Hu X, Zhang X, Gee P, Yan W, Zhao Y, Chen Q, Guo B, Wang H, Zhang YE (2024): Heterologous survey of 130 DNA transposons in human cells highlights their functional divergence and expands the genome engineering toolbox. Cell 187: 3741-3760.