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CHAPTER THREE

The efficient Lamarckian spread of life in the cosmos

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Abstract

In this Chapter we discuss the various mechanisms that are available for the possible transfer of cosmic microbial living systems from one cosmic habitat to another. With the 100 or so habitable planets that are now known to exist in our galaxy alone transfers of cometary dust carrying life including fragments of icy planetoids/asteroids would be expected to occur on a routine basis. It is thus easy to view the galaxy as a single connected "biosphere" of which our planet Earth is a minor component.

Advances in Genetics, Volume 106
ISSN 0065-2660
https://doi.org/10.1016/bs.adgen.2020.03.004

The Hoyle–Wickramasinghe Panspermia paradigm provides a cogent biological rationale for the actual widespread existence of Lamarckian modes of inheritance in terrestrial systems (which we review here). Thus the Panspermia paradigm provides the *raison d'etre* for Lamarckian Inheritance. Under a terrestrially confined neoDarwinian viewpoint such an association may have been thought spurious in the past. Our aim here is to outline the main evidence for rapid terrestrial-based Lamarckian-based evolutionary hypermutation processes dependent on reverse transcription-coupled mechanisms among others. Such rapid adaptation mechanisms would be consistent with the effective cosmic spread of living systems. For example, a viable, or cryo-preserved, living system traveling through space in a protective matrix will of necessity need to *adapt rapidly* and proliferate on landing in a new cosmic niche. Lamarckian mechanisms thus come to the fore and supersede the slow (blind and random) genetic processes expected under neoDarwinian Earth centred theories.

1. The traditional neoDarwinian view of life and evolution

It is useful then to begin by summarizing the widely held traditional view of the evolution of life on Earth. In this way we can sharpen the focus on the set of Lamarckian acquired inheritance processes now discovered which, together with Panspermic "in-falls" of living systems from space, are now replacing the neoDarwinian explanation for the origin life and its further evolution on Earth. A dot point summary would go something like this:

- Life emerged in the period after the Hadean Epoch (about 4 billion years ago) as the first free-living cells, arising from non-living chemistry (Abiogenesis), proliferated on Earth.
- This key Abiogenic event happened 3–4 billion years ago perhaps via an RNA World, in one of Darwin's hypothetical "warm little ponds" or the "primordial soup."
- These free-living primordial cells then proliferated and flourished by Darwinian evolution. They repeatedly duplicated their genomes and genes, with additional slow mutational events occurring. Survival of the fittest of these duplicated derivatives was the origin of new DNA sequences and the rearrangements occurring in their genomes, new species.
- The progression is envisaged to be from the archaeal and prokaryotic bacterial worlds, generating many new cellular species. The production of viruses by most cells went hand in glove with this evolution and further aided cell-cell genetic communication. Thus virus mediated

horizontal gene transfer (HGT) was a key early process aiding cellular diversification and adaptation.

- Darwinian natural selection is seen therefore as preserving all these evolutionary genetic steps which arose by chance and random events. We do not doubt that at least some of these sorts of slow genetic events may have happened.
- The first free living eukaryotic cells occurred by cell-cell fusions between archaeal and prokaryotic cells by symbiosis (Margulis, 1970, 1981). It is then envisaged that these events provided the evolutionary path prior to the explosive emergence of the metazoans and multicellular plant and animal life in the Cambrian period ca 540 million years ago.
- With the apparent exception of the Cambrian explosion itself, however, many of these evolutionary phases envisaged were very slow, taking millions if not hundreds of millions of years.
- Note that the Cambrian "creative disruption" to this linear thinking is not an exception, just a big one. The *actual fossil record*, as well as phylogenetic nucleic acid and protein sequence analyses, show that most novel species and life forms emerge suddenly in a "punctuated" way, either persisting to the present or going to extinction (termed "punctuated equilibrium" by Eldridge and Gould, published in 1972, 1977; the same disrupted events are discussed in Hoyle & Wickramasinghe, 1981, and again in Steele et al., 2018).
- Indeed ever since the explosive events of the Cambrian adaptive radiation two further major extinctions and adaptive radiations are well preserved in the fossil record, and occurred at the Permian/Triassic (P/T) boundary (~252 million years ago) and the Cretaceous/Palaeocene (K/T) boundary (~65.5 million years ago, with the extinction of Dinosaurs).
- Such apocalyptic events seem to have a frequency of occurring approximately every 250 hundred million years, suggesting a cosmic orbiting cycle of our Sun and Solar System around the galactic center of the Milky Way. There are also shorter 30 million year extinction-diversification cycles suggesting an alignment as our star system oscillates through the galactic plane (Clube, Hoyle, Napier, & Wickramasinghe, 1996; Wickramasinghe et al., 2010).

But we need to ask ourselves, is this a credible way to view the evolution of life on Earth? Abiogenesis on Earth, or anywhere in the known observable Universe is highly improbable (the odds against are less than 1 successful event expected in $>10^{5120}$ events, Hoyle & Wickramasinghe, 1999, and outlined in Steele, Al-Mufti, et al., 2019, Steele, Gorczynski, et al., 2019).

An alternative view, which is argued below, is one of scientific pragmatism rather than ideological pursuit of improbable events or just so scenarios. Our key evidence for Lamarckian inheritance, which overcomes the pitfalls inherent to theories of a slow and ponderous neoDarwinian evolutionary progression for the origin of life on Earth, is outlined in Tables 1 and 2.

Our purpose here then is to show that since the 1970s many key lines of scientific evidence have emerged contradicting this comfortable view of life on Earth. We and many colleagues have recently reviewed most of this salient contradictory evidence (Steele et al., 2018; Steele, Al-Mufti, et al., 2019; Steele, Gorczynski, et al., 2019). We conclude that the traditional terrestrial neoDarwinian view of terrestrial evolution is scientifically untenable. At key junctures it does not fit the actually observed data showing that "...living organisms such as space-resistant and space-hardy bacteria, viruses, more complex eukaryotic cells, fertilized ova and seeds have been continuously delivered … to Earth so being one important driver of further terrestrial evolution which has resulted in considerable genetic diversity and which has led to the emergence of mankind" (Steele et al., 2018). Thus the evolution of life on Earth has been driven by seedings from the wider Cosmos. These space-derived "varieties" also further evolve on Earth and drive further diversification. Every few hundreds of millions of years on Earth is marked by major Cosmic bolide "seeding" events presumably as mentioned by passage of our Solar System through giant dust and molecular clouds (e.g., see Hoyle & Wickramasinghe, 1993).

In our view the key hard evidence already exists forming the "Demarcation Data" distinguishing terrestrial neo-Darwinism from the evidence for Cosmic Panspermia. This evidence from the 1970s to 2000 has been marshalled and analyzed by Hoyle and Wickramasinghe (1978, 1979, 1981, 1985, 1993, 1999 which references all key peer-reviewed papers). Wickramasinghe (2018) has reviewed all the key evidence covering the terrestrial atmosphere, bacteria and other micro-organisms, discussing a role for comets as protective incubators and amplifiers of living systems, and highlighted among the evidence the infra-red (IR) analyses of interstellar dust and cometary ejecta among other central issues.

We have also highlighted some important 'Demarcation Data' that distinguishes neo-Darwinism from Cosmic Panspermia (Steele, Al-Mufti, et al., 2019; Steele, Gorczynski, et al., 2019). One key focus is on the internal structure of carbonaceous meteorites showing clear microfossils of both eukaryotic and prokaryotic organisms. These observations have been from independently curated and examined carbonaceous meteorites, dated at

Table 1 Adaptive genetic strategies of environmentally-driven mutators systems (main Ref. Steele, Gorczynski, et al., 2019).

System	Adaptive genetic process	Molecular, enzymatic, cellular processes involved in adaptation	References
Immune system	• Innate immunity (Germline encoded)—to intracellular pathogens (e.g., viruses) and neo-antigens generated in cancer cells by somatic mutation	• AID/APOBEC C-to-U and ADAR A-to-I (G) deaminases mutate pathogen/host genomes. These single nucleotide variants (SNVs) are lesions which generate base pair mismatches which if left unrepaired lead to single nucleotide changes. If the repair process is incomplete it can lead to single stand DNA nicks which if unrepaired lead to chromosome rearrangements and DNA translocations.	Refsland and Harris (2013), Samuel (2011), Schoggins and Rice (2011), Schneider, Chevillotte, and Rice (2014), Lindley (2013), Lindley and Steele (2013, 2018), Lindley, Humbert, Larmer, Akmeemana, and Pendlebury (2016)
	• Acquired adaptive immunity-somatic hypermutation (SHM) of rearranged immunoglobulin (Ig) V regions and, in principle rearranged T cell receptor (TCR) V regions (Termed "VDJs") allowing specific responses to foreign antigens on pathogens (viruses, bacteria) or novel host antigens (neo-antigens) on cancer cells	• AID/APOBEC C-to-U and ADAR A-to-I (G) deaminases initiate and somatically mutate VDJs. Dysregulated Ig SHM like responses typical of cancer genomes. • Can include target site reverse transcription (TSRT) via Y family DNA polymerases, e.g., Pol-η, Pol-κ. • Homologous recombination (HR)	Steele (2016a), Steele and Lindley (2017), Franklin, Steele, and Lindley (2020)

Continued

Table 1 Adaptive genetic strategies of environmentally-driven mutators systems (main Ref. Steele, Gorczynski, et al., 2019).—cont'd

System	Adaptive genetic process	Molecular, enzymatic, cellular processes involved in adaptation	References
	• Origin, maintenance, diversification of germline rearranged V gene repertoires	• AID/APOBEC C-to-U and ADAR A-to-I (G) deaminases initiate and somatically mutate VDJs. • Can include target site reverse transcription (TSRT) via Y family DNA polymerases, e.g., Pol-η, Pol-κ. • Soma-to-germline flow DNA/RNA sequences via vesicles, endogenous retroviral vectors • Homologous recombination (HR)	Steele and Lindley (2018), Steele and Lindley (2020)
Human Genome	• Origin of neutral, benign, beneficial germline variants including those causing human genetic diseases viz. origin of single nucleotide polymorphisms (SNPs) in OMIM and dbSNP databases	• AID/APOBEC C-to-U and ADAR A-to-I (G) deaminases (direct and/or indirect effect germline DNA sequences (protein coding in particular). Elements of other processes listed above viz. Can include Y family polymerases Pol-η, Pol-κ, reverse transcription also (TSRT), and homologous recombination (HR)	Lindley and Hall (2018)

Table 2 Adaptive genetic strategies of environmentally-driven mutators systems (main Ref. Steele, Gorczynski, et al., 2019).

System	Adaptive genetic process	Molecular, enzymatic, cellular processes involved in adaptation	References
Vertebrate immune and endocrine systems	Inheritance acquired tolerance, immunity and behavior	• Acquired transgenerational inheritance • Penetration Weismann barrier • Sire effect-coupled maternal effect • Pavlovian conditioning-couple to acquired inheritance	Gorczynski and Steele (1980, 1981), Gorczynski et al. (1983), Sobey and Conolly (1986), Gorczynski (1992)
	Inheritance of acquired instincts "Dutch Famine"	• Acquired epigenetic inheritance • Acquired epigenetic-genetic effects	Campbell and Perkins (1988), Jablonka & Lamb, 1995), Lindley (2010), Painter et al. (2008), Pembrey, Saffery, and Bygren (2014), Dias and Ressler (2014)
	Inheritance acquired autoimmunity	• Transmission via male of maternal induced autoimmune eye defects (Experiments of Guyer & Smith 1918–1924)	Reprinted in Steele 2016b
Mammalian germ cells	Uptake of foreign DNA and RNA	• Penetration Weismann barrier • Soma-to-Germline flow DNA/RNA with genetic effects on progeny	Spadafora (1998, 2008, 2018), Rassoulzadegan et al. (2006), Fogarty (2002)
Plant hybrid grafts	Acquired inheritance	• Classic pangenesis in hybrid plants	Liu (2018)
Adaptive evolution in bacteria and microorganism	Adaptive hypermutation SOS responses	• Substrate, ligand, stress-induced hypermutation, rapid "Darwinian" selection. Putative involvement Y family DNA polymerases, thus Reverse Transcription (?)	Radman (1974, 1999), Tippin, Phuong Pham, and Goodman (2004), Rosenberg (2001)

>4.5 billion years old. The data have been independently confirmed by experts in four well curated and characterized carbonaceous meteorites: Murchison (Hoover, 2005, 2011; Pflug & Heinz, 1997), Murchison, Orgueil, Mighei (Rozanov & Hoover, 2013), Polonnaruwa (Wallis et al., 2013; Wickramasinghe, Wallis, Wallis, & Samaranayake, 2013). We stress all this, as the scepticism often raised here actually threatens a key corner stone of Science viz. the independent confirmation of evidence—without this criterion modern Science could not function nor progress.

In all these meteorite studies terrestrial contamination has been ruled out. So we must seriously consider these four different and independent "experiments of nature" on their own terms. Eukaryotic fossils with silica-based hard shells, are prominent in these fossils. In the Polonnaruwa meteorite (Wickramasinghe et al., 2013) the frustules of clear diatoms are evident (Fig. 1). Clearly these are features of mature cell biology in astrophysical phenomena that require a coherent explanation. "They strongly imply that complex cell-based life, now immortalized as fossils in carbonaceous meteorites, pre-dates the age of the Earth (and solar system). An explanation based on Panspermia seems unavoidable to us" (Steele, Al-Mufti, et al., 2019; Steele, Gorczynski, et al., 2019).

We have argued pragmatically (Steele, Gorczynski, et al., 2019) that the origins from non-living chemistry of cell-based life in the current known universe are so statistically improbable that our scientific approach should

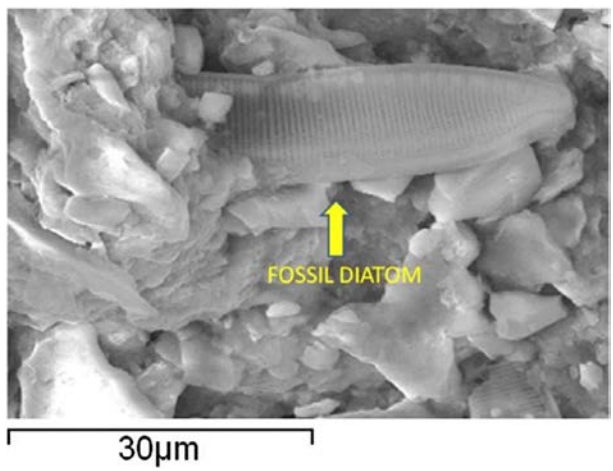

Fig. 1 Eukaryotic microfossil in Carbonaceous meterorite. Voidal-shaped ribbed structure embedded in the rock matrix of the Polonnaruwa carbonaceous meteorite, Wickramasinghe et al. (2013), see also other chemical analyses in Wallis et al. (2013).

Table 3 From Steele, Gorczynski, et al. (2019)—Projected numbers based on Earth equivalents and estimated number of stars in the observable Universe $\sim 10^{22}$.

Cosmic distribution and numbers of living systems	
• Viruses—terrestrial number 10^{31}	10^{53}
• Bacteria/Archaea—terrestrial number $> 10^{30}$	10^{52}
• Single cell eukaryotes—terrestrial number 10^{20}–10^{30}	10^{32}–10^{52}
• Complex Metazoans—terrestrial number $\geq 10^{20}$	10^{42}
• Higher plants, terrestrial number $\geq 10^{7}$ species	10^{29}
• Higher animals, terrestrial number $\geq 10^{7}$ species	10^{29}

not be directed so much toward studying abiogenesis events in the laboratory, but into quantitating the distribution and numbers of living systems in the observable Universe (e.g., Table 3, and Steele, Gorczynski, et al., 2019). Indeed there is much to learn pragmatically about life in the Cosmos by observing what falls to Earth from space (see chapter "Origin of new emergent Coronavirus and Candida fungal diseases—Terrestrial or cosmic?" by Steele et al., this volume), along with other biological evidence for living systems in the near Earth neighborhood, e.g., bacteria in cosmic dust on the external surface of the International Space Station (Grebennikova et al., 2018).

2. The rise of the neoLamarckian acquired inheritance paradigm

We have critically reviewed much of the evidence for Lamarckian inheritance gathered since the 1970s which have established the new Lamarckian evolutionary paradigm (Steele, Gorczynski, et al., 2019).

We have condensed the main lines of this evidence in Tables 1 and 2. These environmentally-induced cellular and molecular processes can now be considered the *primary evolutionary driver mechanisms* for the evolution and ongoing diversification of life on Earth. And, by extension, we argue the case here (see chapter "The sociology of science and generality of the DNA/RNA/protein paradigm throughout the cosmos" by Wickramasinghe et al., this volume) and elsewhere (Wickramasinghe, Wickramasinghe, Tout, Lattanzio, & Steele, 2020) that these DNA and RNA inheritance mechanisms are likely to be general throughout the Cosmos—resulting in the efficient Panspermic dispersal of living systems, in all their variety, throughout the Universe.

Table 4 From Steele, Gorczynski, et al. (2019).

Evidence consistent with Lamarckian evolutionary processes
1. Environmental stimulation as the directional mutational driver
2. Role of epigenetic gene targeting
3. Rapid genetic adaptation
4. Penetration of the *Weismann Barrier*
5. Horizontal gene transfer (HGT)
6. Central role of reverse transcription

The summaries of evidence for horizontal gene transfer (HGT) are covered at the Wikipedia site https://en.wikipedia.org/wiki/Horizontal_gene_ transfer.

The key distinguishing features and driver mechanisms of this neoLamarckian view of life are listed in Table 4.

We now describe pertinent molecular-cellular evidence for Lamarckian acquired-inheritance adaptations across the kingdoms of life—from bacterial cells to higher plants and animals. The review will not be comprehensive because of the vastness of the literature since the 1970s. We will select representative examples for discussion and illumination as outlined in Tables 1 and 2.

2.1 Immune system

2.1.1 Innate immunity

This is the first line of defense against invading pathogens in all cells and is thus termed "Innate" immunity. As the name implies the functions of Innate Immunity are germline selected and encoded and thus not "adaptive" somatically over time, but immediately "reactive" to foreign pathogen entry to cells. Probably a 100 or so genes are co-ordinately upregulated during an Innate Immune response via interferon mediated cytokines, and they are termed Interferon Stimulated Genes (ISGs, Schneider et al., 2014). Key ISG components of Innate Immunity are the cytosine deaminases (AID/APOBEC) converting cytosine in DNA to uracil (C-to-U) and adenosine (ADAR) deaminases converting adenosines to inosines in double stranded (ds)RNA, or in RNA and DNA moieties of RNA:DNA hybrids that occur in Transcription Bubbles (Steele & Lindley, 2017; Zheng, Lorenzo, & Beal, 2017). The inosine bases so formed are mutagenic (A-to-I, read as "G" on replication, reverse transcription or during translation from mRNA to protein sequences, see chapter "The mutagenic source and power of our own evolution" by Lindley, this volume). Thus both mutagenic uracils and

inosines need to be repaired prior to DNA or RNA copying events- when this does not happen it causes G•T, G•U and A•I base pair mismatches in the DNA and RNA helices (leading to C-to-T and A-to-G primary mutations). Downstream DNA repair sequelae of these lesions to single stranded DNA nicks (or staggered double stranded nicks) leads to DNA rearrangements and translocation events (common in progressing cancer genomes). Further, the error prone translesion Y family DNA Polymerases eta (η) and kappa (κ) in mammalian systems are also efficient reverse transcriptases (Franklin, Milburn, Blanden, & Steele, 2004; Franklin et al., 2020) so that error prone reverse transcriptase Y family copying of such lesions can lead to transversion mutations, e.g., A-to-T, A-to-C.

Invading viral genomes replicating in the cytosolic endoplasmic reticulum membranes (so called Replication Factories) or similar membranous sites within the nucleus are the main targets for deamination during the Innate Immune phase (first 24–48 h after infection). The cytosine and adenosine deaminases thus cause mutagenic damage to pathogen genomes. The C-to-U and A-to-I(G) mutational signatures at the appropriate deaminase sequence motifs are literally written all over the viral genomes in the early phase of infection (e.g., see Lindley & Steele, 2018). It is now thought that these aggressive deaminase responses can also cause host genome damage leading to somatic mutations in host cell genes and facilitating cancerous growth on further progression (Lindley, 2013; Lindley & Steele, 2013, Lindley, Humbert et al., 2016, and see chapter "The mutagenic source and power of our own evolution" by Lindley, this volume). It also seems that the components of the Adaptive Immune Response (somatic hypermutation, SHM) are co-opted, if not highjacked, as "Dysregulated Ig -SHM -like responses", now cause off-target mutations across the genome in genes expressed in cells far beyond the lymphoid system.

2.1.2 Acquired immunity

The variable (V) genes of higher vertebrate antibodies, or immunoglobulins (Ig), encode the antigen-binding regions of antibody (and T cell receptor) proteins. They exist as large arrays in the germline DNA. These numerous very similar V sequences (≥50–100 V gene segments) in the germline are normally inactive. However when they are rearranged at the DNA level in a mature somatic B (or T) lymphocyte in the lymphoid and blood circulation they become transcriptionally active. The Vs join with shorter D and J elements forming a transcriptionally active somatic gene encoding rearranged heavy (VDJ) and light (VJ) chains of the HL heterodimers of antibody proteins. There are many possible DNA rearrangement combination in the clonal progenitor cell of a B or T lymphocyte lineage: thus for

antibodies, with say 100 germline Vs, 10 germline Ds, and 5 germline Js in a heavy chain there are $100 \times 10 \times 5$ or 5000 possible heavy chain encoding VDJs with clean joints (no joining errors). For a light chain there would be maybe 100 Vs, 5–10 Js so this will give about 500–1000 VJs (light chains). A viable antigen combining site is formed from a protein heterodimer of one heavy (H) and light (L) chains, essentially by a combinatorial protein association and sorting process in any given B cell. So the potential starting somatic repertoire of antibody specificities is large of the order of 10^6 antibody clonal specificities available for selection by invading antigens early in a response. However such V[D]J genes are also stimulated into somatic hypermutation (SHM), particularly in B lymphocytes (but see Steele & Lindley, 2020).

It is in this "somatic" configuration that V[D]J genes hypermutate following antigenic stimulation. This is a typical "Darwinian" process of rapid mutation, proliferation of antigen-selected B cell survivors with large cellular apoptotic death factors (in so called "Germinal Centres" in peripheral lymphoid organs, such as spleen, lymph nodes).

Thus many mutated B cells are destined to die (>90%) in Germinal Centres. The successful antigen-selected mutants, bearing an antigen-specific receptor on their surface membrane survive to become affinity-improved, clonally expanded, memory B lymphocytes (clonal selection). The daughter cells then enter the vascular circulation and seed other lymphoid organs. All the extant in vivo molecular and cellular evidence indicates the mechanism of Ig somatic hypermutation (SHM) is driven by antigenic stimulation via an AID (APOBEC) and ADAR deaminase-coupled target site reverse transcription process (TSRT), as listed in Table 1.

2.1.3 Germline V repertoires

The origin, maintenance and further diversification of these mammalian germline V arrays, for both immunoglobulins (Ig, the antibodies made by B lymphocytes) and the receptors on T cells (TCRs) which recognize and kill viral/pathogen infected host target cells is a major unsolved problem in immunology and genetics. It now appears that these germ line V gene arrays evolve via a reverse transcriptase coupled soma-to-germline feedback process (Steele & Lindley, 2018, 2020). This we predict can be detected by the active real-time transgenerational penetration of the Weismann Barrier in extended families (Steele & Lloyd, 2015). Thus, all the elements of the deaminase-mediated mutation process and TSRT via Y family DNA polymerases appear involved at some level. The final genetic insertion steps into

the germline DNA would, by necessity, need to be via a targeted homologous recombination process (HR). This step is discussed in the cited references (Table 1, and in Steele, Gorczynski, et al., 2019) and particularly in Steele & Lloyd, 2015).

2.2 Human genome

The origin of the numerous (millions) single nucleotide variations (polymorphisms or SNPs) between the germlines of different human individuals is a major issue in biology, now revealed in this age of rapid and cheap whole genome next generation sequencing. Many of the SNPs in protein-coding regions are functionally neutral, but many are functionally subtle and benign, some are overtly beneficial (and termed "positively Darwinian selected"). These germline variants include those causing human genetic diseases viz. origin of single nucleotide polymorphisms (SNPs) curated in the Online Mendelian Inheritance in Man db (OMIM) and the NCBI dbSNP human genome database (National Center for Biotechnology Information, Bethesda, Maryland, USA). When critically analyzed a vast portion of these SNPs can be accounted for by deamination events at the major known cytosine (AID, APOBEC3G, APOBEC3B) and adenosine (ADAR) deamination motifs (Lindley & Hall, 2018). The important implication is either that AID/APOBEC and ADAR deaminases act in a profligate manner, always active in the transcribed genes of human germline cells, or that these single nucleotide variants originate first in somatic cells and are selected somatically for functional integration into the organism's physiology: that is, AID/APOBEC C-to-U and ADAR A-to-I (G) deaminases are active on expressed protein-coding genes in somatic cells and the successful mutant sequences are then transferred to the germline. Elements of other molecular processes listed appear also to be involved since a RNA-to-DNA reverse transcription step would need to occur for many of the A-site ADAR deamination events (viz. Y family polymerases Pol-h, Pol-k, reverse transcription also (TSRT), and homologous recombination HR).

2.3 Vertebrate immune and endocrine systems

2.3.1 Inheritance acquired tolerance, immunity and behavior

Experiments have demonstrated the inheritance of acquired neonatal tolerance to foreign histocompatibility antigens in mice. Deep neonatal induced tolerance of immune reactivity at the level of cytotoxic T lymphocytes

(CTL) could be induced in neonatal male mice which on mating to females of the same inbred stain, passed on their specific immune tolerance to first and second generation progeny (appearing in the second generation without exposure to the foreign histocompatibility (H-2) antigens used to set up specific tolerance in the original father (Gorczynski & Steele, 1980, 1981). In later experiments the specific H-2 tolerance in progeny generations correlated with specific delayed skin graft rejection (Gorczynski, Kennedy, MacRae, & Ciampi, 1983). Later experiments showed positive paternal transmission was demonstrated in experiments in inbred mice to foreign (rat) erythrocytes, using both repeated high dose neonatal male tolerance (Steele, Gorczynski, & Pollard, 1984) or single shot immunity to the erythrocytes in adult males prior to breeding to normal females (Steele, 1984). These complex transgenerational effects almost certainly involve both genetic and epigenetic regulation resulting in hard genetic inheritance dimensions (as discussed in Steele, Gorczynski, et al., 2019, fig. 2 in that paper).

Acquired inheritance phenomena associated with what is called the "Sire Effect" have been reviewed (Lindley, 2010 pp. 22–29) and the phenomenon was first reported by Gorczynski et al. (1983) when they tested the normal inbred female mice who had raised offspring to male mice of the same inbred strain made neonatally tolerant to repeated doses of foreign lymphoid cells expressing specific H-2 histocompatibility antigens as just described (Gorczynski & Steele, 1980, 1981). When these mothers when bred to normal males of the same inbred strain they produced tolerant or hyporesponsive progeny to the *same H-2 antigens* as used in the original neonatal tolerance regime in the original breeding male.

These mothers also passed on the effect when fostering normal pups, identifying causal factors in the colostrum and milk (Gorczynski et al., 1983). This striking result has implications resurrecting the old observations surrounding the non-Mendelian breeding results caused by male sperm and thus phenomena associated with "Telegony" (Watson, Carroll, & Chaykin, 1983). The "Sire Effect" thus opens a Pandora's Box with wide implications for pure-line animal breeding and wider societal implications (Lindley, 2010 pp. 22).

The "Sire Effect "has real-world practical implications (Lindley, 2010 pp. 26–27). Wild rabbits in rural Australia were in plague proportions in the 1940s and 1950s causing great damage to agriculture, particularly the sheep and cattle industries. To control these wild rabbit populations the Commonwealth Scientific and Industrial Research Organization (CSIRO) released rabbits infected with lethal *Myxomatosis* virus. The virus

was very effective initially in controlling wild rabbit numbers. But the speed with which immunological resistance developed caused further investigations. At first sight it seemed much faster than simple "Darwinian" recovery of a resistant residual population after such a large kill (≥90%). Indeed careful follow up controlled breeding experimental work by Bill Sobey and Dorothy Connolly discovered a significant factor in the rapid spread of resistance: bucks which had recovered from *Myxomatosis* virus when mated to a doe who had not previously been exposed to *Myxomatosis* virus produced litters that were resistant to the lethal effects of the virus- a clear paternal transmission or "Sire Effect" as described by Gorczynski et al. (1983). Thus when a non-immune buck was mated with a doe that had previously been mated to an immune buck a significant number of progeny were born with immunity to *Myxomatosis* virus. Sobey and Conolly concluded that an unknown factor transmitted via the semen of the *Myxomatosis* virus recovered bucks to the normal females which could be further transferred in other matings to normal non-exposed males.

The molecular-cellular mechanisms of the *Myxomatosis* virus sire effect in rabbits, as well as the H-2 antigen-specific maternal influence in the mother's milk acquired by the mother from the original neonatally tolerant male have not been analyzed. Obvious candidates for study can be drawn from an array of epigenetic and genetic transmission effects discussed in Steele, Gorczynski, et al. (2019), fig. 2. They could be related to the small regulatory RNA-mediated spermatozoa effects described by Rassoulzadegan and colleagues (Kiani et al., 2013; Liebers, Rassoulzadegan, & Lyko, 2014; Rassoulzadegan et al., 2006) and other foreign RNA and DNA in semen and associated with spermatozoa reported by Spadafora (Spadafora, 1998, 2008, 2018).

2.3.2 Inheritance acquired instincts

How do instincts arise in evolution? Logic implies an ultimate adaptive Lamarckian cause in ancestors. Strong survival instincts in parents based on prior learnt fear responses must have arisen in our ancestors not by random chance events that were specifically selected, but in a Lamarckian manner, which were then passed on to their progeny *en masse* providing a survival value to the small familial and interbreeding groups of mammals in the wild. Dias and Ressler (2014) showed that parental mice subjected to Pavlovian odor fear conditioning before conception produced offspring with specific behavioral sensitivity to the specific chemical odor used to condition the parents. Unrelated chemical odors did not trigger a conditioned fear response, and these specific acquired transgenerational effects are indeed

inherited via parental gametes. It appears both direct genomic and indirect epigenetic odorant receptor gene targeting appear to act together ("epigenetic-genetic" coupling) to establish what we now recognize as specific instinctual responses involving odorant receptor genes and behavior.

2.3.3 Dutch famine

This well-known consequences of starvation in Holland at the end of World War II are a well documented human epigenetic transgenerational phenomenon, on scale. These extreme starvation episodes underscore the long terms epigenetic inherited effects (Painter et al., 2008). We would also predict that longer term hard inheritance genetic effects are buried in this human data (Steele, Gorczynski, et al., 2019).

2.3.4 Inheritance acquired autoimmunity

A hundred years ago Guyer and Smith at the University of Wisconsin published their classic experiments showing hereditary transmission via male rabbits of antibody induced eye defects though the mother down nine breeding generations viz. maternal induced autoimmune eye defects. A summary of these experimental results by Guyer and Smith are republished in detail with a commentary in Steele (2016b). We are of the view that in the fullness of time these experiments will join the garden pea experiments of Mendel and the plant graft hybrid experiments of Charles Darwin as classics in genetics, particularly acquired inheritance associated with cosmic genetic evolution.

2.4 Mammalian germ cells

2.4.1 Uptake of foreign DNA by spermatozoa and inherited effects in progeny

Corrado Spadafora and colleagues have shown sperm uptake of foreign nucleic acid molecules and transmission of the genetic information to progeny organisms. In some cases they show that a LINE-1-derived reverse transcription step can execute the copying the RNA into DNA. In $\leq$10% of cases the DNA sequences are integrated into the germline genome, while in most cases the sperm-absorbed DNA/RNA exists as extrachromosomal episomes (replicating along with host somatic cells during development and displaying mosaic tissue expression). A role was postulated for exosomes vesicles released into the bloodstream from human tumor xenografts transferring somatic RNA to spermatozoa, implying that there is no physical barrier in spermatozoa to the uptake of DNA or RNA. This work is among the

most precise descriptions of Darwin's "gemmules" in animals published, and is a mode of vesicle transfer which is also utilized in genetic information transfer in plant graft-hybridization, described below (Liu, 2018) and consistent with the current way we now view Lamarckian inheritance. Finally in 2002 Patrick Fogarty reported a striking result of simple intraperitoneal injection of DNA into adult male or female mice. Employing a technique based on P-element transposons and delivering DNA transgenes intravenously in simple vesicles, Fogarty has shown that 50% of progeny from such male mice inherit the gene sequence (Fogarty, 2002). The critical integration event requires a transposase enzyme. This was a clear demonstration of the genetic penetration of the *Weismann Barrier* in mammals in a Lamarckian mode typical of a familiar Horizontal Gene Transfer event.

2.5 Graft-induced heritable changes in plants

2.5.1 Acquired inheritance

Historically graft-induced variations were recorded to occur in ancient China. Charles Darwin however was the first to use the term "graft hybridization". He noted that the formation of breeding hybrids through plant grafting between distinct species or varieties (without the intervention of the sexual organs). Liu (2018) outlines all of these observations that have been confirmed now many times by experts. The results are clear and striking and regularly reproduced by many plant breeders and horticulturists. Indeed, plant hybrid transmission of small regulatory RNAs, mRNAs and other reporter sequences are standard experimental tools in plant molecular genetics and development (Ham & Lucas, 2017). Many such cases of "graft hybrids", were described by Darwin where shoots produced from grafted plants exhibited a combination of characters of both rootstock and scion. It was understandable that he would explain their formation by his theory of Pangenesis involving transmissible and transported "gemmules" in the phloem. Over the past few decades, the existence of graft hybrids has been widely documented, and graft hybridization is considered to be a simple and efficient means of plant breeding. Graft hybridization is now explained by horizontal gene transfer and DNA transformation and the long-distance transport of mRNA and small RNAs considered to be involved in the formation of graft hybrid seeds. We should now add a reverse transcription step to lock in such transported RNA phloem information into the hybrid seed genomes.

2.6 Adaptive evolution in bacteria and microorganisms

2.6.1 Adaptive hypermutation and SOS genetic responses

Developments separate from the above, are less definitive conceptually, involving the penetration of the *Weismann Barrier*, is the work in bacteria and other rapidly multiplying unicellular organisms (e.g., yeast *spp*). In these cases simple Darwinian selection of rare population variants can never be ruled out. However very challenging demonstrations of substrate-induced adaptive evolutionary phenomena in bacteria and yeast have been described (Cairns, Overbaugh, & Miller, 1988; Hall, 1988; Rosenberg, 2001). The data suggest rapid mutator mechanisms in microorganims during the stationary phase (slower replication) which increases the odds of 'selecting' an adaptive mutant. The data have been interpreted as being consistent with a Lamarckian process of adaptive evolutionary genetic change and the authors of the studies suggest a reverse transcriptase-coupled mechanism for the inheritance of acquired characteristics, much like that proposed earlier by Steele and Pollard (1987) for the somatic hypermutation processes summarized in Steele, Gorczynski, et al. (2019) and Table 1.

This work raised the possibility that environmentally induced, non-random mutator processes dependent on a reverse transcriptase step also occur in bacteria and yeast. For bacterial spp. this has been confirmed and many different reverse transcriptase activities have now been described throughout prokaryotes and archaea, reviewed in Steele, Gorczynski, et al. (2019). Indeed Radman (1999) had earlier predicted such error prone polymerase enzymes of evolutionary change (Radman, 1974) as part of the now familiar adaptive "SOS response" in bacteria to a range of environmental stress signals (Tippin et al., 2004). It is intriguing that the Y family DNA Polymerases that figure prominently in the SOS response are all error-prone polymerases and are indeed related by their DNA encoded sequence to the human Y family DNA repair polymerases eta (η), kappa (κ), iota (ι) (Ohmori et al., 2001) all of which have been shown to be efficient reverse transcriptases (Franklin et al., 2004). However none of the other bacterial Y family DNA polymerase members have yet to be examined for their RT activity.

3. Conclusions

We have summarized here some of the new evidence that has accumulated since the 1970s consistent with Lamarckian Acquired Inheritance phenomena from bacteria through to plants and animals. We are of the view

that the "Hypothesis of Lamarck" has now survived some stringent and severe tests earning recognition as a maturing "Theory" of biological evolution. The results of current studies on the molecular mechanisms of these phenomena are variable, and in different stages of advancement. But the mechanisms, and the validity of transgenerational epigenetic-genetic coupled phenomena are, despite our ignorance, much clearer now in many cases than they were 40 years ago. And our discussion and analyses of the relevant extant data in Steele, Gorczynski, et al. (2019) in the context of Cosmic Panspermia, outlined above, clearly needs to be confronted by the scientific mainstream. Lamarckian inheritance of acquired characteristics, which at its core depends on base modified RNA intermediates and reverse transcriptase steps, has successfully run the gauntlet of numerous "Popperian" tests during the past 40 years. We argue then that the effective spread of living systems throughout the Cosmos is both by Lamarckian and Darwinian mechanisms—with the emphasis on Lamarckian evolutionary processes as these provide rapid and "directional" adaptations to new Cosmic niches immediately after the organisms have landed.

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