

Paper 5 of 5

The teem theory of nonMendelian inheritance

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KEYWORDS

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ABSTRACT

Here, the putative belief is challenged that Mendelian inheritance, (first discovered by Gregor Mendel in the 19th century and expanded by Boveri and Sutton, Watson and Crick and others in the 20th century) is the sole mechanism of biological inheritance on this planet. It is argued the DNA molecule contains a second system of hereditary transmission, (the Teemosis Inheritance System) that is complementary to the Mendelian system, but which emerged 3.2 billion years after Mendelian inheritance and which regulates the acquisition and inheritance of teems. It is argued the Teemic Inheritance System is accommodated in non-protein-coding sequences of DNA and regulates the inheritance of emotional information.

Introduction: Genetic inheritance and the central dogma

Throughout the 3.2 billion years of Precambrian evolution, morphology (physical form and structure) and rudimentary innate behaviour (Darwinian reflex instincts) were moderated exclusively by natural selection (NS.) However, in Paper 1, it is argued that while NS is able to configure simple behaviours from random mutations, it is unable to create complex environment-specific innate behaviours because these involve environmental factors, such as the ability to recognise specific predators, prey, food etc. that are external to the genome and to which the mutational process is blind. Rather than relying on the chance allocation of randomly derived mutations to encrypt environmental information into the genome, it is more plausible that the environment has acquired an ‘instructionist’ capacity – to directly translate and encode complex environmental information directly into an organism’s DNA.

So while reflex actions and simple hormonal behaviours are undoubtedly derived from the random assembly of amino acids and proteins precipitated by mutations, in more complex, diverse and fluctuating environments, selective pressures accrue for environment-specific behaviours that require informational flow, (instruction) from the organism’s current environment to its DNA.

This premise is of course at variance with the ‘central dogma’ of biology as formalised by Crick (1958,1970)^{1,2} which asserts that genetic information does not flow from the environment to the genome, but in the opposite direction only - from DNA to RNA to proteins to phenotype. Apart from the enzymic reverse transcriptase activity of retroviruses,³ Mendelian inheritance of physical traits prevents the hereditary transmission of environmentally acquired characters under normal conditions. This ensures environmentally induced modifications in somatic cells (either morphological or behavioural) do not affect (or ‘instruct’) germ cells, thus preventing the inheritance of deleterious phenotypes such as disease, injuries and ageing.^{4,5,6,7}

These conflicting paradigms create a paradoxical situation. While behavioural evolution requires the acquisition and inheritance of environmental information to promulgate complex, environment-specific adaptive behaviours, paradoxically, morphological evolution must prevent the inheritance of acquired traits that would deleteriously contaminate the germ-line. This paradox generated a pervasive evolutionary dichotomy within the Precambrian biosphere.

Throughout most of the Precambrian, we may assume the central dogma reigned supreme, preventing the establishment of an environment-genome feedback in relation to behavioural evolution. However, without environment-genome instruction, I suggest innate behaviour was restricted to rudimentary gene-based reflex behaviours heritable as randomly occurring mutational alleles.

Eventually however, implacable selective pressures for adaptive instincts resulted in the emergence of a second, separate hereditary system within the DNA molecule. While the original Mendelian system continued to regulate the hereditary transmission of morphological information in accordance with the central dogma, I posit a second nonMendelian system emerged to regulate the inheritance of environmentally acquired behavioural information.

The Teemosis Inheritance System

Elsewhere in this issue - Paper 1 such an environment-genome evolutionary process (called teemosis,) is described which emerged emerged 543 mya. By using emotions configured into a linguistic code as the medium of inheritance, teemosis circumvented the central dogma and established a viable alternative evolutionary process to exclusively regulate the acquisition and inheritance of environmental information.

Paradoxically, although teemosis does not moderate the inheritance of physical traits, in Paper 4, it is conjectured that teemosis indirectly contributes to the evolution of morphology in ten different ways.

The evolution of teemosis was achieved by the genetic separation of Mendelian inheritance elements (protein-coding exon genes) from teemic inheritance elements within the DNA molecule. This hypothesis generates a number of core predictions in relation to teemic genetics. Firstly, because nucleic acids are the only means by which inheritance is moderated on this planet, it asserts that teemic inheritance was achieved via a fundamental molecular reorganisation, compartmentalisation and complexification of the DNA molecule. Secondly, the reorganisation to accommodate teemic inheritance must have occurred prior to the evolutionary origins and radiation of teemosis 543 mya.⁸

Collectively, these conjectures generate a core hypothesis of this paper: that the DNA molecule contains two distinct, autonomous but paradoxically synergistic systems of hereditary transmission: what is called the 'Mendelian Inheritance System' (MIS) which exclusively uses coding exon genes to moderate the inheritance of physical traits, (plus a small number of simple gene-based behaviours,) and the Teemosis Inheritance System (TIS) which uses non-protein-coding nucleotide sequences to regulate the inheritance of emotional, behavioural and personality datasets, including complex instincts.

The biological imperative to maintain a genetic separation between the inheritance of physical traits and emotional-behavioural teems appears so consistent it may be used to predict, identify and explain specific genetic TIS elements and functions in DNA, and in so doing, provide empirical support for the core hypotheses. By identifying functional domains and methodology of TIS at the genomic level, it is hoped to extend the unified teem theory of evolution, emotions, perception, motivation, instinct, personality, natural history and the fossil record, (including the unique stratigraphy of the Cambrian explosion,) detailed in this issue to include a new holistic theory of teemic molecular genetics.

Teem theory's assertion that emotional traumas are occasionally encrypted into ncDNA and inherited as emotional information generates twelve predictions that may be used to test the hypothesis that a second nonMendelian system of inheritance exists inside the DNA molecule that uses non-protein-coding nucleotides to encode emotions

and behaviours. In exploring these predictions, we may examine (albeit theoretically) the molecular and genetic mechanisms of the TIS.

1 Teemic DNA does not code for proteins

The first prediction is derived from the genetic incompatibility between morphological and behavioural inheritance, and the need to maintain separation to avoid deleterious consequences of Lamarckian inheritance. That is to say, while teemic information must be inherited vis-a-vis DNA, it must be prevented from coding for amino acids, polypeptides and proteins from which physical cells and traits are derived. This predicts that teemic inheritance only uses DNA material that is heritable, but is not translated into protein products. Does such paradoxical genetic material exist?

The discovery in the late sixties that eukaryotic DNA contained sequences that do not code for protein manufacture,⁹ was followed in 1977 by the independent discovery by Sharp¹⁰ and Roberts¹¹ that eukaryotic genes are interspersed with ‘introns’ - noncoding nucleotides that interrupt protein coding sequences. Eukaryotic introns are transcribed into messenger RNA (mRNA), but are excised from the primary transcript by ribosomes. The ends of the remaining exon sequences are then spliced together by a splicosome and the contiguous exons (minus the introns) are transported from the nucleus to the cytoplasm where protein synthesis occurs. Because introns are not translated into protein products, they do not code for polypeptides or physical traits.^{12,13}

Since then, several other types of non-protein-coding DNA (ncDNA) have been identified that separate and punctuate coding exon genes, (intergenic and introns) including Satellites, Minisatellites, Microsatellites, SINEs, LINEs, Interspersed Elements, 5' and 3' untranslated regions, Pseudogenes, (including unprocessed pseudogenes and processed pseudogenes), Heterogeneous Nuclear RNA (hnRNA), Alu elements, tandem repeats and so on.

Because noncoding introns and intergenic DNA are transcribed into mRNA but not translated into proteins, they were initially assumed to have no evolutionary function and were accordingly termed ‘junk DNA’,¹⁴ ‘selfish DNA’,^{15,16} and ‘ignorant

DNA.’¹⁷ Significantly however, because ncDNA is spliced from the primary RNA transcript prior to translation, (so does not contravene the central dogma,) it is theoretically suitable (and available) to encrypt non-physical coded information from one generation to the next as the transmission medium of TIS. As a core requirement of TIS is to prevent the translation of acquired environmental information into protein products, it argues that noncoding introns and other intergenic ‘junk’ DNA are the principal mediums of teemic inheritance. This is the second core hypothesis of this paper.

2 The evolution of teem compatible DNA

Teem theory predicts that prior to the emergence of teemosis, the molecular structure of DNA supported only one system of inheritance- the Mendelian Inheritance System. Mendelian inheritance is functionally moderated by protein coding genes which are translated via an RNA transcription intermediary into amino acids, polypeptides, proteins and physical cells. For teemosis to emerge as a viable second evolutionary process regulating the hereditary transmission of environmentally acquired information, (which is biologically incompatible with the Mendelian system,) it required the DNA molecule to undergo a significant functional reorganisation to accommodate teemic inheritance elements and maintain their separation from incompatible morphological inheritance elements. In effect, this would have necessitated the gradualistic emergence of new inheritable but noncoding genetic nucleotides to carry the teemic code (Emlan) and separate it from the protein coding genetic material used by the pre-existing Mendelian system. Furthermore, the hypothesis predicts this genomic reorganisation of DNA must have occurred prior to the emergence of teemosis 543 mya.

Is there any evidence of a major functional reorganisation of DNA prior to the basal Cambrian that included the division of the DNA molecule to facilitate two separated noncompatible mediums of inheritance? I suggest there is. Indeed, modern genetics is largely informed by the existence of two separate and distinct forms of DNA - Prokaryotic DNA and Eukaryotic DNA.

Prokaryotic DNA emerged some 3.8 bya, lacks a membrane-bound nucleus and is contained in a single (usually circular) chromosome. It is comprised almost totally of protein coding genes interspersed by short translation stop and start codons. It rarely contains introns. Prokaryotic organisms demonstrate simple genotypes, reproduce asexually and lack a central nervous system and complex perceptual organs. As such, prokaryotes may be assigned as a Darwinian kingdom whose evolution is moderated exclusively by NS. Prokaryotic DNA and prokaryotic phyla were ubiquitous throughout the Precambrian.

Between 2.1 - 1.6 bya, a more advanced form of DNA - 'Eukaryotic DNA' emerged from progenitor prokaryotic DNA.^{18, 19, 20} Eukaryotic DNA contains a nucleated cell and multiple linear chromosomes. Unlike the ancestral prokaryotic DNA, eukaryotic DNA features many orders of magnitude more noncoding material, which is thought to have intrinsically accumulated in eukaryotic genomes through the activity of molecular parasites and genomic slippage.^{21, 22, 23} A significant feature of eukaryotic DNA is the presence of extensive regions of non-protein-coding material. For instance, 98.5% of the human genome is comprised of ncDNA.²⁴

Although noncoding material may have originated as an exaptive by-product of nucleated eukaryotic DNA, it coincidentally provided the raw genetic material that NS could adaptively utilise in a second evolutionary process. To borrow an analogy from media reproduction, eukaryotic DNA provided the 'blank cassette tape' that teemosis would use to inscribe Emlanic code. Eukaryotic DNA contributed to teemosis by facilitating cellular communication and multicellularity which presaged the metazoans arrayed with a CNS and sensory receptors.

3 Only eukaryotes are teemic and display complex behaviour

A corollary of this hypothesis is that only eukaryotes contain eukaryotic DNA, (the kind of DNA used in teemosis,) so only eukaryotes may encode teems. As teems are the only means by which complex innate behaviour and emotions are created and genetically archived, it predicts that eukaryotes but not prokaryotes demonstrate complex innate behaviour and emotions.

This prediction is empirically supported by the well documented behavioural distinction between Monera (bacteria) prokaryotes and the eukaryotic metazoans. Although bacterial and cyanobacterial prokaryotes may demonstrate rudimentary motor behaviour, it is inevitably in response to electro-chemical stimuli. For example, certain bacteria are attracted to light, others to salts, while flagellated bacteria frequently demonstrate chemotactic motility towards chemical attractants and away from chemical irritants. All these behaviours appear to be gene-based Darwinian instincts. By comparison, teemic eukaryotes (additionally possessing a central nervous system, sensory modalities and other teemic adaptations) demonstrate complex and flexible environment specific, instinctive behaviour and affective responses.

Thus, eukaryotic DNA serves as a convenient demarcation between teemic and nonteemic kingdoms. The inability of prokaryotic DNA to support teemosis explains why complex innate behaviour did not emerge throughout the extended Precambrian reign of the prokaryotes.

4 Higher teemic species contain more ncDNA than lower species

If teemosis uses ncDNA to encode complex innate behaviour, personality and emotions in a phylogenetically diverse range of eukaryotic metazoans, (from flatworms to humans,) then selective pressures will gradualistically ensure that the genomes of higher teemic species will contain proportionally more ncDNA than lower teemic species. That is to say, if ncDNA is subject to positive selection in teemic species, lower teemic species such as the flatworm, that demonstrate rudimentary emotional and behavioural repertoires will require less ncDNA than higher teemic species such as primates, while teemic intermediate species, such as the mouse and dog, will contain an intermediate range of ncDNA.

This prediction, it should be noted, is at variance with current biological theory. As ncDNA does not spell out (code for) proteins, it has long been considered an evolutionary parasite with no function in relation to biotic complexity. Therefore, orthodox theory would intuitively predict that ncDNA does not correlate to behavioural or emotional complexity. The only assumed correlation to biological complexity has

been the number of protein coding (exon) genes²⁵ - ie. the more genes, the more complex an organism will be.

Both these suppositions – (that the number of protein-coding genes is correlated to biological complexity, and that ncDNA is genomic detritus and does not scale with complexity,) have recently been challenged. Despite the considerable differences in biological complexity between humans, pufferfish and mice, all three species contain a similar number of protein-coding genes,^{26, 27, 28, 29} challenging the correlation between complexity and number of genes. And in relation to ncDNA functionality, an expanding corpus of genomic sequencing data has revealed the genomes of biologically complex species do indeed contain proportionally more ncDNA than less complex species – precisely as predicted by team theory. Comparisons between the complement of transposable elements in the euchromatic portion of the human, fly and worm genomes reveals the human genome contains a much higher density of transposable elements than the other genomes.³⁰ LINE and SINE elements represent 75% of interspersed repeats in the human genome but only 5-25% in the other genomes.³¹ Indeed, while coding genes demonstrate a remarkable homology between species and even taxa, with respect to their noncoding mobile element content, genomes display a marked dissimilarity. The pufferfish genome for example contains less than 3% mobile element repeats,³² the fruit fly ~3%,³³ and the worm ~10%.³⁴ However, in the more developmentally complex mammals, (such as the mouse and humans, the mobile elements content is significantly higher, in excess of 37% in the mouse³⁵ and over 45% of the human genome.³⁶

Similarly, the density of spliceosomal introns, which are only found in eukaryotic nuclear genomes, increases proportionally with developmental complexity. Simple microbial eukaryotes such as *Dictyostelium* and *Plasmodium* have an estimated one intron per kb of coding sequence rising to 3-4 per kb in fungi and 6-7 per kb in vertebrates.³⁷

A two and half year study by Taft and Mattick 2004 (in press) that analysed the ratio of ncDNA to total genomic DNA for 85 sequenced species found ‘that the amount of noncoding DNA per genome is a more valid measure of the complexity of an

organism than the number of protein-coding genes,”³⁸ a finding that supports a functional ncDNA paradigm. Indeed, one of the most unexpected findings of the Human Genome Consortium was that the human diploid genome was comprised of 98.5% ncDNA, the highest of any species yet sequenced.³⁹ While these findings appear paradoxical, they are consistent with teem theory which classifies Hominidae as the most ‘teemic’ of all families based on observed emotional and behavioural complexity.

5 ncDNA is mobile within the genome

Teem theory asserts that emotional information teemically encrypted into the genome of an individual is inherited and ‘deciphered’ by subsequent generations. That is to say, information is first ‘written’ to the genome, then ‘read’ from it by progeny, processes that infer a linguistic capacity. If so, how does teemosis encrypt transduced emotional information, derived from sensory organs and representing a diverse range of environmental information, into linguistically meaningful arrays of ncDNA? It is suggested the principal means by which teemosis *writes* information into ‘blank’ ncDNA is by shuffling and arranging ncDNA nucleotides into linguistically meaningful chemical patterns, similar to the way that human language arranges letters and words into linguistically meaningful literary sentences.

According to this model, emotions are genetically ‘written’ as precise sequences of linguistically arrayed ncDNA nucleotides. To encode a teem then, requires ncDNA nucleotides to be moved, shuffled, duplicated, deleted and organised into linguistically meaningful new arrays.

This conjecture predicts that ncDNA is not immobile within the genome. Rather, it asserts that ncDNA is genomically fluid and mobile, with teemic components able to be duplicated, deleted, sequentially reorganised and transposed within and between genes and chromosomes to achieve new Emlanic encryptions. Indeed, I suggest the linguistic imperative to be as mobile as the slugs of type used in the printing industry is a seminal feature of teemic ncDNA, and one which has been positively selected for since the basal Cambrian.

‘Mobile ncDNA’ could theoretically perform two evolutionary functions in relation to teemosis. Firstly, it would provide a means by which core ancestral emotions could be homologously duplicated, recombined and organised into new ‘teemic recipes’ describing more complex emotions and emotional representations. This would enable not only emotions such as *resentment* and *pity* to be encrypted from core ncDNA sequences, but complex Emlanic representations such as *thunder*, *water*, *ripeness*, *dance*, *drought* and other transduced elements, circumstances and objects of the external environment. Secondly, ncDNA mobility would allow teems to be positioned within (and contiguous to) coding exon genes in order to exert a regulatory function in respect of those genes. In other words, teems that control hormones, neuropeptides and other physical systems may need to be transposed into regulatory regions of coding genes to effectively control teemic aspects of gene function.

Is there any evidence that mobile ncDNA exists – that ncDNA is duplicated, deleted and transposed between genes and chromosomes? There is. Notwithstanding the prevailing view throughout much of the twentieth century that DNA nucleotides function from a single stable, immobile position on a chromosome, Barbara McClintock discovered *transposable elements* - noncoding ‘jumping genes’ in the genomes of maize over fifty years ago.⁴⁰ This finding was so at variance with prevailing orthodoxy, it took 30 years for the significance of her discovery to be widely appreciated.⁴¹

Transposable elements (TEs) are mobile DNA sequences that are distinguished by their non-protein-coding properties and their ability to move and replicate within genomes. They are widely distributed in bacteria, plants and animals. On the basis of their modes of transposition, TEs are usually divided into four types - three that transpose through RNA intermediates and one that transposes directly as DNA.⁴² Class I elements are retroelements and include long terminal repeat retrotransposons, SINEs (including Alu elements,) and LINEs. Class II elements transpose directly from DNA to DNA and include transposons (eg. the *P* element in *Drosophila*, the *mariner* element in humans and the *Tc1* element in worms, *Caenorhabditis elegans*,⁴³) The number and variety of TEs in eukaryotic genomes is indicated by the 96 separate families of transposable elements found in the *Drosophila melanogaster* genome (Release 3 sequence)⁴⁴ by Kaminker et al (2002.)⁴⁵

Circumstantial support for the hypothesis that transposable elements contribute to Emlanic encryption may be inferred from the non-random distribution of TEs, as non-random distribution is widely considered to be indicative of evolutionary function. If TEs were ‘junk,’ they would tend to accumulate randomly along the genome, whereas each class of TE occupies a distinct area within heterochromatin.^{46, 47} SINE elements, for example, preferentially accumulate in R-banding regions whereas LINE elements occur preferentially in sex chromosomes and G-banding regions.⁴⁸

Teem theory does not assert that TEs are exclusive to teemosis. Rather it is more likely that TEs first emerged in preteemic phyla as a Darwinian means of responding to environmental stress and rapid change, (as in the case of maize,) and was simply adopted by teemic species via NS.

In conclusion, TEs are mobile, noncoding elements that have accumulated extensively in the genomes of eukaryotic metazoans (teemic taxa.) They are highly conserved in all teemic species and nonrandomly distributed. These features appear consistent with a theoretical teemic functionality (genomic encryption,) even if the details of this teemic function are little understood.

6 ncDNA is responsive to environmental stress

The wide distribution of transposable elements in the genomes of eukaryotic metazoans begs the next question; what initiates TEs to replicate, transpose, delete, reorganise and reassemble into linguistic patterns of Emlanic code to encrypt a new teem?

According to teem theory, this process involves binding and receptor molecules initiated by transcriptional activators that are elicited by the ‘teemic trauma’ – an environmental event or circumstance in the life of the individual organism that (when transduced,) generates a high salience emotional response at both the cellular and physiological levels. To reiterate briefly, teem theory holds that powerful emotion (either positive or negative) disrupts genetic homeostasis, triggers the transcriptional activators and guides the encryption of ncDNA into teems. Sometimes these teems end

up in the regulatory areas of genes and if they exert an adaptive regulatory function over the expression of the gene (in respect of the new teem), the new location is selected for.

Accordingly, it is speculated that the teemic trauma functions as an ‘environmental stressor’ which both overwhelms genomic homeostasis, (rendering the ncDNA amenable to modification,) then directs the encryption activity of TEs. The encryption of the TE into a teemic sequence (what Darwinist may call a ‘directed mutation’) will continue as long as the salience of the emotions remains above the ‘teemic threshold.’ Once the salience of the emotions subsides below the threshold, encryption ceases, the TEs stabilise and cellular homeostasis returns. Or, to put it in the context of existing terminology, the directed mutation terminates.

If the encryption of TEs occurs in or is transcribed to germ-line cells, the newly encrypted teem becomes a permanent (inheritable) genetic legacy of one specific, real-time environmental experience. If the encryption occurs in somatic cells, no teem is encoded as the transient TE modification expires with the death of the individual.

This hypothesis generates two testable predictions: firstly, the duplication, deletion, rearrangement and transposition of TEs in teemic species is precipitated by the organismal experience of high salience transduced environmental stress (either positive or negative) – the teemic trauma. Secondly, this trauma, or stress induced TE activity is inheritable.

Before these predictions are tested it is appropriate to note that aligned against them is the putative belief that the genome is resistant to all but the most pernicious environmental stressors. With the exception of ionising and ultraviolet radiation and a number of powerful chemical mutagens, replication appears impervious to environment stressors. Three billion years of positive selection has ensured the exceptional replication fidelity of coding genes, estimated to be less than 10^{-9} replication errors per nucleotide.⁴⁹

Can these two seemingly opposite views be reconciled? I believe so. On closer analysis, it is evident that only the coding exon genes of the MIS display resistance to

environmental stressors. The immutability does not extend to ncDNA utilised by the TIS. Indeed, this differential response to environmental stressors is fundamental to the two distinct systems of inheritance; Mendelian inheritance demands reproductive fidelity and this can only be achieved if coding genes are immune to environmental (Lamarckian) modification under normal conditions. By contrast, teemic inheritance requires environmental information, and the writer is of the opinion that environmental stress is the only functional form of that information.

Once coding genes are excised from the prediction, it is not difficult to find evidence that TEs spontaneously duplicate, delete, transpose and recombine in response to environmental stress, precisely as predicted by teem theory. Since McClintock first demonstrated that transposable elements help the genome to cope with environmental challenges, (stress), sequencing data (particularly over the last decade) has increasingly established that stress-induced mutability is a fundamental characteristic of TEs (including SINEs, LINEs and Alu elements) in eukaryotic metazoans.^{50, 51, 52, 53} In mouse, rabbit and silkworm cells, for example, cell stressors such as heat shock, adeno-virus infection and exposure to genotoxic cycloheximide induce exceptional SINE transcription,^{54, 55, 56, 57, 58}

Significantly the increase in SINE RNA was also observed in live silkworms and mice subjected to physiological stress. To determine if the increase in transposable activity in cells also applied in vivo, Li et al⁵⁹ subjected 18 live anaesthetized mice to sublethal hyperthermic shock by partially immersing the mice in hot water for 25 minutes, and found amounts of noncoding B1 and B2 SINEs taken from liver, spleen, kidney and testis transiently increased by as much as 40-fold. The authors inferred from these observations that SINEs serve an evolutionary function in relation to stress. From the perspective of teem theory however, the anaesthetic used for humane purposes possibly muted the trauma emotions and moderated the results.

Hagen et al⁶⁰ introduced a human Alu element into mouse cells and found that Alu retrotransposition was induced in mouse cells by exposure to genotoxic stress in the form of the topoisomerase II inhibitor etoposide. Heat shock, viral infection and exposure to toxic compounds induce Pol III-directed transcription of Alu repeat

sequences in cultured HeLa and 293 cells.^{61, 62, 63, 64} The finding, by Li and Schmid (2001) that each of six Alu loci they examined demonstrated a unique pattern of expression in response to stress further suggests that TEs are able to differentiate different kinds of stress, which is imperative to any linguistic function.

The conservation of the SINE response to environmental stress in a number of phylogenetically disparate metazoans has been interpreted by Schmid (1998) as indicating a little understood evolutionary function related to the genome's response to stress.⁶⁵ This conservation challenges the putative belief that noncoding SINEs are non-functional. From the standpoint of teem theory, the ability of environmental stressors (transduced into high salience emotions) to alter the configuration of various transposable elements in teemic phyla is consistent with two related teemic functions: to encode new teems and activate existing ones.

The second prediction asserts that stress induced duplications, deletions and transpositions of noncoding TEs may be inheritable to the next generation. This may occur in two ways, either the teemic directed mutation occurs directly in germline ncDNA, or it occurs in somatic cells and is transferred to the germline *in vivo*. While this molecular dynamic remains little understood, some research on *Drosophila* indicates that stress induced somatic induction in TEs in females has effects on subsequent generations, transferred, it is presumed, through the cytoplasm of the eggs.⁶⁶ This maternally inherited effect has been reported in a number of Class II TEs; including mariner elements,⁶⁷ hobo transposons^{68, 69, 70} and Tam (1 and 2) elements,⁷¹ which has been interpreted by Capy et al (2000) as examples of non-Mendelian inheritance.⁷² In their review of the impact of stress on TEs, Capy et al suggest “a relationship may exist between the somatic activity of an element in a given generation and its germ-line activity in the following generation.”⁷³

Perhaps the clearest evidence of germline transmission of ncDNA nucleotides (including TEs) in animals comes from the thousands of individual mutational variations (polymorphisms) of ncDNA that each teemic organism accumulates in each new generation. That is to say, while the human genome acquires an average of 4.2 mutations in coding genes per generation,⁷⁴ it additionally acquires in excess of 1.42

million single nucleotide polymorphisms (SNPs) in its ncDNA, and these are all inherited through the germline. This equates to an average heterozygosity rate of 1 in 1,300 bp.⁷⁵ Similarly, 50% of the youngest human LINE1 element (the L1Hs family),⁷⁶ which includes two subsets (Ta and pre-Ta) are highly polymorphic^{77, 78} suggesting that these descend from the zygote. Indeed, they are so polymorphic, that along with similarly polymorphic Alus, they provide useful markers for tracing population history, human migrations and parentage.⁷⁹

Teem theory does not assert that high salience emotional stress will always precipitate TE activity either in somatic or germline cells. Clearly, emotional response and stress are highly variable between individuals – the emotions that precipitate stress and its genetic concomitants in one individual will not necessarily precipitate the same molecular response in another individual. This is illustrated by several studies with *Drosophila* that demonstrate mobilisation of TEs in some individuals following heat shock,^{80, 81} while other studies found no effect.^{82, 83}

7 ncDNA contains encrypted emotional information

At the hub of teem theory lies the premise that not only does environmental stress periodically precipitate emotion directed modifications in TEs and other ncDNAs, but that these genomic duplications, deletions, reconfigurations and transpositions manifest as linguistically coherent, inheritable information. That is to say, while TE mutational activity is widely regarded to be random, TE activity in response to high salience emotion is non-random and ‘directed,’ and generates linguistically meaningful Emlanic ‘sentences’ that correspond to the high salience emotions that precipitated the directed mutation.

The prediction that ncDNA represents a second genetic language containing linguistically arrayed information sourced from the organism’s current environment is patently at variance with the notion of ‘junk DNA,’ the random nature of mutations, and the prevailing orthodoxy that only one genetic language exists- that based on the Mendelian four-letter nucleotide alphabet (adenine, guanine, cytosine and thymine,) that codes for proteins and amino acid assembly.

The suggestion of a parallel genetic language utilising ncDNA is, however, not without precedent.

Although geneticists have been occupied since the 1950s with decoding the exon language utilised by MIS, by the 1980s, statistical analysis had begun to discern structural differences between coding and noncoding sequences that were indicative of linguistic distinction.^{84, 85, 86} The suggestion that ncDNA may contain a hidden natural language was first postulated by Mantegna et al (1994) from computer based statistical analysis of base pair sequences. Applying Zipf's law⁸⁷ (normally used to analysis human language by ranking word frequencies,) Mantegna argued that "noncoding regions are more similar to natural languages than the coding regions... supporting the possibility that noncoding regions of DNA may carry biological information."⁸⁸ Although these conclusions have been challenged,^{89, 90, 91, 92} a subsequent study, by Stanley et al, (1999) reported a fractal correlation between widely separated noncoding base pairs.⁹³ Significantly, these long-range correlations do not occur in coding sequences.⁹⁴ When combined with the finding that the noncoding sequences appear more complex in more highly evolved species than in less evolved ones,⁹⁵ it suggests ncDNA may incorporate a little understood linguistic function. While Stanley (1999)⁹⁶ argues that a resolution of this debate is hampered by the complexity of DNA sequences and the inadequacy of current analytical methodologies, I additionally suggest that without an understanding of the enigmatic role that ncDNA plays in teemosis, no resolution is possible.

While teem theory predicts the existence of a second genetic code, deciphering the lexicon, grammar and syntax of this ephemeral biological language is far more problematical. For a start, the sheer quantity of ncDNA in the eukaryotic genome presents a significant impediment to analysis - in the human genome for instance, there is 65 times more ncDNA than coding DNA. Also, the Emlanic and Mendelian codes use the same DNA nucleotides and are opportunistically interconnected and synchronitous which makes it more difficult to extrapolate Emlanic linguistic elements from Mendelian elements. Finally, the fact that Emlan additionally regulates the expression of some coding genes blurs the linguistic distinction between Emlanic and Mendelian codes. The writer is therefore of the opinion that deciphering Emlan remains a formidable challenge and will take many years to decipher.

For this reason, I have not attempted here to speculate on precisely which ncDNA elements encrypt teems or in what particular configurations. Besides, the current inventory of noncoding elements, (satellites, microsatellites, minisatellites, SINEs, LINEs, Alus etc) are based on Mendelian genetics and may not correspond to teemic or emlanic structures distinctions. Elucidation of Emlan may not be possible using existing classifications and may require a new classification of ncDNA based on teemic function.

8 ncDNA codes for complex innate behaviour

The primary evolutionary function of TIS is the inheritance of adaptive behaviours, so perhaps the most fundamental prediction of TIS theory is that ncDNA codes for complex innate behaviour. If the teem theory of genetics is to be substantiated, it must demonstrate that complex innate behaviour and emotions are genetically archived in sequences of ncDNA and not in coding exon genes as previously thought.

Testing this hypothesis by demonstrating that a specific ncDNA teemic sequence codes for a complex innate behaviour or emotion is however, problematic. Because the prevailing Darwinian-Mendelian paradigm associates instincts and other innate behaviours exclusively with coding exon genes, no research specifically designed to examine possible ncDNA-instinct links has, to my knowledge, been conducted. However, it is possible that a teem may be isolated by comparing the ncDNA of two closely related (sibling) species that display different (species-specific) innate behaviour. If these behaviours are indeed coded by teems, then an examination of their ncDNA should reveal corresponding different nucleotide sequences.

For example, although the two species of Australian hairy-nosed wombat are morphologically almost identical,⁹⁷ the Northern Hairy-nosed wombat, (*Lasiorhinus krefftii*) tends to live a solitary existence,⁹⁸ while the Southern Hairy nosed wombat (*Lasiorhinus latifrons*) is social, sharing a burrow with between 5 to 10 other individuals.⁹⁹ In theory, these behavioral differences should correspond to distinct ncDNA sequences.

Unfortunately, no DNA analysis has, to my knowledge been conducted of sibling wombat species. However, a considerable corpus of genetic research has been conducted on the north American microtine rodent, or vole, some of which has relevance to this discussion.

The prairie vole (*Microtus ochrogaster*) is highly social, forms stable pair bonds and is monogamous. By contrast, although physically similar to prairie voles, montane voles (*Microtus montanus*) are far less social, do not form enduring pair bonds and are promiscuous. Over a number of years, numerous studies have elucidated the neuroendocrine mechanisms underlying the social behaviour of voles, in particular the role of two octapeptide hormones, oxytocin and vasopressin in regulating social behaviours and emotionality.^{100, 101, 102, 103, 104}

The gene that produces vasopressin in both the prairie vole and montane vole has been identified as the vasopressin V1a receptor gene (V1aR.) and it is \approx 99% identical between the two species.¹⁰⁵ However, in an important study, Hammock and Young (2002)¹⁰⁶ found a 400 nucleotide sequence in the regulatory 5' flanking region of the V1aR gene that differs between the two species. Significantly, this distinguishing sequence was not part of a coding exon gene, it was a noncoding microsatellite sequence. That is to say, sequencing data revealed the monogamous prairie vole's V1aR gene contains a highly repetitive noncoding microsatellite sequence of 400 nucleotides which the nonmonogamous montane vole lacks, (see figure 1A,B.) The suggestion that this microsatellite sequence is responsible for the species-specific variations in social behaviour is supported by the finding that the monogamous pine vole (*Microtus pinetorum*) contains this sequence but the promiscuous meadow vole (*Microtus pennsylvanicus*) does not.

The 400 nucleotide sequence is comprised of “a series of repetitive tandem nucleotide repeats (e.g. CAGA_(N), CATA_(N), AG_(N) and GAGGAGA_(N)) interspersed among nonrepetitive sequences.”¹⁰⁷ While the authors conclude “instability in highly repetitive microsatellite DNA located in the regulatory regions of genes may be a major factor in the variability of region-specific gene expression and phenotype,” from the perspective of team theory, it is argued this 400 nucleotide sequence of noncoding DNA

9 ncDNA codes for personality

Although all members of a teemic species contain similar ncDNA sequences (indicative of shared teems,) individual variations (polymorphisms) periodically accrue in these sequences due to the acquisition of new teems, DNA recombination during meiosis, mutations, genetic drift, replication slippage and environmental mutagens. Paper 1 argued that ncDNA polymorphisms precipitate minor variations in the individual's genetically archived emotions which manifests as 'personality' in teemic phyla. Even a single nucleotide polymorphism may distinguish an individual's emotional response from that of conspecifics, including siblings.

To examine a theoretical example, all female chimpanzees are born with a 'maternal teem' consisting of a specific sequence of ncDNA. This sequence is theoretically identical in all chimps. However, the accumulation of SNPs in each individual's genome alters the expression of the teem and means that no two individual chimps will display precisely the same maternal emotions. This translates to individual differences between chimp mothers in terms of maternal diligence, attention, affection, responsibility, prowess, etc.

By explaining personality as an exaptive by-product of the teemosis process, teem theory provides a plausible explanation for the ubiquitous occurrence of personality in animals. It also challenges the putative belief that personality is unique to humans and other primates.

Finally, the hypothesis- that personality is encoded as polymorphisms of ncDNA asserts that DNA fingerprinting, (DNA profiling) which uses polymorphisms of ncDNA, in particular SNPs to forensically differentiate individuality, paternity and ancestry in metazoans is actually a measurement of individual emotionality or personality. This speculation is consistent with the observation that every human has a slightly different personality – that which makes us unique as individuals.

These conjectures appear to be supported by recent experimental data gained by Westberg et. al. (2003)¹⁰⁹ showing that a dinucleotide repeat polymorphism in the ER

alpha gene in 172 women was significantly correlated to a number of personality traits, including non-conformity, indirect aggression, irritability, psychoticism and suspicion. The authors concluded that “the studied dinucleotide repeat polymorphism of the ER alpha gene may contribute to specific components of personality.”¹¹⁰ See also Melke et. al. (2003)¹¹¹

Over time, it is suggested, teemic polymorphisms gradually proliferate in a population of teemic individuals and contribute to what may be called ‘population personality.’ According to this model, geographically isolated populations of teemic phyla may evolve slight differences in their emotional responses due to the gradualistic accumulation of SNPs. However, because teems are adaptive and highly conserved, genetic drift will not generally delete or add new teems, so speciation does not occur. More typically, polymorphisms alter the expression of conserved teems in isolated populations. For example, one population of kangaroos may be more aggressive than kangaroos in another population. Similarly, in humans, this paradigm may explain perceived differences in ‘national character’^{112, 113} although the difficulties of distinguishing innate personality from culturally acquired behaviours doubtlessly obfuscate any resolution of this question.

The personality hypothesis asserts that the same teem in any two individuals of a species, (such as the one detailed in figure 1B in respect of prairie voles) will reveal a number of SNPs indicative of teemically archived personality. And indeed, a closer inspection of figure 1B reveals the 400 nucleotide teemic sequence of two individual prairie voles (P1 and P2) does indeed differ slightly. These single nucleotide differences, I suggest, equate to minor variations in the teem that regulates the emotions, hormones and neuropeptides that moderate monogamy. In practical terms, these SNPs may predispose individual P1 being slightly more or less monogamous than individual P2.

10 TIS regulates the expression of Mendelian genes

Behaviour in human and nonhuman animals invariably comprises both emotional and physical components. Paper 4 argued that although teemosis only moderates the

inheritance of emotional information, teems also contain encrypted nucleotide instructions that regulate certain physiological responses associated with teemic behaviours and emotions. For instance, when a hostility teem is activated by transduced environmental triggers, in addition to the release of various emotions (anger, annoyance, resentment, fury etc.) the emotions also stimulate neurotransmitters and hormones, causing palpitations, sweating, constriction of blood vessels, pupil dilation, and so on.

These physiological responses have long been considered to be the preserve of proteins, the expression of which is controlled by coding exon genes. However, because most adaptive behaviours are invariably a mix of both emotional and physical elements, and that teemic regulation of associated physiological responses increases the adaptive functionality of teems, teemic regulation has been conserved by NS in most, if not all teemic species. That is to say, although teems do not directly moderate the evolution of hormones, neurotransmitters, enzymes or any physical traits associated with the teemosis process, teems nevertheless may exert a ‘arm’s length’ regulatory control over these physical traits.

The use of emotions to trigger hormones, neurotransmitters and other adaptive physical responses is feasible because of the high speed of emotional transduction. In Paper 2 estimated that transduction pulses (environmental information transduced into emotion by sensory organs) occur approximately 1000 times per second. This estimate is extrapolated from data that reveal human subjects subliminally perceive emotionally salient stimuli flashed for one millisecond – almost a full second before the brain becomes consciously aware of the stimuli. From an evolutionary perspective, this singularly rapid response makes emotional transduction suitable for triggering high speed adaptive teems such as the human anti-spider teem.

The prediction that certain hormones, neurotransmitters and other physical responses to emotions are ultimately regulated by noncoding ‘junk DNA’ is not a view supported by prevailing opinion. However, in 1997, Briten (1997) offered the first evidence that transposable elements exert regulatory functions in a variety of genomes.¹¹⁴ This was followed soon after by the suggestion by Kashi and Soller (1999) that microsatellites (one type of TE) may regulate gene expression.¹¹⁵ It has since been

shown that TEs often duplicate and transport regulatory networks from one gene to a new location in another gene where they have the potential to alter the function of existing regulatory network and thereby moderate gene expression in the new host.¹¹⁶ And recently, Grover et al (2003)¹¹⁷ suggested that Alus (primate-specific ncDNA elements) function as regulatory mechanisms in the human genome and are therefore differentially selected.

In the human apolipoprotein(a) gene, an enhancer (that alters the degree of expression of the gene,) forms part of a noncoding LINE element located 20 kilobases upstream from the transcription start.¹¹⁸ This indicates that LINE elements are an integral part of the host genome.¹¹⁹ And in a study by Westberg et al. (2003)¹²⁰ it was discovered that a dinucleotide noncoding repeat polymorphism in a sample of 172 women altered the function of the estrogen receptor alpha gene that affected the expression of the hormone estrogen which in turn influenced various aspects of behaviour and personality.

Similarly, in a study of panic disorder in women, Ho et al (2003)¹²¹ discovered a noncoding functional polymorphism (G331A) in the promoter region of the progesterone receptor gene that affected the expression of the hormone progesterone. As the polymorphism was higher in panic disorder patients than in controls ($p=0.01$), the data suggests the progesterone receptor gene and the risk of panic disorder in women are correlated to slight variations in ncDNA between the women. And finally, Norris et al, (1995)¹²² has shown the steroid hormone estrogen is regulated by noncoding Alu repeats that function as estrogen receptor-dependent enhancers. The authors concluded that Alu sequences contribute to the regulation of gene transcription in estrogen receptor-containing cells. These findings are consistent with a number of studies that demonstrate tissue-specific regulation of nearby genes, eg.^{123, 124, 125, 126, 127}

This hypothesis does not argue that all coding genes are regulated by teems. Rather, only the small proportion of coding genes that produce and control hormones and other physical responses used in the teemosis process are regulated by teems. While it is beyond the scope of this paper to speculate on precisely how many coding genes in teemic species are regulated by teems, Nekrutenko and Li (2001)¹²⁸ estimated that 1,200

human genes (of an estimated 30,000 genes,) contain transposable elements in their protein-coding regions, although not all these TEs will exert a regulatory role on their host genes in relation to teemosis.

As an example of a teem situated in a regulatory region of a coding gene in order to control the expression of that gene, the theoretical 'vole monogamy teem' may be cited that is situated in the regulatory 5' flanking region of the prairie vole's V1aR gene where it regulates the expression of the hormone vasopressin.

11 ncDNA controls phenotypic plasticity

Paper 4 hypothesised that teemic regulation of gene expression provides a means by which an organism's phenotype may be modified to cope with rapidly fluctuating environments and other genomic challenges. That is to say, teemosis provides the means by which environmental circumstances can generate emotional traumas that initiate a change in phenotype. This may occur when anomalous environmental conditions (AEC) generate an emotional trauma in an individual that is transduced by sensory organs into an Emlanic 'sentence.' The sentence binds to ncDNA receptor molecules, that in turn trigger transcriptional activators that moderate regulatory regions of specific genes and alters their expression. One consequence is to activate methylation to silence the existing phenotype and activate a dormant phenotype. For example, the emotional trauma experienced by numerous amphibian species of tadpoles caused by the evaporation of their ponds can alter the expression of genes that accelerate metamorphosis.

In support of this hypothesis, a study by Streelman and Kocher (2002)¹²⁹ may be cited that found that tilapia fish subjected to high concentrations of salt in their water responded by altering the length of noncoding microsatellites that moderated the expression of two prolactin genes that normally regulate the growth rate of the individuals. As a result, the fish grew to only half their normal size. This research provided the first in vivo evidence "that differences in microsatellites can affect gene expression and that variance in expression has concomitant physiological consequences."¹³⁰ Although only a single example, this study clearly demonstrates that

ncDNA responds to environmental stress by activating hormones that alter the organism's phenotype.

12 Instinct, emotions and personality do not reside in coding exon genes

If teem theory is correct, and complex innate behaviour, emotions and personality in teemic species are archived exclusively in ncDNA as quantum arrays of linguistic emotions (teems), then this axiomatically generates the last of the teemic predictions: - that instincts, emotions and personality do not reside in exon coding genes. That is to say, while the neuropeptides, hormones, neuromodulators, neurotransmitters etc. associated with emotions are doubtlessly encoded in exon genes, the emotions themselves are not encoded in exon genes, but into non-protein-coding teemic sequences (ncDNA.)

This prediction runs counter to the textbook interpretation that has prevailed for over a hundred years – that both physical and behavioural traits are inherited as protein-coding genes. Indeed, thousands of years of animal breeding experiments clearly show that both morphology and behaviour can be dramatically altered by artificially selecting for certain genes, even if the specific nature of the gene was unknown until the twentieth century. The current paradigm is also supported by the reported discovery of coding genes for neuroticism, thrill-seeking, risk-taking, alcoholism, aggression, anxiety and homosexuality and other behavioural propensities. However, while these discoveries have frequently been accompanied by considerable media attention and hyperbole, all these associations have since been challenged, retracted or disproved, although it is conceivable that single genes for complex innate behaviours await discovery.

In the last decade, a revolution in genetics has taken place and we have seen the wholesale sequencing of multifarious genomes from microbial to human. The function of many individual genes is now well understood. Significantly however, while genes have been discovered that exert a secondary effect on emotions (by coding for hormones that are associated with variation in emotional responses,) no single coding gene for a complex innate behaviour or emotion has yet been discovered. No gene for

the human aesthetic appreciation of parklike landscapes has yet been discovered, no gene for a male's preference for a .7 hip to waist ratio in women, no gene for love of dancing, monogamy, jealousy or a host of other emotion based behaviours. While coding 'emotion genes' may yet be discovered, their absence currently supports the hypothesis that emotions are coded elsewhere.

Conclusion

The object of these five papers has been to provide a cursory understanding of the teemosis evolutionary process. Elsewhere, I extrapolate teem theory in greater detail, including an examination of the implications of teem theory for humans, in particular, the role that ncDNA and emotion plays in human disease, including cancer.

As a highly speculative and evolving hypothesis, teem theory undoubtedly contains errors both of fact and theory. However, its core supposition – that emotions play a hitherto unrecognised role in both evolution and genetics is supported by a considerable body of evidence. Indeed, until emotions are holistically integrated into the prevailing physical paradigm of nature, I argue a comprehensive unified theory of life and nature will not be possible.

¹ F.H.C Crick (1958) , The Biological Replication of Macromolecules, In; Symp. Soc. Exp. Biol., XII, P138.

² Francis Crick (1970) Central Dogma of Molecular Biology. Nature, vol. 227, pp561-563. August 8th.

³ Temin, H.M. (1971) The protovirus hypothesis: speculation on the significance of RNA-directed DNA synthesis for normal development and for carcinogenesis. *J. Nat. Can Inst.* 46, III-VII.

⁴ J. Maynard Smith (1975) The Theory of Evolution. 3rd edn, Harmondsworth: Penguin. **PAGE?**

⁵ E. Sober (1984) The Nature of Selection: Evolutionary Theory in Philosophical Focus. The MIT Press. pp101-107

⁶ Richard Dawkins (1988) Universal Darwinism. In: But Is It Science?: The Philosophical Question in the Creation/Evolution Controversy, (Ed Michael Ruse) Prometheus Books. pp208-09

⁷ John Maynard Smith (1998) Evolutionary Genetics (2nd Edition) Oxford University Press. pp8-12

⁸ Paper 3

⁹ Britten, R. J. and Kohne, D. E. 1968. Repeated sequences in DNA. *Science* 161: pp529-540.

¹⁰ S.M. Berget, C. Moore, and P.A. Sharpe. 1977. Spliced segments at the 5'-terminus of adenovirus 2 late mRNA. *Proc. Nat'l. Acad. Sci.* 74:3171-75. In *Microbiology: A Centenary Perspective*, edited by Wolfgang K. Joklik, ASM Press. 1999, p.568

¹¹ Chow, L. T., R. E. Gelinis, T. R. Broker and R. J. Roberts (1977) An amazing sequence arrangement at the 5' ends of adenovirus 2 messenger RNA. *Cell* 12: 1-8. In *Microbiology: A Centenary Perspective*, edited by Wolfgang K. Joklik, ASM Press. 1999, p.574

¹² Berget, S. M., C. Moore and P. A. Sharp (1977) Spliced segments at the 5' terminus of adenovirus 2 late mRNA. *Proc. Natl. Acad. Sci. USA* 74: pp3171-3175.

¹³ Chow, L. T., R. E. Gelinis, T. R. Broker and R. J. Roberts (1977) An amazing sequence arrangement at the 5' ends of adenovirus 2 messenger RNA. *Cell* 12: pp1-8.

¹⁴ Ohno, S. (1972) "So Much Junk DNA" in our Genome. Brookhaven Symposium.

¹⁵ Orgel, L. E. and Crick, F. H. C. (1980) Selfish DNA: the ultimate parasite, *Nature*, 284: pp604-607.

¹⁶ Doolittle W.F., Sapienza C. (1980) Selfish genes, the phenotype paradigm and genome evolution. *Nature* 284: pp601-603.

¹⁷ Dover, G. (1980). Ignorant DNA? *Nature*, 285: pp618-620.

¹⁸ Knoll, A. H. (1992) The early evolution of eukaryotes: a geological perspective. *Science* 256: pp622-627.

¹⁹ Summons R. E and Walter M. R (1990) Molecular fossils and microfossils of prokaryotes and protists from Proterozoic sediments. *Am J Sci*, 290: pp212-244.

²⁰ Han T. M and Runnegar B. (1992) Megascopic eukaryotic algae from the 2.1-billion-year-old Negaunee iron-formation, Michigan. *Science*, 257: pp232-235.

²¹ Richards, R.I. and Sutherland, G.R. (1992) Dynamic mutations: A new class of mutations causing human disease. *Cell* 70: pp709-712.

²² Strand, M., T.A. Prolla, R.M. Liskay, and T.D. Petes (1993) Destabilization of tracts of simple repetitive DNA in yeast by mutations affecting DNA mismatch repair. *Nature* 365: pp274-276

-
- ²³ Heale, S.M. and T.D. Petes (1995) The stabilization of repetitive tracts of DNA by variant repeats requires a functional mismatch repair system. *Cell* 83: pp539-545
- ²⁴ International Human Genome Sequencing Consortium. (2001) Initial sequencing and analysis of the human genome *Nature*, 409, Feb pp860-921.
- ²⁵ Bird, A.P.: (1995) Gene number, noise reduction and biological complexity. *Trends Genet.* 11: pp94-100.
- ²⁶ Venter, J.C., *et al.* (2001) The sequence of the human genome. *Science.* 291: pp1304-51.
- ²⁷ International Human Genome Sequencing Consortium. (2001) Initial sequencing and analysis of the human genome *Nature*, 409, Feb pp860-921.
- ²⁸ Waterston, R.H., *et al.*: (2002) Initial sequencing and comparative analysis of the mouse genome. *Nature.* 420: pp520-62.
- ²⁹ Aparicio, S., *et al.*: (2002) Whole-genome shotgun assembly and analysis of the genome of *Fugu rubripes*. *Science.* 297: pp1301-10.
- ³⁰ Venter, J.C., *et al.* (2001) The sequence of the human genome. *Science.* 291: pp1304-51.
- ³¹ Venter, J.C., *et al.* (2001) The sequence of the human genome. *Science.* 291: pp1304-51..
- ³² Aparicio, S., *et al.*: (2002) Whole-genome shotgun assembly and analysis of the genome of *Fugu rubripes*. *Science.* 297: pp1301-10.
- ³³ Myers E.W, Sutton G.G, Delcher AL, Dew IM, Fasulo DP, Flanigan MJ, Kravitz SA, *et al.* (2000) A whole-genome assembly of *Drosophila*. *Science* 287:2196-2204.
- ³⁴ The *C. elegans* Sequencing Consortium (1998) Genome sequence of the nematode *C. elegans*: a platform for investigating biology. The *C. elegans* Sequencing Consortium. *Science* 282: pp2012-2018
- ³⁵ Mouse Genome Sequencing Consortium. (2002) Initial sequencing and comparative analysis of the mouse genome. *Nature* 420: pp520-562
- ³⁶ International Human Genome Sequencing Consortium. (2001) Initial sequencing and analysis of the human genome *Nature*, 409, Feb. pp860-921.
- ³⁷ Palmer JD, Logsdon J.M: The recent origins of introns. *Curr Opin Genet Dev* 1991, 1: pp470-477.

-
- ³⁸ Ryan J. Taft and John S. Mattick (2004) Increasing biological complexity is positively correlated with the relative genome-wide expansion of non-protein-coding DNA sequences. In press.
- ³⁹ International Human Genome Sequencing Consortium. (2001) Initial sequencing and analysis of the human genome *Nature*, 409, Feb pp860-921.
- ⁴⁰ McClintock, B. (1948) *Carnegie Inst. Wash. Yearbook*. 47, pp155-169 .
- ⁴¹ Margaret G. Kidwell and Damon Lisch (1997) Transposable elements as sources of variation in animals and plants. *Proc. Natl. Acad. Sci. USA* Vol. 94, pp. 7704-7711, July. Colloquium Paper.
- ⁴² International Human Genome Sequencing Consortium. (2001) Initial sequencing and analysis of the human genome *Nature*, 409, Feb pp860-921.
- ⁴³ Margaret G. Kidwell and Damon Lisch (1997) Transposable elements as sources of variation in animals and plants. *Proc. Natl. Acad. Sci. USA* Vol. 94, pp. 7704-7711, July. Colloquium Paper.
- ⁴⁴ Celniker SE, Wheeler DA, Kronmiller B, Carlson JW, Halpern A, Patel S, Adams M, Champe M, Dugan SP, Frise E, *et al.*: Finishing a whole genome shotgun: Release 3 of the *Drosophila melanogaster* euchromatic genome sequence. *Genome Biol* 2002, 3:research0079.1-0079.14.
- ⁴⁵ Joshua S Kaminker, Casey M Bergman, Brent Kronmiller, Joseph Carlson, Robert Svirskas, Sandeep Patel, Erwin Frise, David A Wheeler, Suzanna E Lewis, Gerald M Rubin, Michael Ashburner and Susan E Celniker. (2002) The transposable elements of the *Drosophila melanogaster* euchromatin: a genomics perspective. *Genome Biology*, 3: research 0084.1-0084.20
- ⁴⁶ Pimpinelli, S., M. Berloco, L. Fanti, P. Dimitri, S. Bonaccorsi, E. Marchetti, R. Caizzi, C. Caggese, 1995. Transposable elements are stable structural components of *Drosophila melanogaster* heterochromatin. *Proc Natl Acad Sci U S A* 92: pp3804-8.
- ⁴⁷ Deepak Grover, Partha P. Majumder, Chandrika B. Rao, Samir K. Brahmachari and Mitali Mukerji (2003) Nonrandom Distribution of Alu Elements in Genes of Various Functional Categories: Insight from Analysis of Human Chromosomes 21 and 22. *Mol. Biol. Evol.* 20(9): pp1420-1424.
- ⁴⁸ Wichman, Holly A., Ronald A. Van Den Bussche, Meredith J. Hamilton and Robert J. Baker. (1992) Transposable elements and the evolution of genome organization in mammals. *Genetica* 86:287-293.
- ⁴⁹ Lewin, B. (2000) *Genes VII*. 7th edition. Oxford University Press.
- ⁵⁰ Wessler, S. R. 1996. Plant retrotransposons: turned on by stress. *Current Biol.*, 6, pp959-961.

-
- ⁵¹ Hughes, D.C. (2000) MIRs as agents of mammalian gene evolution. *Trends Genetics* 16: pp60–62.
- ⁵² Kim, C., C. M. Rubin & C. W. Schmid. 2001. Genome-wide remodeling modulates the Alu heat shock response. *Gene* 276: pp127–133.
- ⁵³ Li, T.-Z. & C.W. Schmid (2001) Differential stress induction of individual Alu loci: implications for transcription and retrotransposition. *Gene* 276: pp135–141.
- ⁵⁴ Singh, K., Carey, M., Saragosti, S., Botchan, M. (1985) Expression of enhanced levels of small RNA polymerase III transcripts encoded by the B2 repeats in simian virus 40-transformed mouse cells. *Nature* 314, pp553–556.
- ⁵⁵ Carey, M.F., Singh, K., Botchan, M., Cozzarelli, N.R. (1986) Induction of specific transcription by RNA polymerase III in transformed cells. *Mol. Cell. Biol.* 6, pp3068–3076.
- ⁵⁶ Fornace, A.J., Mitchell, J.B. (1986) Induction of B2 RNA polymerase III transcription by heat shock: enrichment for heat shock induced sequences in rodent cells by hybridization subtraction. *Nucleic Acids Res.* 14, pp5793–5811.
- ⁵⁷ Liu, W.M., Chu, W.M., Choudary, P.V., Schmid, C.W. (1995) Cell stress and translational inhibitors transiently increase the abundance of mammalian SINE transcripts. *Nucleic Acids Res.* 23, pp1758–1765.
- ⁵⁸ Kimura, R.H., Choudary, P.V., Schmid, C.W. (1999) Silkworm Bm1 SINE RNA increases following cellular insults. *Nucleic Acids Res.* 27, pp3381–3387.
- ⁵⁹ Li, T.-H., Spearow, J., Rubin, C.M., Schmid, C.W. (1999) Physiological stresses increase mouse short interspersed element (SINE) RNA expression in vivo. *Gene* 239, pp367–372.
- ⁶⁰ Christy R. Hagen, Rebecca F. Sheffield and Charles M. Rudin (2003) *Human Alu element retrotransposition induced by genotoxic stress*. *Nature Genetics* v35,3, pp219-220
- ⁶¹ Jang, K.L. and Latchman, D.S. (1992) The herpes simplex virus immediate-early protein ICP27 stimulates the transcription of cellular Alu repeated sequences by increasing the activity of transcription factor TFIIC. *Biochem. J.*, 284, pp667–673.HH
- ⁶² Jang, K. L., M. K. L. Collins, and D. S. Latchman (1992) The human immunodeficiency virus Tat protein increases the transcription of human *Alu* repeated sequences by increasing the activity of the cellular transcription factor TFIIC. *J. Acquir. Immune Defic. Syndr.* 5: pp1142-1147.

-
- ⁶³ B Panning and JR Smiley (1993) Activation of RNA polymerase III transcription of human Alu repetitive elements by adenovirus type 5: requirement for the E1b 58-kilodalton protein and the products of E4 open reading frames 3 and 6. *Mol. Cell. Biol*, Vol 13, No. 6. pp3231-3244.
- ⁶⁴ Liu, W.M., Chu, W.M., Choudary, P.V., Schmid, C.W. (1995) Cell stress and translational inhibitors transiently increase the abundance of mammalian SINE transcripts. *Nucleic Acids Res.* 23, pp1758–1765.
- ⁶⁵ Schmid, C.W. (1998) Does SINE evolution preclude Alu function? *Nucleic Acids Res.* 20, pp4541–4550.
- ⁶⁶ Capy P, Gasperi G, Biemont C, and Bazin C. (2000) Stress and transposable elements: co-evolution or useful parasites? *Heredity*, Volume 85(2).August. pp101-106.
- ⁶⁷ Bryan, G. J. And Hartl, D. L. (1988) Maternally inherited transposons excision in *Drosophila simulans*. *Science*, 240, pp215-217.
- ⁶⁸ Bucheton, A. (1979) Non-Mendelian female sterility in *Drosophila melanogaster*: influence of aging and thermic treatments. III. Cumulative effects induced by these factors. *Genetics*, 93, pp131-142.
- ⁶⁹ Ho, Y. T., Weber, S. M. And Lim, J. K. (1993) Interacting hobo transposons in an inbred strain and interaction regulation in hybrids of *D. melanogaster*. *Genetics*, 134, pp895-908.
- ⁷⁰ Kidwell, M. G. 1981. Hybrid dysgenesis in *Drosophila melanogaster*: the genetics of cytotypic determination in a neutral strain. *Genetics*, 98, pp275-290.
- ⁷¹ Coen, E. S., Robbins, T. P. And Almeida, J. (1989) Consequences and mechanisms of transposition in *Antirrhinum majus*. *Mobile DNA*. (Ed. by D. E. Berg). & M. M. Howe, American Society for Microbiology, Washington DC. pp413-436.
- ⁷² Capy P, Gasperi G, Biemont C, and Bazin C. (2000) Stress and transposable elements: co-evolution or useful parasites? *Heredity*, Volume 85(2).August. pp101-106.
- ⁷³ Capy P, Gasperi G, Biemont C, and Bazin C. (2000) Stress and transposable elements: co-evolution or useful parasites? *Heredity*, Volume 85(2).August. pp101-106.
- ⁷⁴ Adam Eyre-Walker and Peter D. Keightley (1999) High Genomic Deleterious Mutation Rates in Hominids. *Nature* 397. pp344-347.
- ⁷⁵ The International SNP Map Working Group. A map of human genome sequence variation containing 1.42 million single nucleotide polymorphisms. *Nature* 409, 928-933 (2001).

-
- ⁷⁶ Smit, A. F., Toth, G., Riggs, A. D., & Jurka, J. (1995) Ancestral, mammalian-wide subfamilies of LINE-1 repetitive sequences. *J. Mol. Biol.* 246, 401-417.
- ⁷⁷ Boissinot, S., Chevret, P. & Furano, A. V. (2000) L1 (LINE-1) retrotransposon evolution and amplification in recent human history. *Mol. Biol. Evol.* 17, 915-928
- ⁷⁸ Sheen, F.-m. *et al.* (2000) Reading between the LINES: Human genomic variation introduced by LINE-1 retrotransposition. *Genome Res.* 10, 1496-1508.
- ⁷⁹ International Human Genome Sequencing Consortium. (2001) Initial sequencing and analysis of the human genome *Nature*, 409, Feb pp860-921.
- ⁸⁰ Ratner, V. A., Zabanov, S. A., Kolesnikova, O. V. And Vasilyeva, L. A. (1992) Induction of the mobile genetic element Dm-412 transpositions in the *Drosophila* genome by heat shock treatment. *Proc. Natl. Acad. Sci. USA*, 89, pp5650-5654.
- ⁸¹ Vasilyeva, L. A., Bubenshchikova, E. V. And Ratner, V. A. (1999) Heavy heat shock induced retrotransposon transposition in *Drosophila*. *Genet. Res.* pp111-119.
- ⁸² Arnault, C. And Dufournel, I. (1994) Genome and stresses: reactions against aggressions, behavior of transposable elements. *Genetica*, 93, pp149-160.
- ⁸³ Arnault, C., Loevenbruck, C. And Biemont, C. (1997) Transposable element mobilization is not induced by heat shocks in *Drosophila melanogaster*. *Naturwissenschaften*, 84, pp410-414.
- ⁸⁴ M.J. Shulman, C.M. Steinberg and N. Westmoreland (1981) The coding function of nucleotide sequences can be discerned by statistical analysis, *Journal of Theoretical Biology*, 88: pp409-420.
- ⁸⁵ Fichant G. and Gautier C. (1987) Statistical method for predicting protein coding regions in nucleic acid sequences // *Comput. Appl. Biosci.* Vol.3.P. pp287-295
- ⁸⁶ Michel CJ. 1986. New statistical approach to discriminate between protein coding and non-coding regions in DNA sequences and its evaluation. *Journal of Theoretical Biology* 120: pp223-236.
- ⁸⁷ Zipf, G. K. (1949) *Human Behavior and the Principle of Least Effort*. Cambridge, Massachusetts: Addison-Wesley Press.
- ⁸⁸ R. N. Mantegna, S. V. Buldyrev, A. L. Goldberger, S. Havlin, C.-K. Peng, M. Simons, H.E. Stanley, (1994) Linguistic features of Noncoding DNA Sequences. *Phys. Rev. Lett.* 73. pp3169-3172.

-
- ⁸⁹ Chatzidimitriou-Dreismann CA, Streffer RM, and Larhammar D. (1996) Lack of biological significance in the ‘linguistic features’ of noncoding DNA — a quantitative analysis. *Nucleic Acids Research* 14:pp1676-1681.
- ⁹⁰ Konopka A.K and Martindale C. (1995) Noncoding DNA, Zipf’s law, and language [letter]. *Science, New Series*. Vol 268, #5215, P789.
- ⁹¹ Tsonis AA, Elsner JB, Tsonis PA. 1997. Is DNA a language? *Journal of Theoretical Biology* pp184:25-9.
- ⁹² Sebastian Bonhoeffer, Andreas V. M. Herz, Maarten C. Boerlijst, Sean Nee, Martin A. Nowak, and Robert and M. May (1996) No Signs of Hidden Language in Noncoding DNA. *Physical Review Letters*. Volume 76, Number 11. P1977.
- ⁹³ H.E. Stanley, S.V. Buldyreva, A.L. Goldberger, D. S. Havlinc, C.-K. Peng and M. Simons (1999) Scaling features of noncoding DNA. *Physica A* 273 pp1-18
- ⁹⁴ S. V. Buldyrev, A. L. Goldberger, S. Havlin, R. N. Mantegna, M. E. Matsa, C.-K. Peng, M. Simons, and H. E. Stanley (1995) Long-range correlation properties of coding and noncoding DNA sequences: GenBank analysis. *Phys. Rev. E* 51, May. pp5084–5091.
- ⁹⁵ S.V. Buldyrev, A.L. Goldberger, S. Havlin, C.-K. Peng, H.E. Stanley, M.H.R. Stanley, M. Simons, (1993) *Biophys. J.* 65. P2673.
- ⁹⁶ H.E. Stanley, S.V. Buldyrev, A.L. Goldberger, S. Havlin, C.-K. Peng, M. Simons (1999) Scaling features of noncoding DNA *Physica A*. 273 pp1-18
- ⁹⁷ Dawson, L. (1983). The Taxonomic Status of small Fossil wombats (Vombatidae: Marsupialia) from Quaternary Deposits, and of related modern wombats. *Proceedings Linnaean Society NSW*, 107: pp99-121.
- ⁹⁸ Johnson, C.N., and Crossman, D.C. (1991). Sexual dimorphism in the northern hairy-nosed wombat, *Lasiiorhinus krefftii* (Marsupialia: Vombatidae). *Australian Mammalogy*, 14: 145-46.
- ⁹⁹ Wells R.T. 1995. Southern Hairy-nosed Wombat, in R. Strahan (Ed.) *The Mammals of Australia* Reed Books, Sydney. pp 20-21.
- ¹⁰⁰ Larry J. Young, Zuoxin Wang and Thomas R. Insel (1998) Neuroendocrine bases of monogamy. *Trends Neurosci.* 21, pp71–75.

-
- ¹⁰¹ Larry J. Young 2002 The Neurobiology of Social Recognition, Approach, and Avoidance. *Biol Psychiatry* 2002;51: pp18–26
- ¹⁰² Larry J. Young, Miranda M. Lim, Brenden Gingrich, and Thomas R. Insel (2001) Cellular Mechanisms of Social Attachment. *Hormones and Behavior* 40, pp133–138
- ¹⁰³ Thomas R Insel and Larry J Young (200?) Neuropeptides and the evolution of social behavior. *Current Opinion in Neurobiology*, 10:784–789.
- ¹⁰⁴ Bruce S. Cushing, Julia O. Martin, Larry J. Young and C. Sue Carter (2001) The Effects of Peptides on Partner Preference Formation Are Predicted by Habitat in Prairie Voles. *Hormones and Behavior* 39, pp48–58
- ¹⁰⁵ Young, L.J. (1999) Oxytocin and vasopressin receptors and species-typical social behaviors. *Horm. Behav.*, 36, pp212-221.
- ¹⁰⁶ Elizabeth A. D. Hammock and Larry J. Young (2002) Variation in the vasopressin V1a receptor promoter and expression: implications for inter- and intraspecific variation in social behaviour. *European Journal of Neuroscience*. Volume 16 Issue 3. August. pp399-402.
- ¹⁰⁷ Elizabeth A. D. Hammock and Larry J. Young (2002) Variation in the vasopressin V1a receptor promoter and expression: implications for inter- and intraspecific variation in social behaviour. *European Journal of Neuroscience*. Volume 16 Issue 3. August. pp399-402.
- ¹⁰⁸ Figure 1A,B and caption reprinted courtesy of: Elizabeth A. D. Hammock and Larry J. Young (2002) Variation in the vasopressin V1a receptor promoter and expression: implications for inter- and intraspecific variation in social behaviour. *European Journal of Neuroscience*. Volume 16 Issue 3. August. pp399-402.
- ¹⁰⁹ Westberg, J Melke, M Landén, S Nilsson, F Baghaei, R Rosmond, M Jansson, G Holm, P Björntorp and E Eriksson (2003) Association between a dinucleotide repeat polymorphism of the estrogen receptor alpha gene and personality traits in women. *Molecular Psychiatry* 8, pp118-122.
- ¹¹⁰ Westberg, J Melke, M Landén, S Nilsson, F Baghaei, R Rosmond, M Jansson, G Holm, P Björntorp and E Eriksson (2003) Association between a dinucleotide repeat polymorphism of the estrogen receptor alpha gene and personality traits in women. *Molecular Psychiatry* 8, pp118-122.
- ¹¹¹ Melke J, Westberg L, Nilsson S, Landen M, Soderstrom H, Baghaei F, Rosmond R, Holm G, Bjorntorp P, Nilsson LG, Adolfsson R, and Eriksson E.A (2003) A polymorphism in the serotonin

receptor 3A (HTR3A) gene and its association with harm avoidance in women. *Arch Gen Psychiatry*. Oct;60(10):pp1017-23.

¹¹² Alex Inkeles (1996) *National Character: A Psycho-Social Perspective*, Transaction Books.

¹¹³ Robert R. McCrae and Juri Allik, Eds. (2002) *The Five-Factor Model of Personality Across Cultures*. Kluwer Academic/Plenum Publishers.

¹¹⁴ Britten, R.J., 1997. Mobile elements inserted in the distant past have taken on important functions. *Gene* 205: 177-82.

¹¹⁵ Kashi, Y. and M. Soller. 1999. *Functional Roles of Microsatellites and Minisatellites*. In: *Microsatellites: Evolution and Applications*. Edited by Goldstein and Schlotterer. Oxford University Press.

¹¹⁶ Kidwell, M.G. and D.R. Lisch (2000). Transposable elements and host genome evolution. *Trends in Ecology and Evolution*. 15: pp95-99.

¹¹⁷ Deepak Grover, Partha P. Majumder, Chandrika B. Rao, Samir K. Brahmachari and Mitali Mukerji. (2003) Nonrandom Distribution of Alu Elements in Genes of Various Functional Categories: Insight from Analysis of Human Chromosomes 21 and 22. *Mol. Biol. Evol.* 20(9):pp1420-1424.

¹¹⁸ Yang, Z., D. Boffelli, N. Boonmark, K. Schwartz & R. Lawn (1998) Apolipoprotein(a) gene enhancer resides within a LINE element. *J Biol Chem* 273: pp891-7.

¹¹⁹ Kidwell, M.G. and D.R. Lisch (2000). Transposable elements and host genome evolution. *Trends in Ecology and Evolution* 15: pp95-99.

¹²⁰ Westberg L, Melke J, Landen M, Nilsson S, Baghaei F, Rosmond R, Jansson M, Holm G, Björntorp P, Eriksson E. (2003) Association between a dinucleotide repeat polymorphism of the estrogen receptor alpha gene and personality traits in women. *Mol Psychiatry*. Jan;8(1): pp118-22.

¹²¹ Ho H-P, Westberg L, Annerbrink K, Olsson M, Melke J, Nilsson S, Baghaei F, Rosmond R, Holm G, Björntorp P, Andersch S, Allgulander C, and Eriksson E. (2003) Association between a functional polymorphism in the progesterone receptor gene and panic disorder in women. *Psychoneuroendocrinology*. Accepted.

¹²² Norris, J., Fan, D., Aleman, C., Marks, J. R., Futreal, P. A., Wiseman, R. W., Iglehart, J. D., Deininger, P. L. & McDonnell, D. P. (1995) *J. Biol. Chem.* 270, pp22777-22782.

-
- ¹²³ J.E. Hambor, J. Mennone, M.E. Coon, J.H. Hanke and P. Kavathas (1993) Identification and characterization of an Alu-containing, T-cell- specific enhancer located in the last intron of the human CD8 alpha gene. *Mol. Cell. Biol.*, Nov, Vol 13, No. 11. pp7056-7070.
- ¹²⁴ I.S. Thorey, G. Cecena, W. Reynolds and R.G. Oshima (1993) Alu sequence involvement in transcriptional insulation of the keratin 18 gene in transgenic mice. *Mol. Cell. Biol.*, Vol 13, No.11. pp6742-6751.
- ¹²⁵ Brini, A. T. , Lee, G. M. & Kinet, J.-P. (1993) Involvement of Alu sequences in the cell-specific regulation of transcription of the gamma chain of Fc and T cell receptors. *J. Biol. Chem.* 268, pp1355-1361.
- ¹²⁶ Toshiyuki Hayakawa, Yoko Satta, Pascal Gagneux, Ajit Varki and Naoyuki Takahata (2001) *Alu*-mediated inactivation of the human CMP- *N*-acetylneuraminic acid hydroxylase gene PNAS. September 25, Vol. 98, # 20, pp11399-11404.
- ¹²⁷ Vansant, G. & Reynolds, W. F. (1995) The consensus sequence of a major Alu subfamily contains a functional retinoic acid response element. *Proc. Natl. Acad. Sci.* Vol 92, August. pp8229-8233
- ¹²⁸ Anton Nekrutenko and Wen-Hsiung Li (2001) Transposable elements are found in a large number of human-protein-coding genes. *Trends in Genetics.* Vol 17, No11. November. pp619-621.
- ¹²⁹ Streelman, J.T, and T.D. Kocher. (2002) *Microsatellite variation associated with prolactin expression and growth of salt-challenged tilapia.* *Physiological Genomics* 9 (1): pp1-4.
- ¹³⁰ Streelman, J.T, and T.D. Kocher. (2002) *Microsatellite variation associated with prolactin expression and growth of salt-challenged tilapia.* *Physiological Genomics* 9 (1): pp1-4.