International Journal of Sciences

Research Article Volume 8 – June 2019 (06)

From Superficial Damage to Invasion of the Nucleosome: Ranking of Morbidities by the *Biosemiotic Depth Hypothesis*

John W. Oller[1], Christopher A. Shaw[2]

[1]University of Louisiana, Department of Communicative Disorders, P.O. Box 43170, Lafayette, Louisiana 70504-3170, USA
[2]University of British Columbia, Neural Dynamics Research Group, Department of Ophthalmology and Visual Sciences, also Department of Pathology, Program in Experimental Medicine, Program in Neurosciences, Vancouver, Canada V5Z 1M9

Abstract: At their most abstract level, according to a certain generalized paradigm in biosemiotic philosophy grounded in well-established mathematical proofs, valid communications from molecules upward must be formally isomorphic to the dynamic true narrative representations (TNRs) of natural language systems that vest those meaningful signs with their functional (pragmatic) content. TNRs, in DNA, RNA, proteins, and higher constructions, therefore, are requisite to health in the individual, in interactions with the larger environment, and with other organisms. In *homo sapiens*, the generalized biosemiotic paradigm proves that morbidities in general must always, in some manner, involve degradation of internal and external communications through TNRs in DNA, RNA, protein language, organelles, cells, tissues, and organ systems. The mathematically grounded paradigm shows that any given TNR can be superveniently degenerated, by very coarse or very fine degrees, to many distinct fictions, errors, lies, and nonsense strings out to the absolute limit of a complete erasure. The depth hypothesis asserts that if the timing and breadth of any degenerative disruption can be held equal, in fact or in principle, the *depth of penetration of any disruptive factor into biosignaling representations* must in theory be pathognomonic of severity in the supervened morbidities. From meiosis through conception to maturity, *ceteris paribus*, corruptions deeper in the developmental hierarchy must be more harmful in the morbidities they supervene. The depth hypothesis suggests a differentiation of autoimmune disorders as deeper than allergies, but less so than prion diseases, tumorigenesis, and metastatic cancers in that order. It suggests, therefore, a potentially useful generalized ranking of morbidities.

Keywords: Aluminum Adjuvants, Autoimmune Diseases, Biosemiotic Depth, Degrading Biosignaling Systems, Etiology of Morbidities, Pragmatic Mapping, TNR-Theory, True Narrative Representations

Introducing a Mathematically Grounded Paradigm of Biosemiotics

Biosemiosis, by mainstream definitions, is the dynamic process of building up meaningful sign systems. It is generally supposed that such sign systems must be constructed from whatever order or chaos actually lies beneath the subatomic level in physics and undergirds the whole of the biosphere [1]–[7]. Moreover, such physical orderliness (or chaos) must either implicitly pre-possess [5] not only the full complexity of the known biosphere but also that of the human language capacity — the consciousness and ability that enables us to discuss meaningful strings of signs in general [8]–[19] — or, the biological sign systems culminating in the human language capacity must somehow develop step-by-step along lines somewhat similar to those proposed by [6].

Beyond the prevailing view that biological codes [13], [15], [20]–[25] in one way or another are essential to life, there is as yet no general consensus on how they come to be as they are, but we know a great deal about how they can be disrupted in ways leading to disorders, diseases, and mortality. In this paper, taking it for granted that known biosemiotic systems bear some profound resemblances to natural language systems with respect to their multi-level grammatical complexities [26]–[30], we focus our attention on how biological signaling systems in general can be damaged by conditions that are generally referred to loosely in the medical professions as "morbidities" — for instance, see the many ways that term is used in the publication known best by its abbreviated title, *MMWR*, standing for the *Morbidity and Mortality Weekly Report* published by the US Centers for Disease Control and Prevention (https://www.cdc.gov/mmwr/index.html).

Published at: http://www.ijsciences.com/pub/issue/2019-06/
DOI: 10.18483/ijSci.2069; Online ISSN: 2305-3925; Print ISSN: 2410-4477

John W. Oller, Christopher A. Shaw (Correspondence)
+1-337-962-4649; 1-604-710-8291

Some theoreticians, notably Roman Jakobson and Lévi-Strauss, as early as 1968, had already speculated that biological language-like systems might prove to be isomorphic in their most abstract forms with the underlying grammars of natural language systems [10]. However, any strong version of that hypothesis has been directly or indirectly rejected by at least some other theoreticians [13], [31], [32] although there is near universal agreement that all of the known biological signaling systems are richly interconnected in a way that certainly resembles ordinary linguistic discourse in many respects. It seems that the theoreticians who insist that linguistic metaphors are either too simple or too complex, have knowingly or accidentally embraced, the assertion by Charles S. Peirce that the whole universe seems to be pervaded by signs, of which human thoughts seem to be the "chief ... mode of representation" though he also asserted that "thought is not necessarily connected with a brain. It appears in the work of bees, of crystals, and throughout the purely physical world" (for the Peircean references see the excellent analysis by Winfred Nöth [29], especially in footnotes 103-104).

The notion that biological and even physical systems profoundly depend upon sign systems of various sorts did not originate with linguists, but was suggested by physicists and biologists through linguistic analogies, metaphors, and the words they chose on their arduous pathway to the discovery of what is still called "the genetic code" [7], [20], [23], [33]–[37]. In 1956, Francis Crick [1] suggested, "if we regard the sequence of base pairs as a *code* [our emphasis throughout this quote], there is nothing in the structure to tell us in which *direction* to *read* it, except the *sequence* of the bases themselves". He supposed that such a "code" might make "'*sense*' if *read* one way and '*nonsense*' if read the other" (p. 537). Three years earlier, George Gamow had written to Linus Pauling: "Ever since I read the article of Watson and Crick last June, I was trying to figure out how a long number *written* in a *fourdigital* [sic] *system* (i.e. nucleic acid molecule) can *determine (uniquely) a correspondingly long word* based on *20-letter-alphabet* (i.e. an enzyme molecule)" [36]. The later result of that line of thinking, searching for a *unique determination* of meaningfulness or functionality in living systems led to the discovery of what is still known as "*the* genetic code" as if there were just that one. This, in spite of the fact that "*the* genetic code" is neither a unique determiner nor is it a complete explanation of the biosphere by any stretch of the imagination , but is known now to be part of a much grander and vastly more complex system of inter-related systems [38]–[45] connecting the whole of the biosphere to the world of physics and chemistry linked all the way upward to the highest of human intellectual capacities manifested in our deeply layered symbol systems. What remains, however, and is still agreed upon at the present day, is the proposition put in many different ways by diverse researchers but none more clearly that Thomas A. Sebeok, that "semiosis presupposes the axiomatic identity of the semiosphere with the biosphere'' [46, p. 68].

Many years later, Marcello Barbieri would ask: ''Is meaning a natural entity? . . . Can we introduce meaning in biology?'' He rejected the idea that biosemiotics involves any non-mechanical interpretation, though he offered no explanation of how any combination of mechanical "codes" which he defined as "rules that establish a correspondence [presumably "uniquely determined" per Gamow's speculation] between two independent worlds" [13, p. 241] could possibly account for something as complex and dynamic as human consciousness and free will. Yet Noam Chomsky [47]–[51], Roger Sperry [52], [53], and others have shown that those most abstruse constructs cannot be dispensed with. More recently, nonetheless Babieri has boldly asserted that "the organic codes . . . are the great *invariants* [our emphasis] of life" and that, therefore, "the study of all codes of life, is also the study of the deep logic of life" [1], [2, p. 248]. As exemplars of "codes", in his 2014 argument, he listed and cited references for the genetic code, metabolic code, Trifonov sequence codes, adhesive code, splicing codes, signal transduction codes, sugar code, histone code, cytoskeleton and compartment codes, neural code, tubulin code, nuclear signaling code, and ubiquitin code, while implying that many others remain to be discovered (p. 244). However, Barbieri's mechanistic approach seems to have no answer whatsoever for the devastating complaints, launched independently by Chomsky and Sperry, against mechanical models in general. Those authors showed [47], [48], [50]–[55] that mechanical models are inadequate explanations of the very simplest conscious acts of free will [50], [56], [57].

Distinct from and yet falling within the rich and diverse range of biosemiotic perspectives, several theories of real (pragmatic) information manifested to competent observers in the concrete world of matter-space and time have been proposed — Barbieri's "code" biology being one among several distinct approaches [58]–[61]. Nevertheless, it is laudable that Barbieri seeks "an objective criterion for the discovery of organic codes" which he supposed must meet three requirements: "an organic code exists if we prove the existence of three entities: (1) two independent worlds of molecules; (2) a potentially unlimited number of arbitrary connections between them implemented by adaptors; and (3) a selection of

adaptors (a set of coding rules) that ensures a specific correspondence" [13, p. 244]. Whereas Barbieri has produced nothing resembling a mathematically general proof of his theory of biological codes, his pursuit of them, narrowly constrained by his insistence on mechanistic modeling, nonetheless, calls to mind general proofs that have been produced along Peircean lines by C. S. Peirce himself in 1897 [62], Tarski 1941, 1949 [63], [64], and more recently by others [65]–[67] (also see Sowa [68]–[70]). On the basis of such mathematical arguments generalized to their limits for all possible meaningful sign systems in the recently developed theory of true narrative representations (TNRs), the nature of meaning in biology can be given a definitive meaning along the lines sought by Barbieri in "biological codes". The difference, however, is that what Barbieri assets is "mechanical" in the "codes" of biology, is so completely fraught with meaning from the level of quantum physics to the human language capacity, that intelligence, consciousness, intentionality, teleology, and free will are essential components interconnecting the hierarchy of systems from top to bottom and through and through.

It comes out that a rich interpretive version of biosemiotics grounded in general mathematical proofs shows that the systems of signs found in the complex molecules of DNAs, RNAs, proteins, and in their distinct higher level composite structures seen in the cells, tissues, and organs of living beings such as ourselves are grounded in the determinative systems of relations most easily discerned in the absolutely commonplace ordinary TNRs of typically successful, though mundane, human discourse [65]–[67], [71], [72]. As an undeniable empirical aspect of such biological sign systems, no reasonable educated person today, not since the "discovery of the genetic code" [23], [30], [33], [35], [36], [73] denies that meaningful biological strings of signs are involved in dynamic interactions with each other and with the body's peptides, organelles, cells, tissues, and organ systems, as well as with other organisms, e.g., the microbiota inside and outside the body [74], [75].

For even a moment of health and well-being — and much more so for a lifetime of mostly healthful days, weeks, and so forth — valid TNRs are required probably from sub-atomic levels and certainly from molecular levels right on upward to the very pinnacle of human consciousness, free will, and intellectual human discourse. Along the lines of Gamow's speculation about "unique determination" of sequences of amino acids in proteins by sequences of base-pairs in nucleic acid, and Barbieri's commitment to determinative "codes" crucial to the existence of living systems, the mathematical arguments of TNR-theory show why biological signaling systems of complex and interrelated codes must undergird the human language capacity through which we interact with each other and without which we could not even try to understand the universe and our place in it [40], [76].

Here we introduce for non-specialists a rapidly developing theoretical paradigm under the scope of the mathematically grounded framework of biosemiotics as expressed in TNR-theory. That whole system of thought embraces the molecular signaling systems of living organisms and extends to the highest levels of discursive representations manifested in the human language capacity. Human discourse occupies, it seems, the very highest level of semiotic systems in general. If it were not for that most general and abstract representational system, we would not be engaged in this discussion in the first place. The particular brand of biosemiotic theory applied here, namely TNR-theory, though universal in its applicability to meaningful sign systems, as already noted, it is grounded in explicit but completely general logico-mathematical proofs by Peirce and others. The basis is found in the unique formal properties of ordinary true representations. In keeping with the rule proposed by Richard Feynman — who famously said, "we are not concerned with where an idea comes from; the sole test of its validity is experiment" [77] — hypotheses drawn from the particular theory of biosemiotics to be examined here have been and are now being actively tested empirically in many contexts [71], [72], [74], [78]–[83].

In this paper, we consider a certain hypothesis derived from TNR-theory that enables us to differentiate the morbidities that impact human beings and to produce a general ranking of them. We pay special attention to those that affect our unique language capacity. We are particularly interested here in the ones that harm the central nervous system (CNS) and in the factors that produce them. Such morbidities and their causal factors are special because they impact our ability to understand ordinary experience, to communicate with each other, and to reason about the material space-time world in which we find ourselves biologically and consciously embodied. Evidently, because of the tendency for errors in biosemiotic processes to accumulate progressively and inevitably over time — owing to the law of entropy from generalized and extended to quantum physics by the physicist and mathematician Edwin Thompson Jaynes [84]–[86] — no individual is exempt from the eventual collapse of all the communication systems on which the body of every living plant and animal depends. Therefore, it is certain the issues dealt with in this paper concern all human beings. The central question here concerns

provenance of the morbidities that eventually must effect the catastrophic biosemiotic systems failure that in ordinary talk is called *death*. It is not a pretty word, but it is one that concerns every human being.

The Depth Hypothesis

The specific hypothesis proposed here allows a ranking of morbidities with respect to their depth of penetration into the signaling systems that enable our organ systems to continue functioning. We argue that a general theory of signs is needed to make sense of the dynamically interrelated biosemiotic systems that are essential to human health and well-being. Such a theory must embrace the most basic meaningful molecules in our bodies right up to the most abstract and the highest meaning systems of the human mind. As we will show, meaningful strings of signs are not only connected from the molecular level right up to the highest functions of the human CNS, but they are necessarily constrained by the same logical principles. At their deepest and most abstract level, TNR-theory shows how and why validly interpreted strings of biological signs many layers deep must be and are isomorphic with the most abstract formal strings of signs manifested as TNRs in mundane human discourse.

In sum, the goal in this paper is to offer a comprehensive overview of morbid conditions, consistent with what is known from experimental/empirical findings enabling the differentiation of major classes of all the morbid conditions trending toward the inevitable limit of mortality. We regard as special test cases, the loosely defined classes of mysterious prion diseases, systemic auto-immunities, tumorigenesis, and metastatic cancers. It is not our purpose here to fine tune the depth hypothesis or the ranking that it entails, but rather to state it as clearly as possible and in doing so to suggest, and to demonstrate from some relevant empirical evidence how it can be further tested and refined.

As Simple as Possible

As Einstein put it in his often quoted dictum of 1929, we seek a theory "that is as simple as possible but no simpler" [87]. The aim is to make the theory as consistent as possible with all the known facts without making it either more or less complex than it needs to be as required both by Ockham's Razor [88] and by Leibniz's principle of the identity of indiscernibles [89], [90]. Einstein noted that the majority of physical theories are "constructive" inasmuch as they "build a picture of some complex phenomena out of some relatively simple proposition" [91, p. 8]. The assertion that *relatively perfect true narrative representations (TNRs) are commonplace*, is that kind of simple, foundational proposition. Once in place, as explained below, that idea enables a series of logico-mathematical proofs by construction and leads to the generation of many empirically testable hypotheses currently being addressed as already noted in citations given above.

The constructive/synthetic theories grounded in "some relatively simple proposition", Einstein contrasted with the less common theories that are analytical — the ones relying "on mathematical formula", i.e., completely general principles that "apply to every case which presents itself" (p. 8). TNR-theory uses both of those approaches: the universal principles to be explained and applied prove *a series of general inequalities ranging from the relatively complete and well-formed nature of every TNR to the myriads of less complete forms that can be derived from TNRs by degenerating them to fictions, errors, lies, nonsense, and complete erasures.* Capsulizing the "relatively simple [synthetic] proposition" and placing it in the context of certain "mathematical formula" — the "analytical" aspect of the theory — it has been proved that *regardless which exemplar of a biological or linguistic TNR may "present itself" (or that any researcher may arbitrarily select), it is always possible to derive from such a representation a series of demonstrably less perfect fictions, errors, lies, and nonsense forms, up to and including a complete erasure. Moreover, TNR-theory proves that TNRs provide the only possible basis for the discovery of any meaning in any sign systems whatsoever.*

What Counts as a TNR?

The mathematical proofs of the whole theory unfold from the undeniable facts that TNRs exist in abundance and that every single one of them — whether in a human language or in a biological language, as suggested by Figure 1 A and B, respectively — takes the form of a representation with three parts which stand in a relatively perfect agreement to each other: (1) there is a symbolic part, *S*, consisting of a complex string or stereoscopic/harmonic system of relations, (2) a pragmatic mapping relation, π, a dynamic moving model, of that complex string/system onto (3) a particular material objective context, *O*, situated in the space-time-material world with which *S* and π agree as completely as they purport to agree. As an example of a TNR, easily checked by any number of observers provided they have a computer and access to the internet, is the sequence of events recorded in the YouTube at this link (https://www.youtube.com/watch?v=E43-CfukEgs&list=PLhLixXCfmuOjmXd4HKMZ_FwIiawD7mtZK&index=120&t=201s), as reported by Brian Cox of the BBC. The recording there concerns a variation on Galileo's experiment where he, or one

of his students, allegedly dropped different sized cannonballs from the Tower of Pisa. The objective was to test Aristotle's claim that the heavier object should fall faster.

Sans the commitment to a strictly mechanical system, the abstract relations constituted by every TNR, do indeed capture the essential components of a "biological code" as described by Barbieri [13]. TNRs also, as shown in the example of the expensive experiment in the Cleveland vacuum chamber with a feather and bowling ball, incorporate as Barbieri argues essential requirements of the long-standing "scientific method" that was so eloquently demonstrated by Galileo's test of Aristotle's false dictum that heavier objects must fall faster than lighter ones. However, by contrast with Barbieri's insistence on a mechanism/model that "uniquely determines" a sequential relation between distinct domains TNR-theory allows for what Peirce (see Sowa [68], [70] for excellent discussion) defined as theorematic reasoning to produce abstract correspondences between the components of a TNR that could not be discovered or produced by any simple mechanism or algorithm. Sowa explains that algorithms employed by so-called "artificial intelligence" systems can be made very good at doing strict deductive reasoning, the type that Peirce termed "corollarial", but with respect to inferential reasoning of the "theorematic" type, they can be beaten by a "good high school student". Experimental reports that measure up to the standard of TNRs can be mundane and uninteresting corollarial tests or they can be original and creative purposeful demonstrations that reach far beyond mere deductions from known facts.

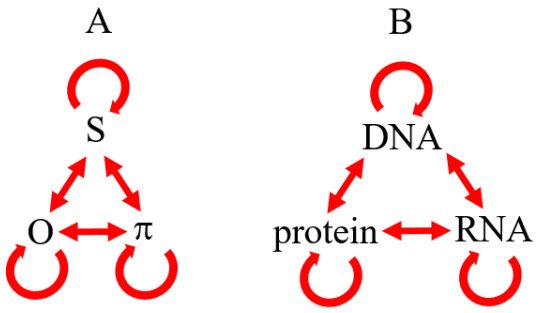

Figure 1. The core semiotic systems in every TNR manifested as an *SπO* relation, A, at the macro-level of any human language, and, B, at the molecular level of biosignaling systems. Such systems enable bodily growth from the most abstract level connected through dynamic physical movements with the concrete material world of space-time producing what appear as a micro-level and a macro-level exponentially growing spiral (see Figure 2).

In the experiment reported by Cox, the test involved dropping a feather and a bowling ball inside the multi-billion-dollar vacuum chamber in Cleveland, Ohio. Any competent observer can see that in the experiment reported by Cox: *the bowling ball and the feather fell at the same rate*. The italicized portion is a TNR. It is true because all the parts of the TNR, the *S*-string *π*-mapped to its *O* by Cox, or by any observer, are all found to stand in agreement with each other. The *SπO* system of relations is as true as it purports to be of the material facts reported. Because those facts are part of a larger sequence of events, the *SπO* system in question is a narrative, a report of events unfolding over some span of time. It is also invariably a representation because the *S* purports to be true of its *O* by virtue of a faithful *π*-mapping of that *S* onto that *O*. Though each component of the *SπO* system of relations takes a rather different form than the other two components — the relatively abstract and general *S*-string is itself, being a string of words in English, profoundly different from the intelligent *π*-mapping through a sequence of actions (for instance, the speaking of Cox and now the tapping on certain keys on a computer by the writer of these words) onto the dynamic concrete material facts observed in the *O*-part of the *SπO* relation. Likewise that *O*-part is entirely different from the other two parts of the *SπO* system of relations. Yet all of them stand in relatively perfect agreement — a kind of harmony that seems to transcend any of the three components. The fact that the harmony in question is real, once it is known in the form of a TNR, one that shows the abstract proposition to be a real manifestation of ordinary truth, is demonstrable in the fact that every such TNR can be paraphrased in many different ways in the same language or can be translated into other languages.

TNRs Have Unique Logical Properties

As soon as the idea underlying the formal nature of every TNR — that is the simple synthetic proposition grounding the theory — was made clear, it was possible to prove analytically (mathematically) that only the *S of a TNR can determine any particular object, O, in a material context of facts by a π-mapping that connects S with that O and thus with the rest of the material world. As a consequence, the π-mapping of that S to that particular O generalizes to all similars exactly to extent of the similarity up to a limit of identity* — engaging Leibniz's principle of the *identity of indiscernibles* [89]. Moreover, only TNRs, among all the meaningful and potentially meaningful representational forms that exist, have the logical properties designated as *determinacy*, *connectedness*, and *generalizability*. *Therefore, only one or more TNRs can provide the necessary basis for the vesting of any meaningful sign system whatsoever with any discoverable trace of meaning.*

TNR-theory Is Not Tautologous

While it has recently been asserted by a critic/reviewer of an earlier draft of this paper that the initial proposition of TNR-theory, and, therefore, its proofs, are tautological, such an objection is easily refuted by empirically examining any TNR whatsoever. It does not matter at all which TNR in particular presents itself or which one might be arbitrarily selected. Every actual and meaningful representational system without exception by its intrinsic nature connects with the material world in a comprehensible and discoverable way through an *SπO* system of relations and thus, in principle and in fact, connects with all other TNRs — directly through their general semantic values and indirectly through their particular pragmatic connections with the material world. Also, only TNRs can adequately express or enable the association of any intelligible meaning with fictions, errors, lies, nonsense strings, or any degree of degeneracy up to and including a complete erasure of the last vestige of a representation. Therefore, every single TNR refutes the charge that the foundational proposition of TNR-theory is, or that ones derived from TNRs, are tautological [65], [66], [92]. They are not tautological nor do they enter the sort of "vicious circles" leading to the "antinomies" enumerated in the *Principia Mathematica* by Whitehead and Russell [93]–[95].

In fact it was proved much earlier, first by Peirce [62], and later by Tarski [63], [64] that all meaningful sign relations are parasitically dependent on those legitimately and competently judged to be true. That underlying principle of TNR-theory was also implicit in Aristotle's often translated axiom: "*Nihil est in intellectu quod non prius fuerit in sensu*" [there is nothing known by the mind that was not first known to the senses] [96, p. 112], [97, p. Book 3, Part 8]. Neither the claim nor its proofs are circular, but more than a few scholars seem to have at least implied that the truth of any ordinary representations that happen to be true must be either trivial and unimportant, or in fact tautologous, even entering a vicious circle.

Avoiding the "Vicious Circle" of Russell's Paradox

Peirce summed up the error of Russell [98] leading to "Russell's Paradox" — the most famous of the logical and mathematical "antinomies" [99] later discussed in the *Principia Mathematica* (Whitehead and Russell, [93]–[95]). Peirce wrote what "puzzles the Hon. Bertrand Russell in his *Principles of Mathematics* is whether a collection which has but a single individual member is identical with that individual" [96, p. 371]. Can an actually existing concrete entity be regarded as the abstract class to which it belongs? Is a class of dogs itself the same as the particular dog or dogs that it may contain? Or, can an abstract general representation, say a description of a person's particular habits, employment, title, or distinctive patterns of dress, be identical with that concrete particular individual person? In supposing that such propositions are meaningful, Russell entered a "vicious circle": to get into it, he chose to regard the semantic value associated with a general mathematical abstraction as the same sort of pragmatically real concrete entity that the abstraction might be used to represent on some particular occasion, or in any of the countless occasions where that singular and unique entity presents itself.

Russell conflated the concrete particular entity referred to by an abstract representation with the semantic value of that abstraction. In doing so, he failed to observe the rule laid down by Peirce that "being and being represented are completely different" [1, p. Draft D-MS L75, 382-387]. As Peirce argued very early in his published writings, whatever exists cannot be judged to be either true or false, it just is what it is [101]–[103]. If it could represent itself, that representation could not be false, but since whatever is present in reality, simply is whatever it is, it cannot present itself otherwise, so, it cannot be false to itself. However, representations that purport to be about material entities other than themselves — say, some distinct sequence of events or some other actual state of affairs — do introduce the possibility of falsehood as distinct from truth. But the raw states of the material world of space and time, just are as they are and cannot logically represent themselves other than they are. They cannot be false.

Meaning Derives Only from TNRs

Once the formal system of every TNR was clarified, it would become possible to prove the following series of inequalities [1] which form the basis for the depth hypothesis in this paper:

$$(S\pi O)_i > (S\pi \underline{O})_i > (S\underline{\pi} O)_i > (S\underline{\pi}\underline{O})_i > \underline{S}_i > \_i \qquad (1)$$

For any instance of a TNR that might present itself, we find a system of relations that may be summed up as $(S\pi O)_i$. If we conceal or remove any aspect of the *O* component so that the removed or hidden part must be imagined, we come to the form underlying every fiction that can be derived from $(S\pi O)_i$ to produce a somewhat less complete system of relations that may be designated as $(S\pi \underline{O})_i$, where the underlining suggests that some part of the represented *O* must be imagined. If all else has been held equal in the construction of such a fiction, it is clear that it must be less complete than the TNR from which it was derived.

Next we come to increasingly degenerated systems of representation designated as errors taking the form, $(\not{S}\ \pi\underline{\not{O}})_i$, where the slashes indicate that mistaking a fiction for a TNR, all else remaining unchanged, involves two further degeneracies. For one, some part of the *S* used to represent the *O* at issue is actually representing some other *O* and all or some of the *O* at issue is different from the one represented. Progressing to a lie derived from an error and intended to be mistaken for a TNR, a further degeneracy appears in the π-mapping as shown in $(\not{S}\not{\pi}\ \underline{\not{O}})_i$. Beyond that level of degeneracy, we come to the sort of nonsense shown in $\underline{\not{S}}_i$ where all that is retained is the surface form of the sort of *S* that might appear in a TNR.

The only further degeneracy that might occur to such a remnant is to erase part or all of it as suggested by $\__i$. The nature of the construction, in all such cases, is such that each element in the rank is necessarily less complete than the one preceding it. Moreover, having proved beforehand that no *S* can gain any determinate significance except through a valid π-mapping connecting it to some particular *O* in the material world the rank suggested in the above series of inequalities completely covers the range not only of all possible meaningful *S*-string/systems of signs, but it extends through the full range of possible nonsense strings and partial erasures up to the limit of complete annihilation of the *S*-string/system. The simplicity, completeness, and generalizability of the proofs of TNR-theory, as noted, may lead some readers to suppose that the system is so obvious that it cannot have any practical applications. That tempting inference, like the facile notion that TNR-theory might be tautologous, is also false.

Testing the Ranking of Symbol Systems

The abstract and completely general series of mathematical inequalities given above at formula (1) follows from the unique logical completeness of TNRs. The ranking of the meaningful elements of that series, $(S\pi O)_i > (S\pi \underline{O})_i > (\not{S}\pi\underline{\not{O}})_i > (\not{S}\not{\pi}\underline{\not{O}})_i$, omitting nonsense strings, $\underline{\not{S}}_i$ and complete erasures, $\__i$, is confirmed empirically by the order in which such systems are acquired by children as they systematically decipher the *S*-strings of any natural language.

Omitting details, milestones in normally progressing language development at the macro-level of the maturing individual from conception forward can be expressed approximately as in Figure 2. At the macro-level of cognitive-emotional-linguistic development, the normally developing child advances from (1) conception to (2) voluntary movements in the womb from the first trimester [104, pp. 12–26] and recognition of the rhythms of the native language [105]–[107]; (3) smiling by the third trimester [104, pp. 98–101]; (4) mapping mom's familiar voice to her unfamiliar face within a few minutes of mom's speaking to the neonate at birth [108]; (5) the normally developing baby by about three months of age can differentiate and produce distinct vowel sounds modeled by an adult [109]; (6) can produce syllabic (canonical) babble by about six months[110] and has acquired a substantial receptive repertoire of words within six to nine months after birth [111]–[114]; (7) produces a first recognizable word by about the first birthday [109], [115], [116]; (8) moves on to two-word constructions (and more) by about the second birthday [117]; (9) differentiates verbal pretending from TNR production by about the third birthday [118]; (10) selectively can correct known errors distinguishing them from pretend communications (fictions) by about the fourth birthday [119]; (11) roughly between the fifth and eighth birthday is able to explain verbally the difference between an error and a deliberate lie [120]; and (12) normally advances to handling the full complexity of adult-level discourse roughly between ages 12 and 18 [121].

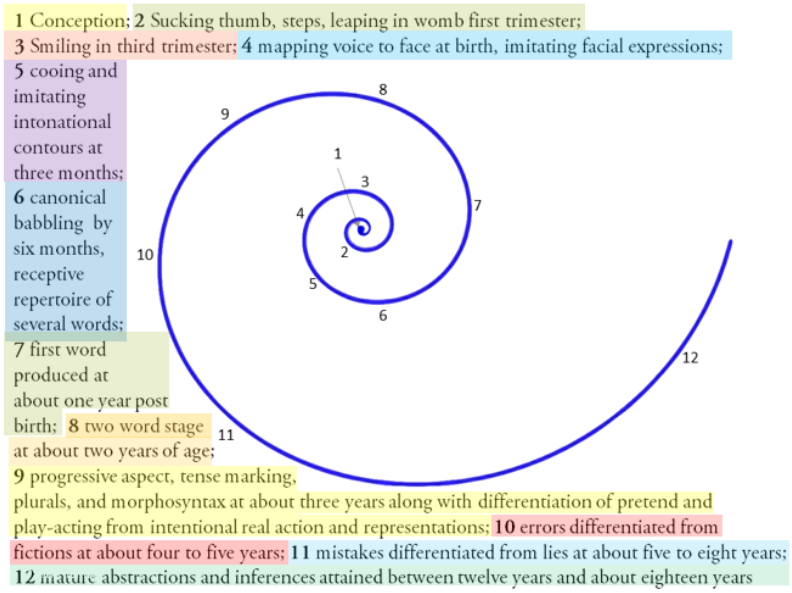

Figure 2. The growth spiral with certain empirically established milestones predicted by TNR-theory.

Empirically established milestones of the cognitive-emotional-linguistic development of the normally developing child conform as precisely as could be expected to the ranking of the meaningful systems by TNR-theory [1]. The normally developing child necessarily first comprehends and then later produces TNRs.

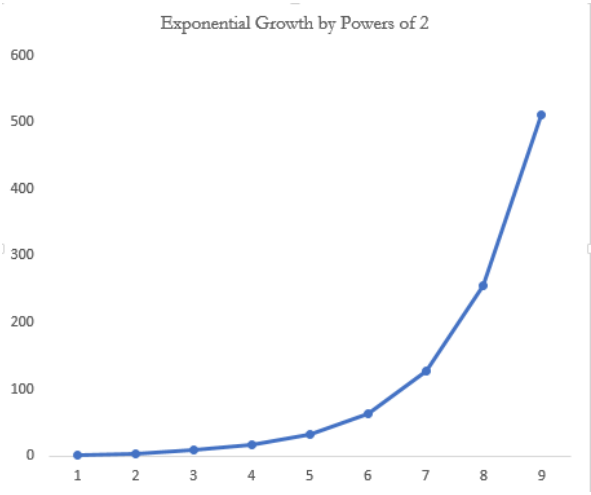

Figure 3. The develomental growth spiral unfurled as a curve hypothetically expressed as an exponential progression by powers of 2 of the number of cells increasing by mitosis.

The rate of progress through the meaningful linguistic strings in the series from TNRs, to fictions, errors, and lies (according to the inequalities in formula 1 above) differ greatly across normally developing children, *but the sequence described does not vary* [109], [115], [116].

Similar to the growth spiral for normal language development there is a micro-level spiral. As constructed in Figure 2, the macro-level growth spiral is hypothesized to approximate a Fibonacci sequence [122], but that hypothetical shape remains to be tested against empirical measurements. By contrast, the micro-level growth spiral must logically approximate growth by powers of 2 with a time-lapse roughly equivalent to the time between the cycles of mitosis that are initiated following conception. That progression, also, is nevertheless subject to experimental verification.

Disrupting Biological TNRs Causes Disease

Another hypothesis that follows directly from TNR-theory is that all morbid conditions affecting human beings from stress "disorders" [123], [124] to life-threatening infectious diseases [125], to poisoning events [81], [83], [126], or traumatic injuries of any kind [127], must involve the disruption of the body's biosignaling systems in some way. The *biosemiotic depth hypothesis* is framed in relation to what is known of the body's biosignaling systems and the many ways they can be disrupted. At the deepest level, throughout the body's development from conception to maturity, the most comprehensive, and best protected level of the representational systems are found in the nuclear DNA which, in view of its coherence and regulatory functions, governs mitochondrial DNA [128], the epigenetic systems, proteomic systems, and so forth all the way out to the body's most superficial epithelial cells. Those limits, from the surface of the skin to the nucleosome, define the sense in which "depth" is to be taken in this paper. In the final analysis, depth from a logical perspective must be a function of the number and density characteristics of the barriers to be penetrated or breached.

It may seem trivial at first to take note of the fact that the most superficial membranous container of the body at the level of the epithelium is also a container of many containers of containers. Yet it is evident that such a container has its origin at the level of the first pair of nucleated stem cells that initiate the development of the post-fertilization blastocyst to be implanted within another deeply embedded container of containers within the matrix. It is also obvious that the integrity and coherence of the whole, throughout the life span, depends at its deepest level on the governing systems in the organism's DNA deeply embedded at the level of the well-guarded nucleosome.

As we penetrate more deeply into the mysteries of that controlling level of biosemiosis, in the smaller and smaller containers within the body, as we approach spaces near the diameter of a water molecule at about 1.9 to 2.75 Ångströms [129], some nontrivial surprises come to light. For instance, biochemists may be surprised by the mathematical fact that the surface area within the smaller and smaller containers becomes larger and larger as the entities become smaller and smaller up to a limit of whatever the smallest containing space may turn out to be. In living organisms that limit is believed to be near the size of the water molecule which can form a container, a hydrological shell, one or more water molecules thick, containing a maximum space of about 3 nm in diameter [129]–[134].

Unsurprisingly, water molecules and their dynamic interactions with each other and with other molecules, seem to be crucially involved in nearly every conceivable biosemiotic interaction approximating the nano-level [131], [132], [135], as also seems to hold in the electro-chemical transmissions of our nerves. Because of the almost unlimited increase in the inner and outer interfacial surface areas of membranes contained within and containing increasingly smaller and smaller containers, molecular entities, and atoms, the extent to which the nano-level and sub-nano-level interactions at those surfaces impact biosemiotic processes may be difficult to over-estimate. Adding to the real physical and biochemical complexities in such micro-domains is the fact that the processes occurring within them typically take place in a time frame ranging from about a micro-second down into the pico-second range [136], [137] and faster [131], [138]–[140]. All of the foregoing should be kept in mind as we examine the essential elements of the very simple, though abstract, mathematical theory of the valid kind of representations, TNRs, on which all coherent communications absolutely depend.

Analogous to Child Language Development

As suggested in Figures 1a and 2a, at its basis, biosemiosis is remarkably similar in its formal dynamics and progress over time to the growth and development of the natural language systems that are acquired by normally developing children all over the world [60], [61]. Biosemiotic interactions also bear some analogy to the artificial language systems deployed in computing. Computer users know about bugs and viruses that can result in anything from temporary inconveniences to the notorious "blue screen of death" which may still precede unrecoverable system failures in some computers. The extreme opposite of the corrupted strings of signs leading to breakdowns in artifacts, as well as to morbidities and mortality in living organisms are the successful communications grounded in valid strings of signs that are essential to our health and well-being. The simplest and most easily understood successful interactions are those that are first understood and later produced by the normally developing human infants that grow and mature into speakers of one or several natural languages.

Breakdowns Produce Disorder, Disease, and Death

In biosemiosis, partial breakdowns statistically and actually must trend toward disorder and disease [78], [79], [82], [141], [142]. Complete breakdowns end in death. In between, the nature of the breakdown in question can be explained by determining the nature, timing, and extent of the injuries resulting in the breakdowns. Of particular importance to the breakdowns leading to disorders, as will be explained, is their place in the unfolding developmental narrative of the organism as defined in the series of inequalities introduced above. As already shown, in natural language acquisition, the inequalities of that series define key milestones of the child's growth spiral as discussed in view of a growing body of research reviewed by Oller et al. [118], [143]. Perhaps more importantly, they also define a rank order in the severity of the degrees of incompleteness in (or damage done to) genetic, epigenetic, and proteomic messages in biosemiotic systems as described by Oller [66].

In morbidities, biosemiotic interactions, are disrupted in key respects. For instance, in the autoimmune disorder systemic lupus erythematosus (SLE), biosemiotic message systems are believed to be damaged in a variety of ways. Among the implicated toxins to be considered below are aluminum compounds [81], [144] and biocides [145]–[154].

As we seek to understand better how the exceedingly complex interactions in the body's biosemiotic systems work, we are forced to support those who

reject the traditional interpretation of the "central dogma" of molecular biology [22]. The dogma was correct in asserting that components of DNA map through RNAs to protein sequences in building organelles, cells, tissues, and the organ systems of our bodies, but it was incorrect in suggesting, as many have understood it, that protein sequences have no power to communicate with DNA [40], [66], [76], [155], [156]. The process of biosemiosis in this regard is now known to be vastly more complex and more dynamic than formerly supposed [23].

In normal development, biosemiosis is a dynamic narrative-like truth-balancing act. It unfolds as a story where certain events must and do occur ahead of others. Because certain events are prerequisite to ones that follow, interventions that disrupt such sequences, or that fail to take account of the necessary progression, are apt to fail. Along the way, at the molecular level, the meanings dynamically present in the intact DNA molecule communicate through a great diversity of RNAs which also interact with each other, and with a multitude of protein strings. In the best case scenario, information in DNA governing the construction of protein strings is communicated faithfully through RNAs and true reports are delivered back to DNA concerning progress in the unfolding narrative expressed as proteins, organelles, cells, and so forth develop in the maturing individual [40].

Disruptive Factors

Factors that can reduce biosemiotic TNRs to errors, lies, and nonsense include radiant energy, chemical toxins, pathogenic invasions, and their interactions. Such factors can disrupt communication between DNA, RNAs, and protein systems. Some medical interventions and experimental genetic modifications can also result in catastrophic breakdowns in biosignalling systems ending in the death of individual patients [157]–[159]. Similarly, both living individuals and future generations can be adversely affected by damage to nuclear and/or mitochondrial DNA [128], [160], [161]. However, mtDNA is evidently governed and subject to successful interactions with nuclear DNA [128], so the latter, effectively resides at the deepest level of the body's biosemiotic systems.

We hypothesize that the depth of penetration of any injurious factor into those biosemiotic systems — *all else being held equal*, including nutritional and environmental parameters as well as the progress of the organism(s) on the normal growth spiral — can serve to differentiate morbidities in general with autoimmune disorders and SLE in focus. On such a basis, we can show that systemic autoimmunities involve a level necessarily deeper than allergies but not so deep as tumorigenesis which itself is not quite so deep as any metastatic cancer. All else being held equal, the hypothesis explored here is that the depth of penetration of damage to (corruption of) biosemiotic systems is pathognomonic. More specifically, it provides a possibly useful basis for differentiating the major classes of known morbidities.

Depth Defined by Position in the Growth Spiral

The most fundamental of the biosemiotic texts conveyed across generations must first be loaded into the parental gametes during the vulnerable multistage process of meiosis [162]. Then, after successful fertilization and conception have taken place, the initial DNA text must be replicated billions of times through similarly vulnerable cycles of mitosis [163]. From conception forward in the developmental spiral, many trillions of successful communications within the developing embryo and between it and its prenatal and postnatal environments must take place [79]. Along the way, gene regulating networks of vast complexity develop and record progress in the DNA of the individual through differential methylation patterns [40], [164], [165].

Whereas all nucleated cells contain the entire dynamic genome of the individual, the differential activation of its components depends on valid communications within the developing organism also taking account of the material environment in which the particular DNA molecule itself, the nucleated cell, the tissue, organ, and the whole body is located. All this must be determined by something like a universal global positioning system that constantly updates the cell's material coordinates within the developing body [166]–[168] relative to the unfolding narrative that represents the whole organism.

It is now clear, and perhaps unsurprising, that the genome is far more dynamic and interactive than it was initially conceived to be by Watson and Crick (1953). Given the known interactions between the dynamic DNA and environmental factors such as the availability of methyl compounds in the diet [155], it is believed that differential methylation throughout the life cycle of the organism, and demethylation at two critical stages, are playing important roles in maintaining the fidelity of the unfolding narrative of the growth spiral [169], [170]. Extensive demethylation during gamete loading and again during the earliest stages of embriogenesis are probably essential to the initiation of well-formed stem cells in the newly developing organism [164], [171].

From the vantage point of TNR theory, it appears as

though much of the history of the distinct narratives of the child's father and mother (up to the time of the meiotic formation of their gametes) may be erased through large scale demethylation in the initiation of the newly developing narrative in the DNA of the child [169]. It is supposed that error corrections are occurring in these large scale demethylations. Likewise, corrections are believed to be occurring in the huge information exchanges taking place during the syndesis phase of gamete loading that must occur during the meiosis of gamete cells in both parents [172]. However, because of the complexities of the highly articulated texts upon which the processes of methylation and demethylation depend, they are especially vulnerable to disruption by radiant energy, toxins, pathogens, and their interactions. Therefore, survival and normal development depends on a valid DNA text correctly transmitted through meiosis in haploid chromosomes from both parents, interpreted and conjugated at the time of fertilization and conception, and from there forward successfully replicated and differentiated through many cycles of mitosis as the organism progresses on the growth spiral.

In mature adults, at the deepest level, gametes are protected by membranous barriers such as the blood testis barrier (BTB) in the male [173], [174] and by a difficult to penetrate membranous barrier in the oocyte of mammalian females [175]. After impregnation the placental barrier helps to guard the developing prenate from damaging metals, viruses, and nanoparticles [176]–[181] and the DNA of the developing individual is encased inside a difficult to penetrate nuclear envelope that must first be disassembled and then reconstructed as two new envelopes are constructed in cell mitosis [182].

Thus, nuclear DNA throughout the life of the organism, though protected by membranes differentially resistant to permeability from outside the epidermis through the epithelial tissues and inward to the deepest level of the nucleolus, becomes particularly vulnerable to damage from toxins and/or attack by pathogens during mitosis. Nuclear DNA has long been known to have special protection by microparasols of melanin shielding the nucleus of epidermal cells from ultra-violet light [183]–[186]. Melanin is not only involved in protection from radiation at the surface but also serves as an antioxidant and chelator of metals and certain toxicants [187] and in the form of neuromelanin is known to be vital to the health of the brain [188]–[190].

Immune Defenses from the Beginning?

As development progresses, the typical prenatal human advances, as suggested in Figure 1, through an amazing series of micro-level biosemiotic milestones somewhat analogous to ones that can more easily be identified at a macro-level in the growth spiral of the whole organism from conception through birth and beyond. From very early on, if all goes well, at the molecular level, the maintenance, repair, and immune resources inherited mainly from the microbiome of the mother seamlessly transition to the rapid development of an increasingly sophisticated capacity of the neonate's self to differentiate its own cells and their parts from non-self entities with the aid of major-histocompatibility/human leukocyte antigen class I (MHC/HLA I). It is extracted from self –DNA and arranged on the surface of cells in complex stereoscopically defined shapes used to mark essentially all of the nucleated self-cells throughout the body. The genomic complex in which that self-identifying information is initially expressed, according to Arango et al., has the distinction of being "the most polymorphic gene cluster of the mammal genome" [191, p. 82].

We can think of that self-defining information in MHC/HLA I at a micro-level as like a birth certificate showing citizenship, a valid address, and employment documentation to identify individual cells, their functions, and authorizations in the rapidly changing contexts of the whole body as it progresses on the growth spiral. Such information is essential to nutrient transport, repairs when needed, defenses against potential invaders, waste disposal, travel (if allowed) across membranes, cells, tissues, and organ systems within the body. As the child grows an increasing array of non-self entities will be encountered, some of them potentially hostile to the survival of the self. According to traditional and current theories of immunity, some non-self entities will already have been singled out for marking by MHC/HLA II through the child's IgG inherited from its mother before birth [176], from mother's microbiome after birth [mostly by vaginal birth] [192], and from mother's IgA if the child happens to be breastfed [193]. However, recent research has shown that the stem cells in umbilical cord blood already possess the genetic requirements for the production of immunoglobulins [194] and contrary to the long-standing view that only B cells can produce IgG and IgA, there is persuasive evidence that mature epidermal cells can do so as well [195]. All of these resources are important to the biosemiotic interactions between the self's maintenance, repair, and defense systems and the non-self entities (along with their peptide components) that the self needs to monitor. Some of those non-self entities or components will need to be captured, interrogated, quarantined, or possibly destroyed and expelled.

Throughout the development and growth process, corruptions of biosemiotic strings especially those that involve MHC/HLA II can result in the sort of confusion where the defense systems of the body mistake harmless antigens for dangerous pathogenic invaders, resulting in allergic reactions which in extreme cases may be fatal [196], or, with additional damage, may result in developmental autoimmune diseases targeting self-peptides, cells, tissues, and organs for immune attack and destruction [197], [198]. When that additional damage to biosemiotics systems occurs, the individual transitions from allergy, potentially fatal if carried to the extreme of anaphylaxis [199], to systemic autoimmune disease where immune defenses are turned upon self-peptides, cells, and tissues [197], [198].

In allergies and in the deeper level autoimmune disorders, disrupting factors such as radiant energy, toxicity, pathogenic impact from viruses, for instance, and their interactions, seem to be involved in causation [144], [200]–[202]. Even something as subtle as seasonal changes in the external environment seem to be impactful in these types of disorders [200]. Nevertheless, in spite of all the maintenance, repair, and defense systems in place, damage to biosignaling systems is inevitable and morbidities occur at multiple levels. Necessary interactions are, as noted earlier, susceptible to injuries from toxins [81], [203]–[210], trauma from radiant energy (particles or waves; [211]), as well as interactive injuries that may spill over from pathogens [212]–[217], and even ruptured membranes owed to bruising of parental gametes can contribute to inappropriately extreme immune responses [218].

Whenever during the normal course of development, the self is attacked by one or more disease agents that are regarded by the body's immune defense systems as capable of rapidly replicating so as to present a potentially mortal threat, provided authorization is granted in consultation with the body's own DNA, the self can perform something resembling mobilization for global warfare through the little-understood MHC/HLA III which interacts with classes I and II (and also the still higher and even less understood MHC/HLA IV [219]). When authorized, the complement cascade, in ways not yet well understood, can develop and equip defenses involving all three classes of MHC/HLA along with an enhanced capacity for rapid clearing of destroyed pathogens and debris from collateral damage after the conclusion of something like a global emergency mobilization [220]. Given the seriousness of a complement cascade in response to one or more pathogenic conditions, it is unsurprising that the research confirms the expectation that extreme autoimmune flare ups commonly involve misunderstood signals inappropriately invoking the complement cascade [221]–[223].

Ranking Morbidities by the Depth Hypothesis

In the light of TNR-theory, it is possible to differentiate and rank morbid conditions according to the depth of penetration into the biosemiotic regulating systems. Autoimmune diseases require injuries that interfere with TNR strings involving the MHC/HLA systems at class II and above. They fall short, however, of the disruption of cell replication and mitosis which can lead to tumorigenic morbidities and with further corruption to metastatic cancers. In fact, the distinction between autoimmune disorders and cancers points the way toward a more comprehensive and detailed differentiation of morbidities in general according to the biosemiotic depth hypothesis:

radiant energy damage < *damage from macrolevel collisions* < *toxic injuries* < *parasitic or pathogenic intrusions* < *collateral damage by defense systems* < *allergies* < *autoimmune disorders* < *prion diseases* < *tumorigenesis* < *metastatic cancers*

The hypothesized scale, in theory *holding all else equal*, ranges from damage at the surface of the body to penetration of the nuclear envelope enabling corruption of mitotic processes leading at an extreme to metastatic cancers. Of course, in addition to depth of penetration into the body's biosemiotic regulating systems, it is also necessary to take account of the timing of damage with respect to the developmental growth spiral. All else being equal, biosemiotic damage occurring earlier in the growth spiral (unless it can be repaired), must be ranked as more harmful than later damage on account of the proportion of self-cells to be impacted downstream [149], [224]. Similarly, if timing and the extent of damage to particular self cells is held equal, earlier and therefore deeper penetration of the damage into regulating systems, *provided it cannot be repaired*, the more harmful it can be downstream. With respect to CNS damage, earlier injuries are commonly repaired more effectively than seemingly comparable damage later in development [225]. However, paradoxically, depending on the timing, extent, and interactive nature of regulatory system damage similar traumatic events during early neuronal migration and pruning may in some instances, e.g., in autism spectrum disorders, be more damaging in children than in adults [141, pp. 193–194]. Nonetheless, taking all the foregoing into account, the most dangerous morbidities for the developing individual and future progeny in the long run must be those that involve penetration of the nuclear envelope containing the crucial nuclear DNA and the gene regulating

networks that it superintends.

Approaching and Penetrating the Nuclear Envelope

Given the vital importance of regulating systems upon which the maintenance, repair, and defense of the individual and future offspring depend, it is noteworthy that the deepest level of biosemiosis within the nuclear DNA, and in some parts of the central nervous system, is not only shielded from damaging radiation and toxins by melanin [183], but is also protected from pathogenic corruption by the network of the body's immune defenses. At the surface of the cell, with the assistance of immune cells, at optimal performance MHC/HLA peptides in classes I and II enable a sharp differentiation of self-cells from identified pathogens before the pathogens have a chance to proliferate and possibly invade the interior of the body and its self-cells, or if an invasion should occur, the self-cell can hopefully be dismantled and the pathogen destroyed before it can replicate and spread.

However, damage to the communication systems involved in the differentiation of self-cells from foreign entities, can increase the likelihood of errors where a harmless surface peptide is mistaken for a class II mark of an invader to be attacked and destroyed by immune cells. This is the classic definition of an allergy. Should the peptide happen to trigger the basophil/mast cell degranulation a life-threatening anaphylactic event may occur [226], [227]. However, for allergies to progress to systemic autoimmune disease, additional corruption must occur at the level of the antigen presenting cells that respond to the mistaken class II marking thus leading to allergic reaction. In the case of systemic autoimmune disease, class I marking on self-cells must be mistaken as class II for many cells in one or more tissues and organ systems of the self. Yet, such confusion remains still outside the self-cell replicating systems guided by systems normally well-protected within the nuclear envelope.

Prion diseases involve oxidative stress of the endoplasmic reticulum just outside the nucleus of self-cells where major protein synthesis takes place [228]–[231], along with damage to the cell's capacity to lyse misfolded or otherwise aberrant proteins [232]. Corruption of nucleolin inside the nuclear envelope is hypothesized to be necessary for tumorigenesis [233], and at a still deeper level, corruption must occur inside the nucleolus itself, in order for metastatic cancer to develop. For instance, certain factors that would normally halt the growth of a benign tumor, and/or the apoptosis or immune destruction of existing defective cells, must be deactivated or destroyed [234]–[239].

To account for at least some of the vast host of injuries that are possible to the highly articulated biosemiotic processes of the body, the increased presence of certain toxins, among them Monsanto's glyphosate (RoundUp) along with other environmental toxins are increasingly being scrutinized. At the level of proteinogenesis, some researchers have argued that non-coding amino acids such as beta-methylamino-L-alanine (BMAA, similar to serine; [240]–[244], canavanine (similar to arginine; [240], [241], [245], and glypohosate (similar to glycine; [145], [246], [247] can lead to erroneous interpretations and are, in some instances, misincorporated into necessary proteins [148], [248] resulting in deformed strings that lead to disease conditions including systemic autoimmunities [245], [249]–[252]. However, the relevant research, at least in the case of BMAA shows that wholesale misincorporation of non-protoeinogenic amino acids is not easily achieved in living cells [253], [254]. BMAA misincorporation is resisted even in bacteria [242], though misincorporation can be humanly engineered and achieved efficiently *in vitro* under special conditions [251], [255], [256].

It is still uncertain when and where misincorporation can occur *in vivo*, though some research suggests that misincorporation of canavanine in place of arginine may happen in the mitochondrial ribosome causing normal protein synthesis to stall [257]. Because misincorporation of BMAA, for one, is blocked in many cases by editing taking place in the mitochoindria [258], [259], a minor level of excitotoxicity of non-coding BMAA, rather than its misincorporation into proteins [243], [254], is believed by some to be causing cell death and contributing to systemic autoimmunities [260], [261].

At any rate, if misincorporation of any nonproteinogenic amino acids ever does occur because of their resemblance to some proteinogenic counterpart, e.g., a molecule of phosphonated glycine (*N*-phosphonomethyl-glycine) could mistakenly be substituted for an achiral glycine molecule in a protein string, as argued by Samsel and Seneff [145], [247] and as described for the particular case of *N*-methyl-dextral-aspartate glutamate receptors by Cattani et al. [148, p. 72], such an erroneous misincorporation would constitute a classic biochemical example of a mistaken identity error, taking the form $\mathcal{S}\pi\underline{\emptyset}$, and subsequently impacting dependent biosemiotic cascades on which the health of consumers of the impacted food crops depend. In the meantime, although the results are disputed by promoters, it appears that glyphosate may be causally associated with loss of fertility, autoimmune diseases, prion disease, and cancers [147], [148], [150], [151], [248], [262]–[268].

Some Specific Implications

One of the implications of the foregoing for the etiology of autoimmune disorders as distinct from cancers suggests why Familial Mediterranean Fever (FMF), and also SLE, might reduce the likelihood of cancers in the persons affected by them [269]–[271]. A straightforward observation that flows from the ranking of morbidities iterated in the previous section is that hyperactive autoimmune targeting of self-cells is as likely to eliminate early developing tumors as any other cells. Therefore, the rate of cancers in persons with such conditions should be, and apparently is, reduced [269]. It is also possible as suggested by Brenner et al. that treatment protocols for autoimmune disorders may have a prophylactic effect in respect to cancers. Furthermore, given that the kinds of damage to DNA that can impact cell replication must take place at the level of mitosis (or deeper in the cell's nuclear DNA) rather than in the MHC/HLA I surface-marking of self-cells, and MHC/HLA II marking of foreign entities, if the autoimmunity happens to engage MHC/HLA III and above in a generalized inflammation attacking the organ systems of the self, tumorigenesis and the possibility of metastatic cancers would likely be pre-empted. A more subtle implication of TNR-theory is that the intentionality, rhetorically suggested tongue-in-cheek by Rida et al. [272] with respect to the deceptive character of cancers learning to be "good at being bad", may be an over-reach.

What mainly distinguishes cancers from allergies and the more serious systemic autoimmune conditions such as SLE, is the power of replication. However, none of the devious twists and turns of metastatic cancerous growths require the foresight that TNR-theory shows must accompany intentionality and self-consciousness in the production of a deliberate lie. Those attributes along with the power to consider possible future outcomes are essential to the child's development of the capacity to differentiate errors from lies. The person lying must consciously intend to deceive the person lied to and replication of the lie itself is essential if that is to happen. Thus, the essential characteristic that distinguishes cancers from autoimmune conditions is the damage to replication systems required for the production of tumors. But thoughtful foresight is not required for cancerous cells. Backing off a step, however, systemic autoimmune conditions seem to entail intentional pursuit of what are perceived by the body's immune cells as enemies. The conditions we loosely term "allergies" involve the body's defense systems mistaking relatively harmless entities for potential invaders and mounting an attack based on that mistake. The potential harm of such an error is augmented if and when self-cells are mistaken for intruders and the "allergy" transitions to autoimmunity.

Concerns with Aluminum Adjuvants

Elemental aluminum is well-established as a toxin to biological systems with a particularly negative impact on the nervous system across the lifespan (for review, see [81]. The toxic actions induced by aluminum can be both acute and chronic. While acute effects are now rare, chronic exposure has been linked to Alzheimer's disease in middle and old age [141], [273], [274] and developmental disorders in children [203], [273], [274].

While there is now little doubt about the potential toxicity of aluminum, arguments against this view tend to take one of two main tacks. The first is that because aluminum is so common in the biosphere, its effects must be benign. However, this view disregards the history of aluminum exposure. Basically, most aluminum on Earth has been bound up in various insoluble forms such as bauxite, rendering it largely inaccessible to organisms. The extraction of aluminum beginning in the 19th century changed the amount of free aluminum in the biosphere and its subsequent widespread use virtually assured that it has entered our lives at many levels, from food processing, deodorants, many medicines, and as an adjuvant in many vaccines. The latter leads to the second critique that since the amount in vaccines is low compared to the current overall ubiquity of aluminum in the environment that it cannot be harmful. Some groups, notably, the Children's Hospital of Philadelphia "Vaccine Education Center" according to their previous website, had speculated that since aluminum can be found in the developing fetus that it must therefore be an "essential" element.

This second critique is also fundamentally flawed since the "small amount" of aluminum in vaccines is there because it can trigger an enhanced immune response with, or without, the presence of some fragment of whatever pathogen(s) the vaccine purports to target for destruction. An additional problem is that those voicing this critique fail to realize that the pharmaco-kinetics of aluminum in the body depend to a great extent on the route of administration. For example, the fate of aluminum ingested is quite different from aluminum injected subcutaneously or into muscle. To assume, as some do, that vaccine adjuvant aluminum can stimulate the immune system, the whole purpose of adjuvants in general, without impacting the central nervous system (CNS), especially during rapid early development, is shortsighted. This argument also ignores a wealth of emerging information on immune-nervous system interactions at various stages of life, but most prominently in early development

[144], [275]–[279].

The above then are some of the problems with aluminum adjuvants: they are not inert in the body, they travel into the CNS through a number of carrier systems, and they have the capacity to induce neurotoxic actions once there [273]–[275]. The main problem, however, is that aluminum disrupts valid TNRs in biosemiosis. In particular, aluminum adjuvants in vaccines, for example, on account of their intentional presentation to the body's defenses, not only induce errors in biosemiotic systems, but qualify as deliberate efforts to misinform the body's immune defenses through a carefully constructed, biochemical deception. Although aluminum is itself antigenic, it has no power to present any valid signal concerning potential invading pathogens to the immune system. It is certainly not any one of the pathogens that the immune system is equipped to protect against. As a result, repeated presentations can only create confusion in the targeting of legitimate pathogens while further disrupting biosemiosis and, as the research shows, the CNS.

Aluminum presents an intentional deception (a lie) when it inexplicably appears in various organs and the lymphatic system along with partial viral or bacterial fragments that are supposed to be the informative components of one or more vaccines. Those pathogenic components also are deceptive insofar as they fall short of the nature of the actual pathogens they are supposed to trick the immune system into arming up against. As a result, the body's semiotic systems are attacked by plethora of deceptions by deliberately incomplete, attenuated or morbid pathogens, at the same as its defense communications are being disrupted by the adjuvant intended to introduce something akin to panic in the body's immune response. The consequence, if repeated often enough, is increasingly likely to be dysregulation which is almost a classical definition of autoimmunity. In turn, when the immune system is undergoing rapid development in infancy and early childhood, it is axiomatic that biosemiotic confusion will impact the CNS where the greatest damage occurs. If the organism survives their initial appearance, errors in biosemiosis and neural development are likely to become magnified through successive stages of development as they are passed from one generation of cells to the next through mitotic divisions.

Conclusions

The growth spiral of normal child development — marked by cognitive, emotional, and especially linguistic advances — is similar in important respects to biosemiotic developments from the molecular level upward. Success in all such developmental advances depends on TNRs correctly expressed and interpreted. Morbidities, including systemic autoimmune disorders, with systemic lupus erythematosus (SLE) as a case in focus, can be differentiated by the depth of penetration of damaging factors into the various biosemiotic systems on which health and well-being depend. It is suggested that theories of and research into the etiology of such morbidities in general, and of autoimmune diseases in particular, can be guided by the examination of factors known or suspected of damaging the critical biosemiotic systems of the body. In the case of SLE, aluminum compounds, particularly adjuvants in some vaccines, and certain biocides used with genetically modified crops destined for farm animals and human consumers of them, are known to produce damage leading to disease conditions.

Moreover, discerning the depth of the damage to biosemiotic systems required to produce allergies as contrasted with the more serious systemic autoimmune disorders, prion diseases, and cancers, we believe, may contribute to a better understanding of morbid conditions in general. Specifically, considering the nature and ranking of the biosemiotic systems impacted in systemic autoimmune disorders as contrasted with metastatic cancers suggest a straightforward, even obvious, hypothesis to explain the reduced likelihood of metastatic cancers in persons with a systemic autoimmune disorder. Because metastatic cancers require the corruption of replication systems at the biosemiotic level of nuclear DNA, whereas autoimmunity only requires the corruption of more superficial strings at the level of MHC/HLA I and II, as expressed at the surface of cells, the deeper damage necessary to cause cancers is pre-empted in self-cells destroyed by autoimmune disease and, for the same reason, is statistically less likely to occur elsewhere in a body impacted by a generalized systemic autoimmune disease.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. The authors are employed in public university systems in the US and Canada, respectively.

Declaration of Conflicting Interests: The authors declare that there are no current conflicts of interest with respect to this paper. The second author, however, wishes to disclose that certain of his laboratory projects, of which this project is not one, have received funds from the Children's Medical Safety Research Institute and that he is a former Chair of the Scientific Advisory Board of that organization.

Acknowledgments

The authors are grateful to various readers who have helped to improve this paper, especially Dr. Stephanie Seneff and Dr. Robert M. Davidson. The ideas expressed here, however, and any remaining errors are our own.

References

1. B.-O. Kueppers, "The nucleation of semantic information in prebiotic matter," in Quasispecies: From Theory to Experimental Systems, vol. 392, E. Domingo and P. Schuster, Eds. Cham: Springer Int Publishing Ag, 2016, pp. 23–42.
2. P. Schuster, "Increase in complexity and information through molecular evolution," Entropy, vol. 18, no. 11, p. UNSP 397, Nov. 2016. https://doi.org/10.3390/e18110397
3. P. Schuster, "Molecular evolution between chemistry and biology," Eur. Biophys. J. Biophys. Lett., vol. 47, no. 4, pp. 403–425, May 2018.
4. Y. Zhong, "A theory of semantic information," China Commun., vol. 14, no. 1, pp. 1–17, Jan. 2017.
5. S. Kozyrev, "Biology as a constructive physics," P-Adic Numbers Ultrametric Anal. Appl., vol. 10, no. 4, pp. 305–311, Oct. 2018. https://doi.org/10.1134/s2070046618040076
6. S. Chatterjee and S. Yadav, "The origin of prebiotic information system in the peptide/RNA world: a simulation model of the evolution of translation and the genetic code," Life, vol. 9, no. 1, p. 25, Mar. 2019. https://doi.org/10.3390/life9010025
7. M. Barbieri, "Code Biology, Peircean Biosemiotics, and Rosen's Relational Biology," Biol. Theory, vol. 14, no. 1, pp. 21–29, Mar. 2019. https://doi.org/10.1007/s13752-018-0312-z
8. J. Uexkull, "The theory of meaning," Semiotica, vol. 42, no. 1, pp. 25-, 1982.
9. D. Favareau, "The biosemiotic turn part 1: a brief history of the sign concept in pre-modernist science," Biosemiotics, vol. 1, no. 1, pp. 5–23, Apr. 2008. https://doi.org/10.1007/s12304-008-9010-8
10. G. Katz, "The hypothesis of a genetic protolanguage: an epistemological investigation," Biosemiotics, vol. 1, no. 1, pp. 57–73, Apr. 2008. https://doi.org/10.1007/s12304-008-9005-5
11. M. Barbieri, "Biosemiotics: a new understanding of life," Naturwissenschaften, vol. 95, no. 7, pp. 577–599, Jul. 2008. https://doi.org/10.1007/s00114-008-0368-x
12. M. Barbieri, "A short history of biosemiotics," Biosemiotics, vol. 2, no. 2, pp. 221–245, Jul. 2009. https://doi.org/10.1007/s12304-009-9042-8
13. M. Barbieri, "From biosemiotics to code biology," Biol. Theory, vol. 9, no. 2, pp. 239–249, Jun. 2014.
14. E. Fernandez, "Taking the relational turn: biosemiotics and some new trends in biology," Biosemiotics, vol. 3, no. 2, pp. 147–156, Aug. 2010. https://doi.org/10.1007/s12304-010-9084-y
15. P. Cobley, "Codes and coding: Sebeok's zoosemiotics and the dismantling of the fixed-code fallacy," Semiotica, vol. 198, pp. 33–45, Feb. 2014. https://doi.org/10.1515/sem-2013-0100
16. K. Kull, "Four ages of understanding: the first postmodern survey of philosophy from ancient times to the turn of the twenty-first century," Chin. Semiot. Stud., vol. 12, no. 3, pp. 341–349, Aug. 2016. https://doi.org/10.3138/9781442675032-007
17. D. Martinelli, "Thomas Albert Sebeok and semiotics," Chin. Semiot. Stud., vol. 12, no. 3, pp. 387–393, Aug. 2016.
18. D. Bardos and G. A. Zemplen, "The shape of biology to come? The account of form and form of account in hoffmeyer's biosemiotics," Tradit. Discov., vol. 43, no. 1, pp. 32–50, Feb. 2017. https://doi.org/10.5840/traddisc20174316
19. T. Maran, A. Sharov, and M. Tønnessen, "The first decade of <emphasis type="italic">Biosemiotics</emphasis>," Biosemiotics, vol. 10, no. 3, pp. 315–318, Dec. 2017. https://doi.org/10.1007/s12304-017-9310-y
20. C. Woese, The Genetic Code the Molecular basis for Genetic Expression. New York: Harper and Row, 1967.
21. M. Yčas, The Biological Code, First Edition edition. Amsterdam: North Holland Publishing Company, 1969.
22. F. H. C. Crick, "Central dogma of molecular biology," Nature, vol. 227, no. 5258, pp. 561–563, Aug. 1970. https://doi.org/10.1038/227561a0
23. F. H. C. Crick, "The genetic code," in What Mad Pursuit: A Personal View of Scientific Discovery, New York, NY: Basic Books, 1988, pp. 89–101.
24. E. N. Trifonov, "The multiple codes of nucleotide-sequences - viewpoint," Bull. Math. Biol., vol. 51, no. 4, pp. 417–432, 1989.
25. M. Barbieri, Ed., Introduction to biosemiotics: the new biological synthesis. Springer Netherlands, 2007.
26. K. Konopka, "Sequences and codes: Fundamentals of biomolecular cryptology," in Biocomputing Informatics and Genome Projects, D. W. Smith, Ed. San Diego, CA: Academic Press, 1994, pp. 119–174. https://doi.org/10.1016/b978-0-08-092596-7.50008-3
27. L. E. Kay, "Who wrote the book of life? Information and the transformation of molecular biology, 1945-55," Sci. Context, vol. 8, no. 4, pp. 609–634, 1995.
28. O. Popov, D. M. Segal, and E. N. Trifonov, "Linguistic complexity of protein sequences as compared to texts of human languages," Biosystems, vol. 38, no. 1, pp. 65–74, 1996. https://doi.org/10.1016/0303-2647(95)01568-x
29. W. Nöth, "Biolinguistics and biosemiotics," in Biosemiotic Perspectives on Language and Linguistics, vol. 13, E. Velmezova, K. Kull, and S. J. Cowley, Eds. Cham Heidelberg New York Dordrecht London: Springer, 2015, pp. 151–168. https://doi.org/10.1007/978-3-319-20663-9_8
30. S. T. Zolyan and R. Zhdanov, "Genome as (hyper)text: From metaphor to theory," Semiotica, no. 225, pp. 1–18, Nov. 2018. https://doi.org/10.1515/sem-2016-0214
31. M. García-Sancho, "The rise and fall of the idea of genetic information (1948-2006)," Genomics Soc. Policy, vol. 2, no. 3, Dec. 2006. https://doi.org/10.1186/1746-5354-2-3-16
32. U. E. Stegmann, "'Genetic coding' reconsidered: an analysis of actual usage," Br. J. Philos. Sci., vol. 67, no. 3, pp. 707–730, Sep. 2016. https://doi.org/10.1093/bjps/axv007
33. C. R. Woese, The Genetic Code: the Molecular basis for Genetic Expression. New York, NY: Harper & Row, 1967.
34. M. Barbieri, "What is code biology?," Biosystems, vol. 164, pp. 1–10, Feb. 2018.
35. M. M. Rakocevic, "The cipher of the genetic code," Biosystems, vol. 171, pp. 31–47, Sep. 2018. https://doi.org/10.1016/j.biosystems.2018.05.009
36. G. Gamow, "Letter from George Gamow to Linus Pauling. October 22, 1953. - Correspondence - Linus Pauling and the Race for DNA: A Documentary History," 22-Oct-1953.
37. G. Gamow, Possible mathematical Relation between Deoxyribonucleic Acid and proteins. København: Munksgaard, 1954.
38. M. J. Simons and A. J. Pellionisz, "Genomics, morphogenesis and biophysics: triangulation of Purkinje cell development," Cerebellum Lond. Engl., vol. 5, no. 1, pp. 27–35, 2006. https://doi.org/10.1080/14734220500378581
39. S. V. Petoukhov, "The genetic code, 8-dimensional hypercomplex numbers and dyadic shifts," ArXiv11023596 Q-Bio, Feb. 2011.
40. J. Pellionisz, "The decade of fractogene: from discovery to utility - proofs of concept open genome-based clinical applications," Int. J. Syst. Cybern. Inform., pp. 17–28, 2012.
41. J. Pellionisz, R. Graham, P. A. Pellionisz, and J.-C. Perez, "Recursive genome function of the cerebellum: geometric unification of neuroscience and genomics," in Handbook of the Cerebellum and Cerebellar Disorders, M. Manto, Ed. Berlin: Springer, 2013, pp. 1381–1423. https://doi.org/10.1007/978-94-007-1333-8_61
42. Cattani and G. Pierro, "On the Fractal Geometry of DNA by the Binary Image Analysis," Bull. Math. Biol., vol. 75, no. 9, pp. 1544–1570, Sep. 2013. https://doi.org/10.1007/s11538-013-9859-9
43. Di Ieva, F. Grizzi, H. Jelinek, A. J. Pellionisz, and G. A. Losa, "Fractals in the neurosciences, part I: General principles and basic neurosciences," Neuroscientist, vol. 20, no. 4, pp. 403–417, Aug. 2014. https://doi.org/10.1177/1073858413513927
44. Di Ieva, P.-J. Le Reste, B. Carsin-Nicol, J.-C. Ferre, and M. D.

Cusimano, "Diagnostic Value of Fractal Analysis for the Differentiation of Brain Tumors Using 3-Tesla Magnetic Resonance Susceptibility-Weighted Imaging," Neurosurgery, vol. 79, no. 6, pp. 839–846, Dec. 2016. https://doi.org/10.1227/neu.0000000000001308
45. S. Liu et al., "Relationship between necrotic patterns in glioblastoma and patient survival: fractal dimension and lacunarity analyses using magnetic resonance imaging," Sci. Rep., vol. 7, no. 1, p. 8302, 16 2017. https://doi.org/10.1038/s41598-017-08862-6
46. T. A. Sebeok, "Biosemiotics: its roots, proliferation and prospects," in Essential Readings in Biosemiotics: Anthology and Commentary, D. Favareau, Ed. Dordrecht: Springer Netherlands, 2001, pp. 217–236. https://doi.org/10.1007/978-1-4020-9650-1_6
47. N. A. Chomsky, "Language and Mind," 1968. [Online]. Available: https://www.marxists.org/reference/subject/philosophy/works/us/chomsky.htm. [Accessed: 18-Sep-2015].
48. N. A. Chomsky, Reflections on Language. New York: Pantheon, 1975.
49. N. A. Chomsky, Language and Mind, 3 edition. Cambridge ; New York: Cambridge University Press, 2006.
50. N. A. Chomsky, "The machine, the ghost, and the limits of understanding: Newton's contributions to the study of mind," presented at the The CSMN Annual Lecture on Mind in Nature, Center for the Study of Mind in Nature, University of Oslo, 2011.
51. N. A. Chomsky, "Science, mind, and limits of understanding." Jan-2014.
52. R. W. Sperry, "Changing concepts of consciousness and free will," Perspect. Biol. Med., vol. 20, no. 1, pp. 9–19, 1976. https://doi.org/10.1007/bf01115112
53. R. W. Sperry, "Some effects of disconnecting the cerebral hemispheres," Nobelprize.org, 08-Dec-1981. [Online]. Available: http://www.nobelprize.org/nobel_prizes/medicine/laureates/1981/sperry-lecture_en.html. [Accessed: 09-Jul-2015].
54. M. Piattelli-Palmarini, J. Uriagereka, and P. Salaburu, Eds., Of minds and language: A dialogue with Noam Chomsky in the Basque Country, 1 edition. Oxford: Oxford University Press, 2011. https://doi.org/10.1017/s0022226713000108
55. R. W. Sperry, "Consciousness, freewill and personal identity," in Brain, Behaviour and Evolution, D. A. Oakley and H. C. Plotkin, Eds. Methuen and Company, 1979, pp. 219–228. https://doi.org/10.4324/9781315149523-10
56. N. Chomsky, Cartesian Linguistics: A Chapter in the History of Rationalist Thought, 1st ed. New York, NY: Harper & Row, 1966.
57. N. A. Chomsky, "Of minds and language," Biolinguistics, vol. 1, pp. 9–27, 2007.
58. E. D. Weinberger, "A theory of pragmatic information and its application to the quasi-species model of biological evolution," Biosystems, vol. 66, no. 3, pp. 105–119, Sep. 2002. https://doi.org/10.1016/s0303-2647(02)00038-2
59. M. Barbieri, "What is Information?," Biosemiotics, vol. 5, no. 2, Aug. 2012.
60. J. W. Oller, "Pragmatic information," in Biological Information: New Perspectives, 1 edition., Robert J. Marks_II, J. C. Sanford, W. A. Dembski, and B. L. Gordon, Eds. New Jersey: World Scientific Publishing Company, 2013, pp. 64–86.
61. R. Maleeh, "Pragmatic information as a unifying biological concept," Information, vol. 5, no. 3, pp. 451–478, Sep. 2014. https://doi.org/10.3390/info5030451
62. S. Peirce, "The logic of relatives," The Monist, vol. 7, no. 2, pp. 161–217, Jan. 1897.
63. Tarski, "The concept of truth in formalized languages," J. Symb. Log., vol. 6, pp. 73–89, 1941.
64. Tarski, "The semantic conception of truth," in Readings in Philosophical Analysis, H. Feigl and W. Sellars, Eds. New York, NY: Appleton, 1949, pp. 341–374.
65. J. W. Oller, "The antithesis of entropy: biosemiotic communication from genetics to human language with special emphasis on the immune systems," Entropy, vol. 12, no. 4, pp. 631–705, Mar. 2010. https://doi.org/10.3390/e12040631
66. J. W. Oller, "Biosemiotic entropy: Concluding the series," Entropy, vol. 16, no. 7, pp. 4060–4087, Jul. 2014. https://doi.org/10.3390/e16074060
67. J. W. Oller, "How grammatical relations are determined," in Proceedings of the 22nd Forum of the Linguistic Association of Canada and the United States, San Antonio, Texas, August 8-12, 1995, B. Hoffer, Ed. Chapel Hill, NC: Linguistic Association of Canada and the United States, 1996, pp. 37–88.
68. J. F. Sowa, "Commentary on 'Existential Graphs: MS 514 by Charles Sanders Peirce,'" 19-Oct-2017. [Online]. Available: http://www.jfsowa.com/peirce/ms514.htm. [Accessed: 07-Jan-2019].
69. J. F. Sowa, "Peirce's tutorial on existential graphs," Semiotica, vol. 186, no. 1–4, pp. 345–394, Aug. 2011. https://doi.org/10.1515/semi.2011.060
70. J. F. Sowa, "Existential Graphs: The simplest notation for logic ever invented," 2017.
71. J. W. Oller, L. Chen, S. D. Oller, and N. Pan, "Empirical predictions from a general theory of signs," Discourse Process., vol. 40, no. 2, pp. 115–144, 2005. https://doi.org/10.1207/s15326950dp4002_2
72. J. W. Oller and L. Chen, "Episodic organization in discourse and valid measurement in the sciences," J. Quant. Linguist., vol. 14, no. 2–3, pp. 127–144, 2007.
73. J. D. Watson and F. H. C. Crick, "A structure for deoxyribose nucleic acid," Nature, vol. 171, pp. 731–738, Apr. 1953.
74. R. R. Dietert and J. Dietert, "The completed self: an immunological view of the human-microbiome superorganism and risk of chronic diseases," Entropy, vol. 14, no. 12, pp. 2036–2065, Oct. 2012. https://doi.org/10.3390/e14112036
75. R. R. Dietert and E. K. Silbergeld, "Biomarkers for the 21st century: Listening to the microbiome," Toxicol. Sci., vol. 144, no. 2, pp. 208–216, Apr. 2015.
76. https://doi.org/10.1093/toxsci/kfv013
77. J. Pellionisz, "The principle of recursive genome function," The Cerebellum, vol. 7, no. 3, pp. 348–359, Sep. 2008.
78. R. P. Feynman, "The Feynman Lectures on Physics," 1964-1963. [Online]. Available: http://www.feynmanlectures.caltech.edu/I_01.html. [Accessed: 17-Sep-2018].
79. R. M. Davidson and S. Seneff, "The initial common pathway of inflammation, disease, and sudden death," Entropy, vol. 14, no. 12, pp. 1399–1442, Aug. 2012. https://doi.org/10.3390/e14081399
80. Gryder, C. Nelson, and S. Shepard, "Biosemiotic entropy of the genome: mutations and epigenetic imbalances resulting in cancer," Entropy, vol. 15, no. 1, pp. 234–261, Jan. 2013. https://doi.org/10.3390/e15010234
81. M.-W. Ho, "The new genetics and natural versus artificial genetic modification," Entropy, vol. 15, no. 11, pp. 4748–4781, Nov. 2013. https://doi.org/10.3390/e15114748
82. A. Shaw, S. Seneff, S. D. Kette, L. Tomljenovic, J. W. Oller, and R. M. Davidson, "Aluminum-induced entropy in biological systems: implications for neurological disease," J. Toxicol., vol. 2014, p. 491316, 2014. https://doi.org/10.1155/2014/491316
83. M. Kosoy, "Deepening the conception of functional information in the description of zoonotic infectious diseases," Entropy, vol. 15, no. 5, pp. 1929–1962, May 2013. https://doi.org/10.3390/e15051929
84. Kennedy, S. Seneff, R. M. Davidson, J. W. Oller, B. E. Haley, and R. D. Masters, "Environmental toxicants and infant mortality in America," Peertechz J. Biol. Res. Dev., vol. 1, no. 1, pp. 36–61, 2016. https://www.peertechz.com/articles/OJBS-1-105.php
85. T. Jaynes, "Information theory and statistical mechanics. I," Phys. Rev., vol. 106, no. 4, pp. 620–630, May 1957. https://doi.org/10.1103/physrev.106.620
86. T. Jaynes, "Information Theory and Statistical Mechanics. II," Phys. Rev., vol. 108, no. 2, pp. 171–190, Oct. 1957. https://doi.org/10.1103/physrev.108.171
87. E. T. Jaynes, "New engineering applications of information theory," in Proceedings of the First Symposium on Engineering, John Wiley & Sons, Inc., 1963, pp. 163–167.
88. S. Viereck, "What life means to einstein: an interview," The Saturday Evening Post, p. 17, 26-Oct-1929.

89. "Occam's razor," Wikipedia. 08-May-2019.
90. W. Leibniz, "Discourse on Metaphysics," 1686. [Online]. Available: http://www.anselm.edu/homepage/dbanach/leibniz-discourse.htm#I. [Accessed: 29-Dec-2014].
91. F. Chernoff, "Leibniz's principle of the identity of indiscernibles," Philos. Q., vol. 31, no. 123, pp. 126–138, Apr. 1981. https://doi.org/10.2307/2218719
92. Einstein, "Time, space, and gravitation," Science, vol. 51, no. 1305, pp. 8–10, 1920 1919.
93. W. Oller, "Reasons why some methods work," in Methods that work: ideas for literacy and language teachers, Second., J. W. Oller, Ed. Boston, MA: Heinle and Heinle Publishers, 1993, pp. 374–385. https://doi.org/10.1017/s0272263100014339
94. N. Whitehead and B. Russell, Principia Mathematica - Volume One. San Bernardio, CA: Rough Draft Printing, 1910.
95. N. Whitehead and B. Russell, Principia Mathematica - Volume Three. San Bernardio, CA: Rough Draft Printing, 1913.
96. N. Whitehead and B. Russell, Principia Mathematica - Volume Two. San Bernardio, CA: Rough Draft Printing, 1912.
97. S. Peirce, "Lowell Lectures. 1903, Lecture 5 ms., Robin Catalogue #469. Published: [Peirce 1976, HI/1, 333-354] as Lowell Lectures. 1903, Lecture V (469-470).," in The new elements of mathematics, vol. III, 4 vols., C. Eisele, Ed. The Hague/Paris: Mouton, 1903, pp. 333–354. https://doi.org/10.1515/9783111563398.329
98. Aristotle, "Στην ψυχή [On the Soul]," The Internet Classics Archive, vol. Book 3, Part 8. Daniel C. Stevenson, Web Atomics, MIT, ca-350AD.
99. Russell, Principles of Mathematics. W W Norton & Co Inc, 1903.
100. D. Irvine and H. Deutsch, "Russell's Paradox," in The Stanford Encyclopedia of Philosophy, Winter 2016., E. N. Zalta, Ed. Metaphysics Research Lab, Stanford University, 2016.
101. S. Peirce, "Logic, Considered as Semeiotic: An Overview of Charles Peirce's Philosophical Logic, Constructed from Manuscript L75, Version 1," Peirce's Arisbe, 1998-1902. [Online]. Available: http://www.iupui.edu/~arisbe/menu/library/bycsp/L75/ver1/l75v1-09.htm. [Accessed: 18-Dec-2018]. https://doi.org/10.2979/trancharpeirsoc.50.4.523
102. S. Peirce, "Lecture VIII: Forms of Induction and Hypothesis. Ms 105.," in Writings of Charles S. Peirce: A Chronological Edition, August 1, 1982., vol. 1, 8 vols., M. Fisch, C. J. W. Kloesel, C. E. Moore, D. D. Roberts, L. A. Ziegler, and N. P. Atkinson, Eds. Bloomington, IN: Indiana University Press, 1865, pp. 256–271.
103. S. Peirce, "On a new list of categories," Proc. Am. Acad. Arts Sci., vol. 7, pp. 287–298, 1868.
104. S. Peirce, "Questions concerning certain faculties claimed for man," J. Specul. Philos., vol. 2, pp. 103–114, 1868.
105. S. Campbell, Watch Me Grow! London: Carroll & Brown Publishers Limited, 2004.
106. Langus, J. Mehler, and M. Nespor, "Rhythm in language acquisition," Neurosci. Biobehav. Rev., vol. 81, pp. 158–166, Oct. 2017. https://doi.org/10.1016/j.neubiorev.2016.12.012
107. T. Nazzi, J. Bertoncini, and J. Mehler, "Language discrimination by newborns: Toward an understanding of the role of rhythm.," J. Exp. Psychol. Hum. Percept. Perform., vol. 24, no. 3, pp. 756–766, 1998. https://doi.org/10.1037//0096-1523.24.3.756
108. Provasi, D. I. Anderson, and M. Barbu-Roth, "Rhythm perception, production, and synchronization during the perinatal period," Front. Psychol., vol. 5, Sep. 2014. https://doi.org/10.3389/fpsyg.2014.01048
109. Z. Sai, "The role of the mother's voice in developing mother's face preference: Evidence for intermodal perception at birth," Infant Child Dev., vol. 14, no. 1, pp. 29–50, Mar. 2005. https://doi.org/10.1002/icd.376
110. W. Oller, "Milestones in language development," in Encyclopedia of Language Development, P. J. Brooks and V. Kempe, Eds. Thousand Oaks, CA: Sage Publications, Inc., 2014, pp. 377–382. https://sk.sagepub.com/reference/encyclopedia-of-language-development/n123.xml
111. K. Oller, L. A. Wieman, W. J. Doyle, and C. Ross, "Infant babbling and speech," J. Child Lang., vol. 3, no. 01, Feb. 1976. https://doi.org/10.1017/s0305000900001276
112. Bergelson and D. Swingley, "At 6-9 months, human infants know the meanings of many common nouns," Proc. Natl. Acad. Sci., vol. 109, no. 9, pp. 3253–3258, Feb. 2012. https://doi.org/10.1073/pnas.1113380109
113. Bergelson and D. Swingley, "The acquisition of abstract words by young infants," Cognition, vol. 127, no. 3, pp. 391–397, Jun. 2013. https://doi.org/10.1016/j.cognition.2013.02.011
114. Bergelson and D. Swingley, "Young toddlers' word comprehension is flexible and efficient," PLoS ONE, vol. 8, no. 8, p. e73359, Aug. 2013. https://doi.org/10.1371/journal.pone.0073359
115. Bergelson and R. N. Aslin, "Nature and origins of the lexicon in 6-mo-olds," Proc. Natl. Acad. Sci. U. S. A., vol. 114, no. 49, pp. 12916–12921, Dec. 2017. https://doi.org/10.1073/pnas.1712966114
116. J. W. Oller, S. D. Oller, and Liang Chen, "Milestones in impaired and unimpaired first language acquisition: why the sequence cannot easily be violated," presented at the Tenth International Congress for the Study of Child Language, Frie University of Berlin, Henry Ford Building, Berlin, Germany, 28-Jul-2005. DOI: 10.13140/RG.2.1.4628.7848
117. S. D. Oller, "Meaning matters: A clinician's/student's guide to general sign theory and its applicability in clinical settings," J. Commun. Disord., vol. 38, no. 5, pp. 359–373, Sep. 2005. https://doi.org/10.1016/j.jcomdis.2005.03.002
118. J. L. Ruark and C. A. Moore, "Coordination of lip muscle activity by 2-year-old children during speech and nonspeech tasks," J. Speech Lang. Hear. Res. JSLHR, vol. 40, no. 6, pp. 1373–1385, Dec. 1997. https://doi.org/10.1044/jslhr.4006.1373
119. J. W. Oller, S. D. Oller, and L. C. Badon, Milestones: Normal Speech and Language Development Across the Lifespan, Paper and DVD edition. San Diego: Plural Publishing, 2006.
120. Carpenter, J. Call, and M. Tomasello, "A new false belief test for 36-month-olds," Br. J. Dev. Psychol., vol. 20, no. 3, pp. 393–420, Sep. 2002. https://doi.org/10.1348/026151002320620316
121. Berthoud-Papandropoulou and H. Kilcher, "Is a false belief statement a lie or a truthful statement? Judgments and explanations of children aged 3 to 8," Dev. Sci., vol. 6, no. 2, pp. 173–177, Apr. 2003. https://doi.org/10.1111/1467-7687.00268
122. Piaget, "Excerpt from The psychology of intelligence.," in Language and Experience: Classic Pragmatism, J. W. Oller, Ed. Lanham, MD: University Press of America, 1947, pp. 203–216.
123. Persaud and J. P. O'Leary, "Fibonacci Series, Golden Proportions, and the Human Biology," Austin J. Surg., vol. 2, no. 5, p. 7, 2015.
124. P. Shonkoff and A. S. Garner, "The lifelong effects of early childhood adversity and toxic stress," Pediatrics, vol. 129, no. 1, pp. E232–E246, Jan. 2012. https://doi.org/10.1542/peds.2011-2663
125. P. Gil and R. Rupprecht, "Attachment research. Current aspects of attachment theory and development psychology as well as neurobiological aspects in psychiatric and psychosomatic disorders," Nervenarzt, vol. 74, no. 11, pp. 965–971, Nov. 2003.
126. Steiman and N. Watemberg, "Apparent life-threatening events: patients' health status at 5 years of age," Isr. Med. Assoc. J. IMAJ, vol. 17, no. 11, pp. 673–677, Nov. 2015.
127. A. Shaw and M. S. Petrik, "Aluminum hydroxide injections lead to motor deficits and motor neuron degeneration," J. Inorg. Biochem., vol. 103, no. 11, pp. 1555–1562, Nov. 2009. https://doi.org/10.1016/j.jinorgbio.2009.05.019
128. U. S. Uchendu, B. I. Omalu, D. X. Cifu, and L. E. Egede, "Repeated concussions: time to spur action among vulnerable veterans," Am. J. Public Health, vol. 106, no. 8, pp. 1366–1368, Aug. 2016. https://doi.org/10.2105/ajph.2016.303293
129. J. St. John, "The control of mtDNA replication during differentiation and development," Biochim. Biophys. Acta BBA - Gen. Subj., vol. 1840, no. 4, pp. 1345–1354, Apr. 2014. https://doi.org/10.1016/j.bbagen.2013.10.036

130. P. M. Wiggins, "Life depends upon two kinds of water," Plos One, vol. 3, no. 1, p. e1406, Jan. 2008. https://doi.org/10.1371/journal.pone.0001406
131. F. Chaplin, "A proposal for the structuring of water," Biophys. Chem., vol. 83, no. 3, pp. 211–221, Jan. 2000.
132. Laage, T. Elsaesser, and J. T. Hynes, "Water dynamics in the hydration shells of biomolecules," Chem. Rev., vol. 117, no. 16, pp. 10694–10725, Aug. 2017. https://doi.org/10.1021/acs.chemrev.6b00765
133. Franzese and V. Bianco, "Water at biological and inorganic interfaces," Food Biophys., vol. 8, no. 3, pp. 153–169, Sep. 2013.
134. F. Chaplin, "Water's hydrogen bond strength," in Water and Life: The Unique Properties of H2O, R. M. Lynden-Bel, S. C. Morris, J. D. Barrow, J. L. Finney, and C. L. Harper, Eds. Boca Raton, FL, USA: CRC Press, 2010, pp. 69–86. https://doi.org/10.1201/ebk1439803561
135. Okajima, M. Ando, and H. Hamaguchi, "Formation of 'nano-ice' and density maximum anomaly of water," Bull. Chem. Soc. Jpn., vol. 91, no. 6, pp. 991–997, Jun. 2018. https://doi.org/10.1246/bcsj.20180052
136. P. M. Wiggins, "Water in complex environments such as living systems," Phys. -Stat. Mech. Its Appl., vol. 314, no. 1–4, pp. 485–491, Nov. 2002.
137. M. Stadler, F. Demmel, J. Ollivier, and T. Seydel, "Picosecond to nanosecond dynamics provide a source of conformational entropy for protein folding," Phys. Chem. Chem. Phys., vol. 18, no. 31, pp. 21527–21538, Aug. 2016. https://doi.org/10.1039/c6cp04146a
138. S. Fujiwara et al., "Ligation-dependent picosecond dynamics in human hemoglobin as revealed by quasielastic neutron scattering," J. Phys. Chem. B, vol. 121, no. 34, pp. 8069–8077, Aug. 2017. https://doi.org/10.1021/acs.jpcb.7b05182
139. S. Boutet et al., "High-resolution protein structure determination by serial femtosecond crystallography," Science, vol. 337, no. 6092, pp. 362–364, Jul. 2012.
140. J. Tielrooij, S. T. van der Post, J. Hunger, M. Bonn, and H. J. Bakker, "Anisotropic water reorientation around ions," J. Phys. Chem. B, vol. 115, no. 43, pp. 12638–12647, Nov. 2011. https://doi.org/10.1021/jp206320f
141. J. Tielrooij, N. Garcia-Araez, M. Bonn, and H. J. Bakker, "Cooperativity in ion hydration," Science, vol. 328, no. 5981, pp. 1006–1009, May 2010. https://doi.org/10.1126/science.1183512
142. A. Shaw, Neural Dynamics of Neurological Disease. John Wiley & Sons, Inc., 2017.
143. R. M. Davidson, A. Lauritzen, and S. Seneff, "Biological water dynamics and entropy: A biophysical origin of cancer and other diseases," Entropy, vol. 15, no. 9, pp. 3822–3876, 2013. https://doi.org/10.3390/e15093822
144. J. W. Oller, S. D. Oller, and S. N. Oller, Milestones: Normal Speech and Language Development Across the Life Span, 2nd ed. San Diego, CA: Plural Publishing, Inc., 2014.
145. Watad et al., "The autoimmune/inflammatory syndrome induced by adjuvants (ASIA)/Shoenfeld's syndrome: descriptive analysis of 300 patients from the international ASIA syndrome registry," Clin. Rheumatol., vol. 37, no. 2, pp. 483–493, Feb. 2018. https://doi.org/10.1007/s10067-017-3748-9
146. Samsel and S. Seneff, "Glyphosate pathways to modern diseases VI: Prions, amyloidoses and autoimmune neurological diseases," J. Biol. Phys. Chem., vol. 17, no. 1, pp. 8–32, Mar. 2017. https://doi.org/10.4024/25sa16a.jbpc.17.01
147. Huhn, "More and enhanced glyphosate analysis is needed," Anal. Bioanal. Chem., vol. 410, no. 13, pp. 3041–3045, May 2018. https://doi.org/10.1007/s00216-018-1000-3
148. H. C. Van Bruggen et al., "Environmental and health effects of the herbicide glyphosate," Sci. Total Environ., vol. 616, pp. 255–268, Mar. 2018.
149. Cattani et al., "Developmental exposure to glyphosate-based herbicide and depressive-like behavior in adult offspring: Implication of glutamate excitotoxicity and oxidative stress," Toxicology, vol. 387, pp. 67–80, Jul. 2017. https://doi.org/10.1016/j.tox.2017.06.001
150. E. Gallegos, M. Bartos, C. Bras, F. Gumilar, M. C. Antonelli, and A. Minetti, "Exposure to a glyphosate-based herbicide during pregnancy and lactation induces neurobehavioral alterations in rat offspring," Neurotoxicology, vol. 53, pp. 20–28, Mar. 2016. https://doi.org/10.1016/j.neuro.2015.11.015
151. M. Milesi et al., "Perinatal exposure to a glyphosate-based herbicide impairs female reproductive outcomes and induces second-generation adverse effects in Wistar rats," Arch. Toxicol., vol. 92, no. 8, pp. 2629–2643, Aug. 2018. https://doi.org/10.1007/s00204-019-02386-w
152. Garcia-Espineira, L. Tejeda-Benitez, and J. Olivero-Verbel, "Toxicity of atrazine- and glyphosate-based formulations on Caenorhabditis elegans," Ecotoxicol. Environ. Saf., vol. 156, pp. 216–222, Jul. 2018. https://doi.org/10.1016/j.ecoenv.2018.02.075
153. Antoniou et al., "Teratogenic effects of glyphosate-based herbicides: divergence of regulatory decisions from scientific evidence," J. Environ. Anal. Toxicol., vol. 2012, Jun. 2012. https://doi.org/10.4172/2161-0525.s4-006
154. Q. Mao et al., "The Ramazzini Institute 13-week pilot study on glyphosate and Roundup administered at human-equivalent dose to Sprague Dawley rats: effects on the microbiome," Environ. Health, vol. 17, p. 50, May 2018. https://doi.org/10.1186/s12940-018-0394-x
155. Kim, J. Perez, S. Ferguson, and I. Campbell, "The specific incorporation of labeled aromatic-amino-acids into proteins through growth of bacteria in the presence of glyphosate - application," Febs Lett., vol. 272, no. 1–2, pp. 34–36, Oct. 1990. https://doi.org/10.1016/0014-5793(90)80442-l
156. R. A. Waterland, M. Travisano, K. G. Tahiliani, M. T. Rached, and S. Mirza, "Methyl donor supplementation prevents transgenerational amplification of obesity," Int. J. Obes., vol. 32, no. 9, pp. 1373–1379, Sep. 2008. https://doi.org/10.1038/ijo.2008.100
157. R. A. Waterland, "Epigenetic mechanisms affecting regulation of energy balance: many questions, few answers," Annu. Rev. Nutr., vol. 34, no. 1, pp. 337–355, Jul. 2014. https://doi.org/10.1146/annurev-nutr-071813-105315
158. J. Perper, L. Kuller, and Y. Shim, "Detection of fatal therapeutic misadventures by an urban medicolegal system," J. Forensic Sci., vol. 38, no. 2, pp. 327–338, Mar. 1993. https://doi.org/10.1520/jfs13412j
159. Starfield, "Is US health really the best in the world?," JAMA, vol. 284, no. 4, pp. 483–485, Jul. 2000. https://doi.org/10.1001/jama.284.4.483
160. Anderson, R. Davis, G. B. Hanna, and C. A. Vincent, "Surgical adverse events: a systematic review," Am. J. Surg., vol. 206, no. 2, pp. 253–262, Aug. 2013. https://www.ncbi.nlm.nih.gov/pubmed/23642651
161. R. Chiaratti, B. M. Garcia, K. F. Carvalho, T. S. Machado, F. K. da S. Ribeiro, and C. H. Macabelli, "The role of mitochondria in the female germline: Implications to fertility and inheritance of mitochondrial diseases: Role of mitochondria in the female germline," Cell Biol. Int., vol. 42, no. 6, pp. 711–724, Jun. 2018. https://doi.org/10.1002/cbin.10947
162. K. Pal, P. S. Ambulkar, B. R. Sontakke, J. E. Waghmare, M. R. Shende, and A. M. Tarnekar, "Role of nuclear and mitochondrial genes in human male infertility: a review," The Nucleus, vol. 60, no. 2, pp. 209–220, Aug. 2017. https://doi.org/10.1007/s13237-017-0209-4
163. Conti and F. Franciosi, "Acquisition of oocyte competence to develop as an embryo: integrated nuclear and cytoplasmic events," Hum. Reprod. Update, vol. 24, no. 3, pp. 245–266, Jun. 2018. https://doi.org/10.1093/humupd/dmx040
164. Bournique, M. Dall'Osto, J.-S. Hoffmann, and V. Bergoglio, "Role of specialized DNA polymerases in the limitation of replicative stress and DNA damage transmission," Mutat. Res.-Fundam. Mol. Mech. Mutagen., vol. 808, pp. 62–73, Mar. 2018. https://doi.org/10.1016/j.mrfmmm.2017.08.002
165. L. Tan and Y. G. Shi, "Tet family proteins and 5-hydroxymethylcytosine in development and disease," Dev. Camb. Engl., vol. 139, no. 11, pp. 1895–1902, Jun. 2012. https://doi.org/10.1242/dev.070771
166. W. Dean, "DNA methylation and demethylation: A pathway to gametogenesis and development: DNA methylation dynamics in mouse embryos," Mol. Reprod. Dev., vol. 81, no. 2, pp. 113–125, Feb. 2014. https://doi.org/10.1002/mrd.22280

167. J. Briscoe and S. Small, "Morphogen rules: design principles of gradient-mediated embryo patterning," Development, vol. 142, no. 23, pp. 3996–4009, Dec. 2015. https://doi.org/10.1242/dev.129452
168. J. Simons and A. J. Pellionisz, "Genomics, morphogenesis and biophysics: Triangulation of Purkinje cell development," Cerebellum, vol. 5, no. 1, pp. 27–35, Mar. 2006. https://doi.org/10.1080/14734220500378581
169. M. Turing, "The chemical basis of morphogenesis," in Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences, Vol. 237, No. 641. (Aug. 14, 1952), pp. 37-72., Biological Sciences., vol. 237, 641 vols., London, UK: The Royal Society, 1952, pp. 37–72. https://doi.org/10.1098/rstb.1952.0012
170. K. Hogg and P. S. Western, "Refurbishing the germline epigenome: Out with the old, in with the new," Semin. Cell Dev. Biol., vol. 45, pp. 104–113, Sep. 2015. https://doi.org/10.1016/j.semcdb.2015.09.012
171. L. Prokopuk et al., "Loss of maternal EED results in postnatal overgrowth," Clin. Epigenetics, vol. 10, no. 1, Dec. 2018. https://doi.org/10.1186/s13148-018-0526-8
172. R. M. Kohli and Y. Zhang, "TET enzymes, TDG and the dynamics of DNA demethylation," Nature, vol. 502, no. 7472, pp. 472–479, Oct. 2013. https://doi.org/10.1038/nature12750
173. J. B. Fernandes et al., "FIGL1 and its novel partner FLIP form a conserved complex that regulates homologous recombination," PLOS Genet., vol. 14, no. 4, p. e1007317, Apr. 2018. https://doi.org/10.1371/journal.pgen.1007317
174. G. Stanton, "Regulation of the blood-testis barrier," Semin. Cell Dev. Biol., vol. 59, pp. 166–173, Nov. 2016. https://doi.org/10.1016/j.semcdb.2016.06.018
175. Wen et al., "Signaling pathways regulating blood–tissue barriers — Lesson from the testis," Biochim. Biophys. Acta BBA - Biomembr., vol. 1860, no. 1, pp. 141–153, Jan. 2018. https://doi.org/10.1016/j.bbamem.2017.04.020
176. L. P. Cheeseman, J. Boulanger, L. M. Bond, and M. Schuh, "Two pathways regulate cortical granule translocation to prevent polyspermy in mouse oocytes," Nat. Commun., vol. 7, p. 13726, Dec. 2016. https://doi.org/10.1038/ncomms13726
177. J. P. van den Berg, E. A. M. Westerbeek, F. R. M. van der Klis, G. A. M. Berbers, and R. M. van Elburg, "Transplacental transport of IgG antibodies to preterm infants: A review of the literature," Early Hum. Dev., vol. 87, no. 2, pp. 67–72, Feb. 2011. https://doi.org/10.1016/j.earlhumdev.2010.11.003
178. J. L. Oei et al., "Amphetamines, the pregnant woman and her children: a review," J. Perinatol., vol. 32, no. 10, pp. 737–747, Oct. 2012. https://doi.org/10.1038/jp.2012.59
179. E. Wood and C.-D. Walker, "Fetal and neonatal HPA axis," Compr. Physiol., vol. 6, no. 1, pp. 33–62, Jan. 2016. https://doi.org/10.1002/cphy.c150005
180. H. Nielsen, A. Larsen, and A. L. Nielsen, "DNA methylation alterations in response to prenatal exposure of maternal cigarette smoking: A persistent epigenetic impact on health from maternal lifestyle?," Arch. Toxicol., vol. 90, no. 2, pp. 231–245, Feb. 2016. https://doi.org/10.1007/s00204-014-1426-0
181. Kozikowska et al., "Mercury concentrations in human placenta, umbilical cord, cord blood and amniotic fluid and their relations with body parameters of newborns," Environ. Pollut., vol. 182, pp. 256–262, Nov. 2013. https://doi.org/10.1016/j.envpol.2013.07.030
182. V. Kulvietis, V. Zalgeviciene, J. Didziapetriene, and R. Rotomskis, "Transport of nanoparticles through the placental barrier," Tohoku J. Exp. Med., vol. 225, no. 4, pp. 225–234, 2011. https://doi.org/10.1620/tjem.225.225
183. M. I. Linder et al., "Mitotic disassembly of nuclear pore complexes involves CDK1- and PLK1-mediated phosphorylation of key interconnecting nucleoporins," Dev. Cell, vol. 43, no. 2, pp. 141-156.e7, Oct. 2017. https://doi.org/10.1016/j.devcel.2017.08.020
184. Y. Miyamura et al., "The deceptive nature of UVA-tanning versus the modest protective effects of UVB-tanning on human skin," Pigment Cell Melanoma Res., vol. 24, no. 1, pp. 136–147, Feb. 2011. https://doi.org/10.1111/j.1755-148x.2010.00764.x
185. Y. Huang et al., "Mimicking melanosomes: polydopamine nanoparticles as artificial microparasols," ACS Cent. Sci., vol. 3, no. 6, pp. 564–569, Jun. 2017.
186. J.-C. Beani, "Ultraviolet A-induced DNA damage: role in skin cancer," Bull. Acad. Natl. Med., vol. 198, no. 2, pp. 273–295, Feb. 2014. https://reference.medscape.com/medline/abstract/26263704
187. Kobayashi et al., "Supranuclear melanin caps reduce ultraviolet induced DNA photoproducts in human epidermis," J. Invest. Dermatol., vol. 110, no. 5, pp. 806–810, May 1998. https://doi.org/10.1046/j.1523-1747.1998.00178.x
188. D. Simon, L. Hong, and D. N. Peles, "Insights into melanosomes and melanin from some interesting spatial and temporal properties," J. Phys. Chem. B, vol. 112, no. 42, pp. 13201–13217, Oct. 2008. https://doi.org/10.1021/jp804248h
189. L. Zecca et al., "The neuromelanin of human substantia nigra: structure, synthesis and molecular behaviour," J. Neural Transm.-Suppl., no. 65, pp. 145–155, 2003. https://link.springer.com/chapter/10.1007/978-3-7091-0643-3_8
190. A. Zucca et al., "Interactions of iron, dopamine and neuromelanin pathways in brain aging and Parkinson's disease," Prog. Neurobiol., vol. 155, pp. 96–119, Aug. 2017. https://doi.org/10.1016/j.pneurobio.2015.09.012
191. H. Lee, S.-Y. Baek, S. Y. Chun, J.-H. Lee, and H. Cho, "Specific visualization of neuromelanin-iron complex and ferric iron in the human post-mortem substantia nigra using MR relaxometry at 7T," Neuroimage, vol. 172, pp. 874–885, May 2018. https://doi.org/10.1016/j.neuroimage.2017.11.035
192. M.-T. Arango et al., "HLA-DRB1 the notorious gene in the mosaic of autoimmunity," Immunol. Res., vol. 65, no. 1, pp. 82–98, Feb. 2017. https://doi.org/10.1007/s12026-016-8817-7
193. M. F. Jennewein, B. Abu-Raya, Y. Jiang, G. Alter, and A. Marchant, "Transfer of maternal immunity and programming of the newborn immune system," Semin. Immunopathol., vol. 39, no. 6, pp. 605–613, Nov. 2017. https://doi.org/10.1007/s00281-017-0653-x
194. S. L. Bridgman et al., "Infant gut immunity: a preliminary study of IgA associations with breastfeeding," J. Dev. Orig. Health Dis., vol. 7, no. 01, pp. 68–72, Feb. 2016. https://doi.org/10.1017/S2040174415007862 https://doi.org/10.1017/S2040174415007862
195. Liu et al., "Immunoglobulin gene expression in umbilical cord blood-derived CD34(+) hematopoietic stem/progenitor cells," Gene, vol. 575, no. 1, pp. 108–117, Jan. 2016. https://doi.org/10.1016/j.gene.2015.08.046
196. Jiang et al., "IgG and IgA with potential microbial-binding activity are expressed by normal human skin epidermal cells," Int. J. Mol. Sci., vol. 16, no. 2, pp. 2574–2590, Jan. 2015. https://doi.org/10.3390/ijms16022574
197. D. Finkelman, M. V. Khodoun, and R. Strait, "Human IgE-independent systemic anaphylaxis," J. Allergy Clin. Immunol., vol. 137, no. 6, pp. 1674–1680, Jun. 2016. https://doi.org/10.1016/j.jaci.2016.02.015
198. Bodis, V. Toth, and A. Schwarting, "Role of human leukocyte antigens (HLA) in autoimmune diseases," Rheumatol. Ther., vol. 5, no. 1, pp. 5–20, Jun. 2018. https://doi.org/10.1007/s40744-018-0100-z
199. Gianfrani, L. Pisapia, S. Picascia, M. Strazzullo, and G. Del Pozzo, "Expression level of risk genes of MHC class II is a susceptibility factor for autoimmunity: New insights," J. Autoimmun., vol. 89, pp. 1–10, May 2018. https://doi.org/10.1016/j.jaut.2017.12.016
200. D. Finkelman, M. V. Khodoun, and R. Strait, "Human IgE-independent systemic anaphylaxis," J. Allergy Clin. Immunol., vol. 137, no. 6, pp. 1674–1680, Jun. 2016. https://doi.org/10.1016/j.jaci.2016.02.015
201. Watad et al., "Seasonality and autoimmune diseases: The contribution of the four seasons to the mosaic of autoimmunity," J. Autoimmun., vol. 82, pp. 13–30, Aug. 2017. https://doi.org/ 10.1016/j.jaut.2017.06.001
202. N. L. Bragazzi et al., "Advances in our understanding of immunization and vaccines for patients with systemic lupus erythematosus," Expert Rev. Clin. Immunol., vol. 13, no. 10, pp. 939–949, 2017. https://doi.org/10.1080/1744666x.2017.1361321

203. Dardiotis and D. P. Bogdanos, "Epstein-Barr virus: in search of a causal or a casual relationship between the virus and the disease?," Isr. Med. Assoc. J., vol. 20, no. 2, pp. 111–113, Feb. 2018.
204. G. Dórea, "Exposure to mercury and aluminum in early life: developmental vulnerability as a modifying factor in neurologic and immunologic effects," Int. J. Environ. Res. Public. Health, vol. 12, no. 2, pp. 1295–1313, Jan. 2015. https://doi.org/10.3390/ijerph120201295
205. R. Snapp, D. B. Boyer, L. C. Peterson, and C. W. Svare, "The contribution of dental amalgam to mercury in blood," J. Dent. Res., vol. 68, no. 5, pp. 780–785, May 1989. https://doi.org/10.1177/00220345890680050501
206. J. Vimy, Y. Takahashi, and F. L. Lorscheider, "Maternal-fetal distribution of mercury (203Hg) released from dental amalgam fillings," Am. J. Physiol., vol. 258, no. 4 Pt 2, pp. R939-945, Apr. 1990. https://doi.org/10.1152/ajpregu.1990.258.4.r939
207. L. Lorscheider, M. J. Vimy, A. O. Summers, and H. Zwiers, "The dental amalgam mercury controversy — inorganic mercury and the CNS; genetic linkage of mercury and antibiotic resistances in intestinal bacteria," Toxicology, vol. 97, no. 1–3, pp. 19–22, Mar. 1995. https://doi.org/10.1016/0300-483x(94)02964-v
208. E. Haley, "Mercury toxicity: Genetic susceptibility and synergistic effects," Med. Veritas, vol. 2, pp. 535–542, 2005. https://doi.org/10.1588/medver.2005.02.00070
209. C. Marques, J. V. E. Bernardi, J. G. Dórea, M. de Fatima R Moreira, and O. Malm, "Perinatal multiple exposure to neurotoxic (lead, methylmercury, ethylmercury, and aluminum) substances and neurodevelopment at six and 24 months of age," Environ. Pollut., vol. 187, pp. 130–135, Apr. 2014. https://doi.org/10.1016/j.envpol.2014.01.004
210. J. G. Dórea, "Methylmercury in colostrum and milk of Japanese mothers," Chemosphere, vol. 137, p. 221, Oct. 2015. https://doi.org/10.1016/j.chemosphere.2015.06.100
211. Y. Park et al., "Exposure to lead and mercury through breastfeeding during the first month of life: A CHECK cohort study," Sci. Total Environ., vol. 612, pp. 876–883, Jan. 2018.
212. Sage and N. Shikazono, "Radiation-induced clustered DNA lesions: Repair and mutagenesis," Free Radic. Biol. Med., vol. 107, pp. 125–135, Jun. 2017. https://doi.org/10.1016/j.freeradbiomed.2016.12.008
213. E. Depuydt, J. Beert, E. Bosmans, and G. Salembier, "Human Papillomavirus (HPV) virion induced cancer and subfertility, two sides of the same coin," Facts Views Vis. Obgyn, vol. 8, no. 4, pp. 211–222, Dec. 2016.
214. Shamriz and Y. Shoenfeld, "Infections: a double-edge sword in autoimmunity," Curr. Opin. Rheumatol., vol. 30, no. 4, pp. 365–372, Jul. 2018. https://doi.org/10.1097/bor.0000000000000490
215. Garolla, D. Pizzol, and C. Foresta, "The role of human papillomavirus on sperm function," Curr. Opin. Obstet. Gynecol., vol. 23, no. 4, pp. 232–237, Aug. 2011. https://doi.org/10.1097/gco.0b013e328348a3a4
216. C. Freitas, F. C. Mariz, M. a. R. Silva, and A. L. S. Jesus, "Human papillomavirus vertical transmission: review of current data," Clin. Infect. Dis., vol. 56, no. 10, pp. 1451–1456, May 2013. https://doi.org/10.1093/cid/cit066
217. Gimenes et al., "Male infertility: a public health issue caused by sexually transmitted pathogens," Nat. Rev. Urol., vol. 11, no. 12, pp. 672–687, Dec. 2014. https://doi.org/10.1038/nrurol.2014.285
218. Damke et al., "Male Partners of Infertile Couples with Seminal Infections of Human Papillomavirus Have Impaired Fertility Parameters," Biomed Res. Int., p. 4684629, 2017. https://doi.org/10.1155/2017/4684629
219. U. Schagdarsurengin, P. Western, K. Steger, and A. Meinhardt, "Developmental origins of male subfertility: role of infection, inflammation, and environmental factors," Semin. Immunopathol., vol. 38, no. 6, pp. 765–781, Nov. 2016. https://doi.org/10.1007/s00281-016-0576-y
220. J. Gruen R., "Human MHC class III and IV genes and disease associations," Front. Biosci., vol. 6, no. 1, p. d960, 2001. https://doi.org/10.2741/gruen
221. Milner M., "Genetic organization of the human MHC class III region," Front. Biosci., vol. 6, no. 1, p. d914, 2001. https://doi.org/10.2741/milner
222. Ballanti et al., "Complement and autoimmunity," Immunol. Res., vol. 56, no. 2–3, pp. 477–491, Jul. 2013.
223. Bajic, S. E. Degn, S. Thiel, and G. R. Andersen, "Complement activation, regulation, and molecular basis for complement-related diseases," Embo J., vol. 34, no. 22, pp. 2735–2757, Nov. 2015. https://doi.org/10.15252/embj.201591881
224. Tedesco et al., "Pathogenic role of complement in antiphospholipid syndrome and therapeutic implications," Front. Immunol., vol. 9, p. 1388, Jun. 2018.
225. Hakem, "DNA-damage repair; the good, the bad, and the ugly," EMBO J., vol. 27, no. 4, pp. 589–605, Feb. 2008. https://doi.org/10.1038/emboj.2008.15
226. A. Shaw and J. McEachern, Eds., Toward a Theory of Neuroplasticity, 1 edition. Philadelphia: Psychology Press, 2001.
227. J. K. Lee and P. Vadas, "Anaphylaxis: mechanisms and management," Clin. Exp. Allergy, vol. 41, no. 7, pp. 923–938, Jul. 2011.
228. Liu and S. K. Sathe, "Food allergen epitope mapping," J. Agric. Food Chem., vol. 66, no. 28, pp. 7238–7248, Jul. 2018. https://doi.org/10.1021/acs.jafc.8b01967
229. Y. M. Taalab et al., "Mechanisms of disordered neurodegenerative function: concepts and facts about the different roles of the protein kinase RNA-like endoplasmic reticulum kinase (PERK)," Rev. Neurosci., vol. 29, no. 4, pp. 387–415, Jun. 2018. https://doi.org/10.1515/revneuro-2017-0071
230. Z. A. Shah, D. Zhao, T. Hussain, N. Sabir, and L. Yang, "Regulation of microRNAs-mediated autophagic flux: a new regulatory avenue for neurodegenerative diseases with focus on prion diseases," Front. Aging Neurosci., vol. 10, p. 139, May 2018. https://doi.org/10.3389/fnagi.2018.00139
231. Scheckel and A. Aguzzi, "Prions, prionoids and protein misfolding disorders," Nat. Rev. Genet., vol. 19, no. 7, pp. 405–418, Jul. 2018. https://doi.org/10.1038/s41576-018-0011-4
232. Kanata et al., "MicroRNA alterations in the brain and body fluids of humans and animal prion disease models: current status and perspectives," Front. Aging Neurosci., vol. 10, p. 220, Jul. 2018. https://doi.org/10.3389/fnagi.2018.00220
233. Majumder and O. Chakrabarti, "Lysosomal quality control in prion diseases," Mol. Neurobiol., vol. 55, no. 3, pp. 2631–2644, Mar. 2018. https://doi.org/10.1007/s12035-017-0512-8
234. G. Hovanessian, C. Soundaramourty, D. El Khoury, I. Nondier, J. Svab, and B. Krust, "Surface Expressed Nucleolin Is Constantly Induced in Tumor Cells to Mediate Calcium-Dependent Ligand Internalization," Plos One, vol. 5, no. 12, p. e15787, Dec. 2010. https://doi.org/10.1371/journal.pone.0015787
235. M. Haschka, G. Karbon, L. L. Fava, and A. Villunger, "Perturbing mitosis for anti-cancer therapy: is cell death the only answer?," Embo Rep., vol. 19, no. 3, p. UNSP e45440, Mar. 2018. https://doi.org/10.15252/embr.201745440
236. L. M. Ogawa and S. J. Baserga, "Crosstalk between the nucleolus and the DNA damage response," Mol. Biosyst., vol. 13, no. 3, pp. 443–455, Mar. 2017. https://doi.org/10.1039/c6mb00740f
237. Luchinat et al., "Identification of a novel nucleophosmin-interaction motif in the tumor suppressor p14arf," Febs J., vol. 285, no. 5, pp. 832–847, Mar. 2018. https://doi.org/10.1111/febs.14373
238. Di Matteo et al., "Structural investigation of nucleophosmin interaction with the tumor suppressor Fbw7 gamma," Oncogenesis, vol. 6, p. e379, Sep. 2017.
239. M. S. Lindstrom, D. Jurada, S. Bursac, I. Orsolic, J. Bartek, and S. Volarevic, "Nucleolus as an emerging hub in maintenance of genome stability and cancer pathogenesis," Oncogene, vol. 37, no. 18, pp. 2351–2366, May 2018. https://doi.org/10.1038/s41388-017-0121-z
240. D. Scott and M. Oeffinger, "Nucleolin and nucleophosmin: nucleolar proteins with multiple functions in DNA repair," Biochem. Cell Biol., vol. 94, no. 5, pp. 419–432, Oct. 2016. https://doi.org/10.1139/bcb-2016-0068
241. B. J. Main, C. J. Italiano, and K. J. Rodgers, "Investigation of the interaction of beta-methylamino-L-alanine with eukaryotic

and prokaryotic proteins," Amino Acids, vol. 50, no. 3–4, pp. 397–407, Apr. 2018. https://doi.org/10.1007/s00726-017-2525-z
242. B. J. Main, R. A. Dunlop, and K. J. Rodgers, "The use of L-serine to prevent beta-methylamino-L-alanine (BMAA)-induced proteotoxic stress in vitro," Toxicon, vol. 109, pp. 7–12, Jan. 2016. https://doi.org/10.1016/j.toxicon.2015.11.003
243. R. van Onselen, N. A. Cook, R. R. Phelan, and T. G. Downing, "Bacteria do not incorporate beta-N-methylamino-L-alanine into their proteins," Toxicon, vol. 102, pp. 55–61, Aug. 2015. https://doi.org/10.1016/j.toxicon.2015.05.014
244. R. van Onselen and T. G. Downing, "BMAA-protein interactions: A possible new mechanism of toxicity," Toxicon, vol. 143, pp. 74–80, Mar. 2018. https://doi.org/10.1016/j.toxicon.2018.01.011
245. Rauk, "beta-N-Methylamino-L-alanine (BMAA) not involved in Alzheimer's disease," J. Phys. Chem. B, vol. 122, no. 16, pp. 4472–4480, Apr. 2018. https://doi.org/10.1021/acs.jpcb.8b01641
246. K. J. Rodgers and N. Shiozawa, "Misincorporation of amino acid analogues into proteins by biosynthesis," Int. J. Biochem. Cell Biol., vol. 40, no. 8, pp. 1452–1466, 2008. https://doi.org/10.1016/j.biocel.2008.01.009
247. Samsel and S. Seneff, "Glyphosate's suppression of cytochrome P450 enzymes and amino acid biosynthesis by the gut microbiome: pathways to modern diseases," Entropy, vol. 15, no. 4, pp. 1416–1463, Apr. 2013. https://doi.org/10.3390/e15041416
248. Samsel and S. Seneff, "Glyphosate pathways to modern diseases V: Amino acid analogue of glycine in diverse proteins," J. Biol. Phys. Chem., vol. 16, pp. 9–46, 2016. https://doi.org/10.4024/03sa16a.jbpc.16.01
249. D. Cattani et al., "Mechanisms underlying the neurotoxicity induced by glyphosate-based herbicide in immature rat hippocampus: Involvement of glutamate excitotoxicity," Toxicology, vol. 320, pp. 34–45, Jun. 2014. https://doi.org/10.1016/j.tox.2014.03.001
250. M. G. Zavala-Cerna, E. A. Martinez-Garcia, O. Torres-Bugarin, B. Rubio-Jurado, C. Riebeling, and A. Nava, "The clinical significance of posttranslational modification of autoantigens," Clin. Rev. Allergy Immunol., vol. 47, no. 1, pp. 73–90, Aug. 2014. https://doi.org/10.1007/s12016-014-8424-0
251. J. J. Hogan, G. S. Markowitz, and J. Radhakrishnan, "Drug-induced glomerular disease: immune-mediated injury," Clin. J. Am. Soc. Nephrol., vol. 10, no. 7, pp. 1300–1310, Jul. 2015. https://doi.org/10.2215/cjn.01910215
252. G. Worst et al., "Cell-free expression with the toxic amino acid canavanine," Bioorg. Med. Chem. Lett., vol. 25, no. 17, pp. 3658–3660, Sep. 2015.
253. J. Akaogi et al., "Role of non-protein amino acid L-canavanine in autoimmunity," Autoimmun. Rev., vol. 5, no. 6, pp. 429–435, Jul. 2006.
254. R. van Onselen, S. Downing, G. Kemp, and T. Downing, "Investigating beta-N-Methylamino-L-alanine misincorporation in human cell cultures: a comparative study with known amino acid analogues," Toxins, vol. 9, no. 12, p. 400, Dec. 2017. https://doi.org/10.3390/toxins9120400
255. R. van Onselen, L. Venables, M. van de Venter, and T. G. Downing, "beta-N-Methylamino-L-Alanine toxicity in PC12: excitotoxicity vs. misincorporation," Neurotox. Res., vol. 33, no. 1, pp. 15–23, Jan. 2018. https://doi.org/10.1007/s12640-017-9743-8
256. M. D. Vaughan, Z. Su, E. Daub, and J. F. Honek, "Intriguing cellular processing of a fluorinated amino acid during protein biosynthesis in Escherichia coli," Org. Biomol. Chem., vol. 14, no. 38, pp. 8942–8946, 2016. https://doi.org/10.1039/c6ob01690a
257. G. Worst et al., "Residue-specific incorporation of noncanonical amino acids into model proteins using an escherichia coli cell-free transcription-translation system," Jove-J. Vis. Exp., no. 114, p. e54273, Aug. 2016. https://doi.org/10.3791/54273
258. Konovalova, T. Hilander, F. Loayza-Puch, K. Rooijers, R. Agami, and H. Tyynismaa, "Exposure to arginine analog canavanine induces aberrant mitochondrial translation products, mitoribosome stalling, and instability of the mitochondrial proteome," Int. J. Biochem. Cell Biol., vol. 65, pp. 268–274, Aug. 2015. https://doi.org/10.1016/j.biocel.2015.06.018
259. Hilander et al., "Editing activity for eliminating mischarged tRNAs is essential in mammalian mitochondria," Nucleic Acids Res., vol. 46, no. 2, pp. 849–860, Jan. 2018. https://doi.org/10.1093/nar/gkx1231
260. E. Kartvelishvili, M. Peretz, D. Tworowski, N. Moor, and M. Safro, "Chimeric human mitochondrial PheRS exhibits editing activity to discriminate nonprotein amino acids," Protein Sci., vol. 25, no. 3, pp. 618–626, Mar. 2016. https://doi.org/10.1002/pro.2855
261. G. Parks, G. Cooper, M. Dooley, M. Park, E. Treadwell, and G. Gilkeson, "Childhood agricultural and adult occupational exposures to organic dusts in a population-based case–control study of systemic lupus erythematosus," Lupus, vol. 17, no. 8, pp. 711–719, Aug. 2008. https://doi.org/10.1177/0961203308089436
262. G. Parks, J. A. Hoppin, A. J. De Roos, K. H. Costenbader, M. C. Alavanja, and D. P. Sandler, "Rheumatoid arthritis in agricultural health study spouses: associations with pesticides and other farm exposures," Environ. Health Perspect., vol. 124, no. 11, Jun. 2016. https://doi.org/10.1289/ehp129
263. R. Mesnage, M. Arno, M. Costanzo, M. Malatesta, G.-E. Séralini, and M. N. Antoniou, "Transcriptome profile analysis reflects rat liver and kidney damage following chronic ultra-low dose Roundup exposure," Environ. Health, vol. 14, no. 1, Dec. 2015. https://doi.org/10.1186/s12940-015-0056-1
264. M. Milan et al., "Ecotoxicological effects of the herbicide glyphosate in non-target aquatic species: Transcriptional responses in the mussel Mytilus galloprovincialis," Environ. Pollut., vol. 237, pp. 442–451, Jun. 2018. https://doi.org/10.1016/j.envpol.2018.02.049
265. R. Mesnage, B. Bernay, and G.-E. Séralini, "Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity," Toxicology, vol. 313, no. 2–3, pp. 122–128, Nov. 2013. https://doi.org/10.1016/j.tox.2012.09.006
266. Y. A. Bali, S. Ba-Mhamed, and M. Bennis, "Behavioral and immunohistochemical study of the effects of subchronic and chronic exposure to glyphosate in mice," Front. Behav. Neurosci., vol. 11, p. 146, Aug. 2017. https://doi.org/10.3389/fnbeh.2017.00146
267. N. Yu et al., "Circular RNA expression profiles in hippocampus from mice with perinatal glyphosate exposure," Biochem. Biophys. Res. Commun., vol. 501, no. 4, pp. 838–845, Jul. 2018.
268. Ji, L. Xu, Z. Wang, X. Fan, and L. Wu, "Differential microRNA expression in the prefrontal cortex of mouse offspring induced by glyphosate exposure during pregnancy and lactation," Exp. Ther. Med., vol. 15, no. 3, pp. 2457–2467, Mar. 2018. https://doi.org/10.3892/etm.2017.5669
269. Javier Baier, C. Eugenia Gallegos, R. Raisman-Vozari, and A. Minetti, "Behavioral impairments following repeated intranasal glyphosate-based herbicide administration in mice," Neurotoxicol. Teratol., vol. 64, pp. 63–72, Dec. 2017. https://doi.org/10.1016/j.ntt.2017.10.004
270. R. Brenner et al., "Familial Mediterranean Fever and incidence of cancer: an analysis of 8,534 israeli patients with 258,803 person-years," Arthritis Rheumatol., vol. 70, no. 1, pp. 127–133, Jan. 2018. https://doi.org/10.1002/art.40344
271. W. Schroeder and S. M. Sheikh, "The complex genetics of common variable immunodeficiency," J. Investig. Med. Off. Publ. Am. Fed. Clin. Res., vol. 52, no. 2, pp. 90–103, Mar. 2004. https://doi.org/10.1136/jim-52-02-17
272. S. Georgin-Lavialle et al., "Familial Mediterranean fever," Rev. Med. Interne, vol. 39, no. 4, pp. 240–255, Apr. 2018.
273. C. G. Rida, G. Cantuaria, M. D. Reid, O. Kucuk, and R. Aneja, "How to be good at being bad: centrosome amplification and mitotic propensity drive intratumoral heterogeneity," Cancer Metastasis Rev., vol. 34, no. 4, pp. 703–713, Dec. 2015.https://doi.org/10.1007/s10555-015-9590-0
274. L. Tomljenovic and C. A. Shaw, "Do aluminum vaccine adjuvants contribute to the rising prevalence of autism?," J. Inorg. Biochem., vol. 105, no. 11, pp. 1489–1499, Nov. 2011.

https://doi.org/10.1016/j.jinorgbio.2011.08.008
275. L. Tomljenovic and C. A. Shaw, "Aluminum vaccine adjuvants: are they safe?," Curr. Med. Chem., vol. 18, no. 17, pp. 2630–2637, 2011. https://doi.org/10.2174/092986711795933740
276. C. A. Shaw and L. Tomljenovic, "Aluminum in the central nervous system (CNS): toxicity in humans and animals, vaccine adjuvants, and autoimmunity," Immunol. Res., vol. 56, no. 2–3, pp. 304–316, Jul. 2013. https://doi.org/10.1007/s12026-013-8403-1
277. N. Agmon-Levin, G. R. V. Hughes, and Y. Shoenfeld, "The spectrum of ASIA: 'Autoimmune (Auto-inflammatory) Syndrome Induced by Adjuvants,'" Lupus, vol. 21, no. 2, pp. 118–120, Feb. 2012. https://doi.org/10.1177/0961203311429316
278. C. Perricone, S. Colafrancesco, R. D. Mazor, A. Soriano, N. Agmon-Levin, and Y. Shoenfeld, "Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) 2013: Unveiling the pathogenic, clinical and diagnostic aspects," J. Autoimmun., vol. 47, pp. 1–16, Dec. 2013.https://doi.org/10.1016/j.jaut.2016.05.011
279. S. Esposito, E. Prada, M. V. Mastrolia, G. Tarantino, C. Codecà, and D. Rigante, "Autoimmune/inflammatory syndrome induced by adjuvants (ASIA): clues and pitfalls in the pediatric background," Immunol. Res., vol. 60, no. 2–3, pp. 366–375, Dec. 2014.https://doi.org/10.1007/s12026-014-8586-0
280. S. Goldman and N. Z. Miller, "Relative trends in hospitalizations and mortality among infants by the number of vaccine doses and age, based on the Vaccine Adverse Event Reporting System (VAERS), 1990-2010," Hum. Exp. Toxicol., vol. 31, no. 10, pp. 1012–1021, Oct. 2012. https://doi.org/10.1177/0960327112440111