

The Widespread Implications of a Nano-Bio Communication System

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Abstract

This paper proposes that human biological information can be in part transferred from one person to another by tiny particles or nano-sized droplets that are smaller than pollen. The transfer can take place by secretions in any form, such as perspiration or breath. The particles, typically nano-size, lipid-encapsulated vesicles, contain fragments of DNA and other genetic material and are called exosomes (EXs). Thus, one person can transfer essential attributes, both physical and mental, to another person that the person may not have had previously and that may be useful for survival. It is pointed out that this has been occurring for millions of years of evolution. Furthermore, the EXs are related to the synaptic vesicles in neuron-to-neuron communication and can cross biological barriers such as the blood-brain barrier. The EXs represent a universal nano communication system providing a rather newly identified unifying interaction principle in nature. This paper both summarizes and speculates on the relevance of this rapidly developing field to prevailing views of human biological and cultural evolution.

Les Implications Généralisées d'un Système de Communication Nano-Bio

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Résumé

Ce document explique que de l'information biologique humaine puisse être en partie transférée d'une personne à une autre par de minuscules particules, à savoir des gouttelettes de taille nanométrique, plus petites que le pollen. Le transfert peut avoir lieu par des sécrétions sous plusieurs formes, comme la sueur ou le souffle. Ces particules, des vésicules lipidiques-encapsulées généralement de taille nano, qui contiennent des fragments d'ADN et d'autre matériel génétique, sont appelées Exosomes (abrégié en EX). Ainsi, une personne peut transférer des attributs essentiels, autant physiques que mentaux, à une autre personne qui n'en possédait pas auparavant, et qui peuvent lui être utiles pour sa propre survie. L'article met en évidence que cela se produit depuis des millions d'années d'évolution. En outre, les EX étant associés à des vésicules synaptiques dans une communication de neurone à neurone, peuvent franchir les barrières biologiques tels que la barrière hémato-encéphalique. Les EX représentent donc un système de communication nano universelle fournissant un principe - identifié assez récemment - d'interaction unificatrice dans la nature. Cet article résume et en même temps s'interroge sur la pertinence de ce domaine, qui se développe rapidement, par rapport à la vision dominante de l'évolution biologique et culturelle humaine.

Las Extensas Implicaciones de un Systems de Comunicaciones Nano-Bio

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Resumen

Este artículo propone que la información biológica humana puede ser transferida de una persona a otra a través de pequeñas partículas o nano gotitas más pequeñas que el polen. La transferencia puede suceder por cualquier forma de secreción, tal como el sudor o el aliento. Las generalmente nano-partículas, vesículas lípido encapsuladas, contienen fragmentos de ADN y otro material genético y son llamados Exosones (EXs). Por consiguiente, una persona puede transferir atributos esenciales, ambos físicos y mentales, a otra persona que no los haya tenido anteriormente y puedan ser útiles para sobrevivir. Cabe resaltar que esto viene ocurriendo por millones de años de evolución. Aun mas, los exones están relacionados con las vesículas sinápticas de comunicación de neuronas a neuronas y pueden atravesar barreras biológicas tal como la barrera sanguínea del cerebro. Los Exones representan un sistema de nano comunicación aportando un principio relativamente nuevo de interacción y unificación en la naturaleza. Este artículo, ambos resume y especula en la importancia de este rápidamente en desarrollo campo a los prevalecientes puntos de vista en la evolución cultural y biológica humana.

As Implicações Generalizadas de um Sistema de Comunicação com Nano-Bio

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Sumário

Este artigo propõe que a informação biológica humana pode ser em parte transferida de uma pessoa para outra, por pequenas partículas, ou gotículas nanométricas, que são menores que o pólen. A transferência pode ocorrer por secreções de qualquer forma, como transpiração ou respiração. As partículas (tipicamente tamanho nano, bolhas encapsuladas em lipídios) contêm fragmentos de DNA com outros materiais genéticos e são chamados de exossomos (EXs). Assim, uma pessoa pode transferir atributos essenciais para outras pessoas, tanto físicos como mentais, que podem ser úteis para a sobrevivência. Nota-se que isso vem ocorrendo há milhões de anos de evolução. Além disso, os EXs estão relacionados às vesículas sinápticas na comunicação entre os próprios neurônios e podem atravessar barreiras biológicas, como a barreira hematoencefálica. Os EXs representam um sistema universal de nano-comunicação que fornece um princípio de interação unificadora recentemente identificado na natureza. Este artigo resume e especula sobre a relevância desse campo em rápido desenvolvimento, para as visões predominantes da evolução biológica e cultural do ser humano.

Die weitreichende Auswirkungen eines Nano-Bio Kommunikationssystems

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Zusammenfassung

Die biologischen Informationen des Menschen können teilweise von einem Mensch auf einen anderen übertragen werden. Diese Abhandlung beschreibt, dass dies geschehen kann mit Hilfe von sehr kleinen Partikeln bzw. Nanotröpfchen, die kleiner sind als Pollen.

Verschiedenartigen Sekreten wie Schweiß oder Atem können diese Informationen übertragen. Die Größe dieser Partikeln ist üblicherweise im Nano Bereich, sie sind lipid-verkapselte Vesikel und enthalten DNA Fragmente oder sonstiges genetisches Material. Man nennt sie Exosomes (EXs). Demzufolge kann eine Person wesentliche Eigenschaften, sowohl physische als auch mentale, auf eine andere Person, die sie vorher noch nicht hatte, übertragen, was sehr nützlich für das Überleben sein könnte. Es hat sich herausgestellt, dass dies bereits vor Jahrmillionen in der Evolution geschah. Des Weiteren agieren die EXs ähnlich wie die synaptischen Vesikel in der Neuron zu Neuron Kommunikation und können biologische Hindernisse, wie z.B. die Blut-Hirn Schranke, überqueren.

Die EXs stellen ein universales Nano Kommunikationssystem dar und bieten ein ziemlich neu identifiziertes vereinigendes Interaktionsprinzip in der Natur.

Diese Abhandlung bietet einen Überblick und spekuliert über die Relevanz dieses sich schnell entwickelnden Forschungsgebiets sowie über seine vorherrschenden Vorstellungen der biologischen und kulturellen Entwicklung des Menschen.

Introduction

The biological inheritance mechanism, including the one in humans, is associated with the linear and long DNA polymer molecule. The DNA sustains life from one generation to another by being transmitted in fertilization by specific cells called gametes. In the nucleated eukaryotic cells, the DNA localizes to the mitochondria and to the cellular nuclei. There, in this kind of DNA, integrated genetic information becomes converted into specific biological functions. This occurs so that the DNA sequences will become transcribed as the messenger RNAs (mRNAs). The mRNAs are then translated to the wealth of the protein species. The proteins compose at one end the enzymes that make the biochemical reactions possible in our body. Such reactions provide the fundament for the various metabolic events in the human body. Besides metabolism, the enzymes are involved in synthesis of the structural proteins of the human body, such as collagens. These provide the physical support for the bones and the ligaments that join the muscles to the bones (Myllyharju 2008, 402-417).

Today, scientists have developed cost-effective sequencing technologies that enable them to identify rapidly all of the human genome-level information present in the DNA (Cao et al. 2018, 17-32). This capacity is currently changing the prevailing views of the modes of action and transfer of biological information within the human body. The knowledge has opened exciting research lines to reveal how the individuals are connected to each other and other living organisms in nature. This paper summarizes some of these recent developing megatrends. Based on recently published data, this paper goes on to speculate on the new

horizons that the secreted nano- and micro-size mobile genetic information droplets have opened up. Collectively the field can be expected to have a great impact on science and human culture.

The Human Genomic “Dark Matter” as the Dominant Information of Life

Presently the information within the genomic DNA of all species, including humans, can be identified by so-called deep sequencing, typically taking around one day (Cao et al. 2018, 17-32). The Human Genome Project set up the foundations for the so-called genomic era. This process aimed to reveal the entire composition of the DNA book of life, that is, the exact structure of the DNA, the order of all its building-block nucleotide sequences.

The next step in the large body of international work was to identify how the genomic information, called transcriptome, is used in cells. The transcriptome represents all those RNA types that are generated from the genomic DNA in the process of transcription. In other words, this research line identifies the genetic words that are being said from the DNA and in specific those DNA types that are expressed from the DNA. The transcriptome thus represents the collective quantitative and qualitative composition of the specific RNA types that are made from the DNA (Costa-Silva, Domingues, and Lopes 2017, e0190152). Based on such an approach, the global activity of the whole genome can be revealed in the human body and other species as well.

Strikingly, when all the cellular RNA sequences were compared to that of the DNA information, this led yet to an unexpected finding. It turned out that only a small portion, around 1.5 percent of the mammalian genomic sequences, is in fact encoded as the protein encoding mRNA types. Thus, this means that more than 97 percent of human genomic information produces so called non-coding genetic information. To date, scientists have revealed that most of the DNA is actually read as a wealth of different types of RNA molecular fragments. Such RNA can be either protein-encoding ones or those that do not code for proteins, serving therefore as the non-coding RNAs (ncRNA). The degree to what types of RNAs are being made in a given cell is based on the specific physical conditions that the cells are exposed to during their life cycle ((Bhartiya and Scaria 2016, 59-68; Shi et al. 2016, 1471-1478; Goodhead and Darby 2015, 102-109). The ncRNAs have a key role to serve as the cellular marionette strings to regulate the protein coding mRNA expression. This occurs in part via control of the mRNA stability. Together, the human genome contains a wealth of mini-genes that do not code for the classic information transfer components that is the proteins.

Human Genomic Information is in Part Secreted Inside Invisible Droplets Called Exosomes

Another surprise for the scientists came when it turned out that ncRNA types can also be secreted from the cells. As a result, such RNA fragments can end up in body fluids, such as blood. Via body fluids, the RNA can spread widely systemically, that is, at the level of the whole body from their site of secretion. Besides these findings, it was noted that the ncRNAs can become packed inside of very small cellular droplets. These droplets are then secreted out from the cells. These information structures can be of nano- and micro-size (30-1000 nm) and were named as the exosomes (EXs), even though other names are also used ((Iraci et al. 2016, 171; Kalra, Drummen, and Mathivanan 2016, 170; Nakamura et al. 2016, 48; Lotvall and Valadi 2007, 156-158).

The RNAs are not the only type of components that can be packed in the EXs. The others are DNA and proteins such as enzymes, lipids, sugars, and metabolites. All these are critical for the control of physiology. Cells secrete the EXs especially when they are exposed to stimuli. It is important to note that the molecular content of the EXs can vary depending on the exact nature of stimuli that our body is encountering. Together, based on the current view in the field, the EX system appears to provide a mechanism by which the cells and the organs maintain their metabolic balance that is homeostasis (Figure 1) (Paolicelli, Bergamini, and Rajendran 2018). The EX system is, however, also relevant in regards to diseases, but this aspect is not discussed in detail in this paper.

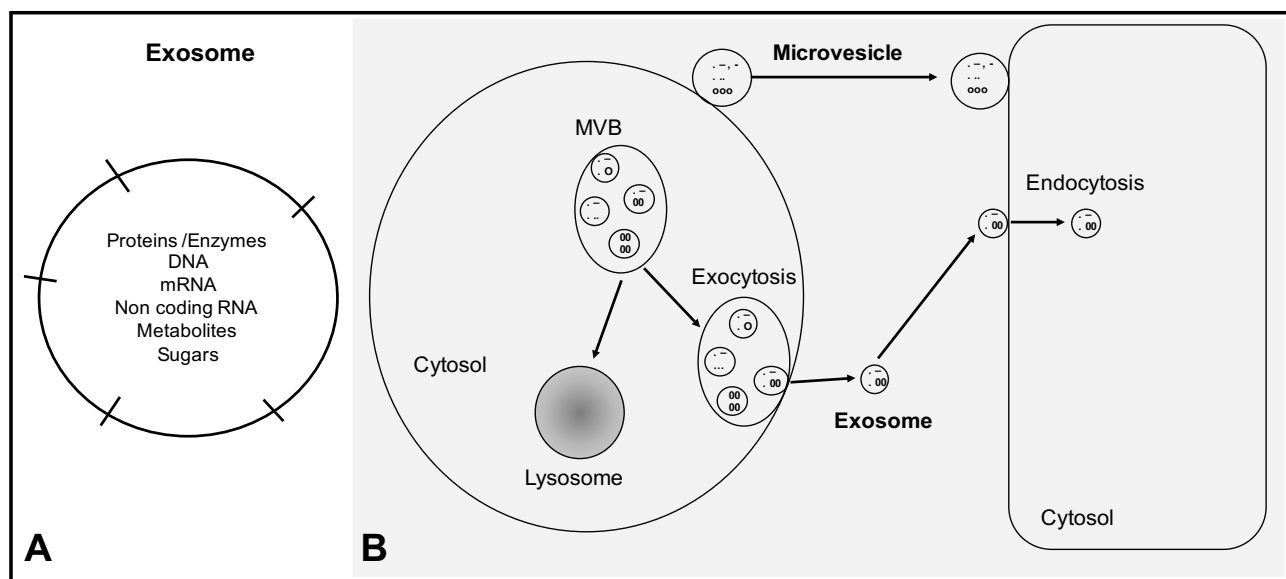


Figure 1. Schematic illustration of a cell and the secreted extracellular nano vesicle element, exosome (EX) biological communication system. A) One EX is depicted. The EX is a nano size (30-100 nm) “sac” that contains integrated surface proteins serving to target and bind a given EX to a target cell in the organ of the body (for a review, please see (van Niel, D'Angelo, and Raposo 2018, 213-228; Panagiotou et al. 2018)). The EX interior contains a wealth of key biomolecules (see the text for details). **B)** The EXs are initially generated inside the cells in the Multi Vesicular Body (MVB) by encapsulation of the MVB lipid membrane. Thereafter, the MVB is either enzymatically destroyed in the Lysosome or fused to the plasma membrane of the donor cell. The fusion releases the EXs to the body fluids to be transmitted to distant cells. The secreted EXs bind and fuse to a target cell membrane. This fusion releases the EX’s content to the cell, and molecules such as the microRNAs (miRNAs), a non-coding form of RNAs, regulate cellular metabolism and fate via control of the mRNA stability (Makarova et al. 2016, 33-49). Since the EX can cross the biological barriers such as the Blood Brain Barrier (BBB), they provide also a novel way to connect “the body and the mind.” Given this property, the EXs provide a kind of mobile “biological symbol function” that is involved in horizontal and vertical transfer of such regulatory biological information ((Lee et al. 2016, 51991-52002; Lo Cicero, Stahl, and Raposo 2015, 69-77; Valadi et al. 2007, 654-659).

According to the current view, EX-mediated communication is universal in nature. Human body fluids such as serum, saliva, and cerebrospinal fluid, in addition to urine, feces, and gut microbes, all contain millions of the EXs. Such EXs are expected to differ in their qualitative

and quantitative molecular content (Figure 1). It is important to note that the EXs are also an integral part of our food and drinks, such as milk and fruit juices (Shandilya et al. 2017, 9506-9513; Pérez-Bermúdez et al. 2017, 40-50). Due to these reasons the EXs also connect our body to the outside world in a fundamental way. Thus, by their nature the EXs can serve as useful and flexible vessels of biological information transfer in the human body. They can transport both genetic and other types of biomolecular information both short and long distances. The genetic EX materials are represented as the m/ncRNA and DNA types. The other molecular products include enzymes, peptides, and metabolites that can be secreted by the EXs between the bodily cells. It can be concluded that the EXs represent a robust and at least an epigenetic machinery that regulate the cells in a profound way and not only in humans, but also in the other species and between them as well ((Bakhshshandeh, Kamaledin, and Aalishah Khadijeh 2017, 31-36; Maas, Breakefield, and Weaver 2017, 172-188; Vyas and Dhawan 2017, 1567-1576; Orench-Rivera and Kuehn 2016, 1525-1536; Coakley, Maizels, and Buck 2015, 477-489; Muraca et al. 2015, 343-348; Tzelos et al. 2016, 84-92).

Qualitative Different Invisible Exosome Droplets as “Physiological Notes in Control of Life”

For a non-biology expert to obtain a view of the significance of the EXs and their function, we may illustrate this by using music as a metaphor (Hancock 2008, 205-208). According to this analogy, of the millions of individual EXs in the human body, each of the EXs may contain its unique molecular regulatory capacity (for a review, please see van Niel et al. 2018, 213-228; Panagiotou et al. 2018). Thus, each of the EXs may be viewed as a kind of a musical note of the physiological composition of life. Once a given cell is exposed to stimuli, it will respond by secreting a series of EXs. These and the sequence of their secretion in a flow of influence serve to balance the cellular response to the stimuli. Thus, a given target cell advances the physiological music that is reflected as the changes in the cellular EX-regulated metabolic profiles. In other words, since the ncRNAs of the EXs regulate multiple target mRNAs to maintain the cellular homeostasis via control of mRNA stability, such an EX-coordinated symphony would provide a concrete way for how they can advance the cellular music by translating the EX spray to a given physiological composition in a reacting cell.

The invisible Postal Coded Exosome Droplets Transfer Information Between Cells

At present, it is still poorly understood how the different physiological conditions lead to formation of specific EXs with certain molecular compositions (Cocucci and Meldolesi 2015, 364-372; Villarroya-Beltri et al. 2014, 3-13). The EXs are encapsulated by a lipid membrane that is obtained from the cell of an EX's origin. Several types of proteins are either superficial or integral and thus cross the membrane inside the EX droplets.

The role of such EX proteins is to serve as a postal address with a lock-key type of mechanism. In this idea, the protein keys that are present at the EX surface provide an exact recognition at the target cell membrane by the corresponding binding proteins (Figure 1). After the target-cell binding, the EX will be taken in by the cell. Inside a cell, the EX will be opened by certain enzymes. This releases the EX's content to the cell to regulate its behavior (Maas et al. 2017, 172-188). By having this kind of a described mechanism, the EXs represent in nature a complex but only-recently-recognized universal cellular information transfer system. The ways that the EXs are targeting common or unique cell

types is being actively studied (Figure 1). In summary, the EXs provide an important and ancient transport system in living organisms. Based on their composition we can understand rather well how the EXs expose their influence on the cells.

The Invisible Exosome Droplets Connect the Body and the Mind

One relevant feature of the EXs is that, unlike many of the currently identified biological signaling systems, the EXs represent the natural vehicles that can cross over the biological vasculature-related barriers such as the ones in the brain, the gut, the placenta, and the kidney. The blood-brain barrier (BBB) represents one critical barrier that has been considered very restrictive. This means that only few molecular types can cross the BBB. There is now evidence that the EXs indeed provide means to cross the BBB (András and Toborek 2016, e1131804). Thus, besides linking the cellular control in a new way in the human body, the EXs also serve to connect the functionalities of the brain to the rest of the body via an EX's molecular cargo.

When considering our currently dominant view of how the human brain is thought to function, the neuronal electro-chemical signal transfer and the synaptic vesicles (SVs) are critical. The SVs transfer the neural signal from cell to cell in the neurons. The EXs provide here a new mechanism in the synaptic cell-cell signaling, and they are also similar in structure to the SVs. In addition to this the EXs widely mediate the cell-cell communication, not only between the neuronal cells but also between other cell types in the brain. (Rajendran et al. 2014, 15482-15489; Smalheiser 2007, 35).

The capacity of the EXs to cross the BBB has opened important science-and-philosophy-related questions and challenges. Since the EXs can transmit molecular regulatory information between the brain and the rest of the body, this fact is relevant for the classic "body-mind dilemma" (Urban 2018, 228-240; Scudellari et al. 2018, e139). The dilemma illustrates the failure in our conceptual understanding to be able to explain in mechanistic detail how the mind could be connected to the control of cell behavior in the rest of the human body. Given this, the mind has been considered by some in many ways to be separate from the body. In other words, our ideas, imaginations, meditations, visualizations, and thinking are considered to be only subjective representations without clear objective value and have no known direct connection to the environment from which they come. Given this, we have failed to establish a scientifically sound bridge between the brain and the body. We can conclude that the identification of the EXs that can cross the BBB with a significant load of molecular genetic information provide an important conceptual opening for studies on how our subjective mind's related reactions may be embodied.

Based on the above discussions of the nature of the EXs, they can be expected to be relevant in providing opportunities to learn how psychology impacts diseases when they are psychosomatic (Liew et al. 2017, 11-19; Li et al. 2017, 17-28; Tsilioni, Panagiotidou, and Theoharides 2014, 882-888; Demertzi et al. 2009, 1-9). Depending on the neural actions that are associated with our thoughts, emotions, and memory, these actions may indeed be considered to be qualitatively and quantitatively differently composed and secreted EXs in order to reach a better understanding of human cognition. Together by being able to cross the BBB, the EXs may translate one's mindset. This may mean EX-mediated translation of the somatic cellular actions via the (epi)genetic-mediated control mechanism.

The impact of the EX can be extended beyond the brain since the EXs can also cross other biological barriers, such as the gut, the lung, the placenta, and germ cells in the reproductive organs (Miranda et al. 2018, 34-43; Sáez et al. 2018, 26-35; Vyas and Dhawan 2017, 1567-1576; El Andaloussi et al. 2013, 391-397). Due to these reasons, the EXs may serve to mediate the epigenetic control also across the barriers more broadly. Such a mechanism would thus be based on the transfer and target-cell release of the ncRNAs inside the EXs. Given the properties of the EXs, they are prime candidates to mediate horizontal or trans-generational information transfer. This process could operate during pregnancy. The maternal influence here leads to epigenetic programming of the fetal cells, such as occurs in stress and famine, for example (van der Harst, de Windt, and Chambers 2017, 590-606; Vaiserman, Koliada, and Jirtle 2017, 38). Since the EXs are involved in the control of embryonic development (Krause et al. 2018, 1422675; McGough and Vincent 2016, 2482-2493), the EXs may thus play a role in the transfer of the developmental programming important in mediating the environmental load to the embryo (Aljunaidy et al. 2017, R399; Krautkramer et al. 2017, 30-50).

The Invisible Exosome Droplets as Putative Bioaerosol Signals

Since small EXs are present in most human body fluids, including saliva, cerebrospinal fluid, tears, and urine, the EXs may turn relevant when considering social interactions (Hari et al. 2015, 181-193). Such an idea is based on the known property of infective viruses, such as the influenza virus that spreads between individual as bioaerosols. Thus, since the EXs are of the size of viruses and are present in the saliva and therefore are present in the breath, it seems plausible that the EXs also could serve as bioaerosols. Thus, the EXs may indeed represent a new type of a player in social interactions. Here the EXs would be exchanged between people who are in somewhat close proximity. The EXs distributed by one person may be inhaled by a recipient. By being transferred across the lung barrier, the EXs may enter into the blood circulation. Via the EX postal code, an EX can end up in a given organ. It should, however, be considered that the immune system of the host may also eradicate the EXs after being recognized as foreign bodies (Lässer et al. 2011, 9).

It is not only breath but our food and drinks such as milk, fruit juices, and berries that also contain the EXs. These may similarly have the capacity to enter into the body via crossing biological barriers. Thus, it seems evident that EXs provide several levels by which humans are connected to the rest of the natural world. Given these points we may think differently about sayings such as “listen to your gut feelings,” or “the skills of a person were inherited already in their mother’s milk.” The EX knowledge may explain scientifically the well-preserved sayings by being their biological representations (Zempleni et al. 2017, 3-10).

We may expand the impact of the emerging nanobiological EX communication even beyond the communication between human beings. The EXs are present in urine and feces, and they serve as universal mediators in nature. Indeed, the EXs are also connected, for example, to viruses, bacteria, yeasts, parasites, and spores (Gandolfi et al. 2013, 4727-4736; Jaenicke 2005, 73). On the grounds of this data, due to their small size, the EXs may be more significant in nature, even at the level of the biome. In the troposphere, the bioaerosols serve as so-called nucleation centers. These are involved in the formation of clouds and rain dynamics (Wolf et al. 2015, 662-671). Interestingly, depending on their composition and size, bioaerosols can spread very long distances, some even across the Earth.

The EXs can also be rather stable, so much so that the EXs of dried milk, for example, can be reactivated in solution. Moreover, since the ncRNAs are already small fragments, they sustain their activity better than the mRNA in harsh conditions, such as under radiation and ultraviolet exposure (Yahyapour et al. 2018, 34-45; Ge et al. 2014, 1568-1575). Given the known EX properties, it may be hypothesized that “a breath in a given location” may putatively influence another living organism in a more distant location. Here the target inhales the EXs and in this way such a biological nanoparticle would enter the body fluids.

If the aforementioned speculations are someday supported with experimental data, this would open a new level of sociobiological studies. If EXs indeed can function as regulatory bioaerosols together with certain other types of aerosols, this may promote a broader view that the atmosphere and cloud dynamics may have had an impact on biological evolution in a manner that involves the EXs (Jelonek, Widlak, and Pietrowska 2016, 656-663; Xu et al. 2015, 1355-1363). In this scenario, the function of rain would be to bring to Earth the sun/cosmic-energy-radiated EX nano bioaerosol particles. These could impact the nucleic acids by causing mutations, and the mutated nucleic acids could be an evolutionary raw material for a species when inhaled.

Invisible Exosome Droplets and Charles Darwin’s Pangenesis Theory

During the time of Gregory Mendel (late nineteenth century), the father of genetics, Charles Darwin, considered the possibility that inheritance within humans would be mediated by small particles synthesized by every cell in the body. These “gemmules,” as he named them, were believed to transport biological inheritance to germ-line cells. Darwin named his theory “pangenesis” (Liu and Li 2016, 19-22; Holterhoff 2014, 661-695; Li, Wang, and Liu 2014, 387-388).

The currently known behavior of EXs and their biology is in line with the idea that the EXs are somewhat similar to the gemmules named by Darwin in his pangenesis theory. When we consider the mechanism of evolution, the EX system provides in fact an elegant way to test on a micro scale, and thus at the level of a few cells, the usefulness of the novelties that the EX-modified cells may have encountered. Thus if, for example, the atmospheric-derived and radiation-subjected EX RNA/DNA had any beneficial effects in a recipient’s cell, the host would have the capacity to multiply the information. If the EX-derived information had any harmful consequences in a given cell, as is likely the case, there would need to be a mechanism to eradicate the EX cargo novelty. How would this be possible?

Could the EX RNA/DNA be incorporated to become part of the host DNA? It may be relevant in this context that the breast milk-secreted droplets transmit the so-called reverse transcriptase (RT) enzyme (Irmak, Oztas, and Oztas 2012, 20). The role of the RT that is linked to certain viral infections in the body is to convert the RNA to become incorporated to the DNA chain. By this way the EX-derived genetic innovation would become maintained in a cell permanently.

It is also known that fragments of DNA can become incorporated directly to the genomic DNA via a process called DNA interference (DNAi) (Omotezako, Onuma, and Nishida 2015, 20150435). Besides this process, the genome contains an abundance of so-called jumping genes, the transposons. The transposons represent genomic information that moves from one place to another (Shapiro 2017, 1-17; Lapp and Hunter 2016, 237-249). The so-called CRISPR approach represents yet another natural genome editing machinery that may have an

impact in the EX mediated control (Zhang et al. 2017, 230-241). Together, these mechanisms may be connected to the EX-mediated control in evolution.

The properties of EXs, including their ability to cross the BBB and transmit information between the environment and a host, may indeed serve as machinery in the process of evolution. The EXs may provide a possible mechanism to couple the brain, mind, and consciousness with an internal evolutionary process. Here the described elements also integrated to EX dynamics may serve as the mediators to promote human and other species' adaptations (Eaton et al. 2015, 1165-1171; Smythies, Edelstein, and Ramachandran 2014, 133). These questions remain to be studied in the future in detail.

Invisible Exosome Droplets and Esotericism

Given that the EXs are present not only in humans but also in the other living organisms, they may provide a common biological symbolic function; in other words, they could be “the letters of life” that connect all living organisms together in an invisible way. Indeed, the novel nano biological field represented by the secreted nano- and micro-size EX vesicles that are lipid encapsulated molecular cargo tools in our body may also be relevant to the esoteric sciences. For example, the EX biological symbolic function may be seen as an analogy of creative words, the idea of the *logos*. For the world to become a reality, words needed to be expressed, spelled out. This possibility suggests that the idea within the primordial creation may be reflected in the notion of the *Musica Universalis*, the Harmony of the Spheres (Zhu, Dacso, and O'Malley 2018, 727-752). Musical vibrations can be in harmony when a certain musical composition is being played on instruments. Similarly, the harmonies or disharmonies may play the life tone via the EXs, using them as the notes of life. The comparison of matter to music can be visualized in a cymatics setup (Misseroni et al. 2016, 23929), where the EXs could serve as the particles organized by life's creative forces (Kwon et al. 2012, 1260-1264).

Together with other factors, the emergence of personalities may be influenced by the actions of billions of EX-based bio-language elementary particles having an impact on the body and mind. This possibility is in line with reports that, for example, heart transplant recipients start to express properties of a person who donated the organ (Pearsall, Schwartz, and Russek 2000, 65-72). Moreover, the exchange of EXs among people and within nature in general might even impact biological and cultural evolution.

Conclusion

By now it is evident that nano- and micro-vesicle EX mediated communication is universal in nature. This signaling system serves as a link between live organisms. The EX research field has opened up exciting opportunities. The EXs may provide ways to identify even finer and more subtle but relevant energetic regulatory forces in control of life.

Even though a wealth of research work has been conducted in developmental biology, we still fail to understand how shapes and forms become assembled during the process of organ morphogenesis. In this context, the process named “cymatics” provides a demonstration of how energy such as sound waves can serve as a formative force. In cymatics, small particles become organized in a specific way. The organization, or the generated particle cluster shapes, depends on the exact frequencies of the sound exposed to the particles in a vibrating surface (Misseroni et al. 2016, 23929). Given this, the identification of the EXs may provide

a way to look for those frequencies that in a genetic-program-dependent manner may be involved in organizing the cells to 3D organoids (derived from reprogrammed stem cells) or organs such as the kidney becoming constructed during embryogenesis.

When we consider esotericism, the EXs may serve as the biological evolutionary raw material through which human consciousness evolves via the spiritual work, for example. Hence, in conducting ritual exercises such as meditation or intonation, this may lead to the activation, formation, and secretion of certain types of EXs. Such newly assembled EXs with specific molecular signature may then go on to translate the impact of the daily exercise to the gradual development of new neural circuits that are connected to the emergence of new mental capabilities in the end. This process is also influenced by the food we eat, the environment we live in, and with whom we interact. In clinical medicine, the EXs provide opportunities to develop diagnostics and therapies. These exciting questions can be approached with the experimental skills available in the scientific communities.

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