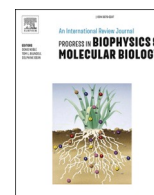


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Uterosomes: The lost ring of telegony?

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ABSTRACT

Telegony refers to the appearance of some characteristics of the female's previously mated male in her subsequent offspring by another male. According to evidence, telegony may occur either through the infiltration of sperm into the somatic tissues of the female genital tract or the presence of fetal genes in the mother's blood. It is highlighted that sperm penetrates into the mucosa of the uterine and possibly alters the genetic structure, affecting the embryo and enduring from one pregnancy to the next, which may be one of the potential mechanisms of telegony. Uterine fluid, uterine gland-derived histotroph, supplies key nutrients for successful embryo implantation and it is important during the first trimester, especially, because of its susceptibility to maternal states. The presence of EVs in uterine fluid (uterosomes) was reported in mice, sheep, and humans, including a wide range of biomolecules, such as proteins, and non-coding RNAs. In this review article, we presented a new idea to explain telegony. Based on our idea, after the previous male sperm entry into the female reproductive system, those sperm which do not participate in fertilization penetrate into the somatic cells of the uterus and store their genetic/epigenetic information there. The sperm of the next partner reaches a location in the female reproductive canal where it exchanges information with the uterosomes and obtains the proteins and non-coding RNAs required for fertilization, development, and implantation.

1. Introduction

1.1. Telegony

Telegony, as one of the most interesting genetic phenomena, refers to the appearance of some characteristics of female's previously mated male in her subsequent offspring by another male (Burkhardt, 1979). August Weismann (1893) coined the term 'telegony' and mentioned that 'spermatozoa had reached the ovary after the first sexual union had occurred and had penetrated into certain ova which were still immature.' The maturation of these oocytes may coincide with the second intercourse which might lead to the birth of offspring. In his classic book *The Germ-Plasm*, he described telegony as a 'doubtful phenomenon of heredity,' adding that the reported examples of telegony were based on a 'misconception,' and recommending that further trials be conducted to answer this matter (Weismann, 1893).

Darwin (Darwin and Murray, 1868) gathered some asserted instances of what he attributed to "the direct action of the male element on the female form" and for the first time described telegony in Chapter 11

of his book *The Variation of Animals and Plants under Domestication* (Darwin and Murray, 1868). He regarded this phenomenon to be of particular significance for unraveling the mechanisms of heredity. Besides, he mentioned that "it is certain that ovaria are sometimes affected by a previous impregnation, so that the ovules subsequently fertilized by a distinct male are plainly influenced in character" (Darwin and Murray, 1868). "My evidence is adequate to show the reality of a former sire imposing his effect on a future offspring, despite the fact that this fact is one of comparably infrequent occurrence," Romanes said of telegony." (Romanes, 1893). The existence of telegony was reported in a wide spectrum of species such as horses (Douglas, 1821; Finn, 1893), pigs (Giles, 1815; Lowe, 1896), dogs (Cornevin, 1891; Darwin and Murray, 1868), cats (Lowe, 1896), sheep (Darwin and Murray, 1868; Finn, 1893), mice (Gorczyński et al., 1983), rabbits (Parer et al., 1995; Sobey and Conolly, 1986; Williams and Moore, 1991; Zhelnin, 1964), flies (Crean et al., 2014), beetles (Pascoal et al., 2018), and humans (Cornevin, 1891; Flint, 1877; Lingard, 1884; Lowe, 1896; Webber, 1896).

In the 80s and 90s, the phenomena of telegony were noted in the immune system of mice and rabbits. First and foremost, Gorczyński et al.

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(1983) reported the aberrant hyporesponsiveness to particular alloantigens in the second generation offspring born to neonatally tolerant male despite subsequent mating with “normal” (nontolerant) males. Rabbit offspring sired by non-immune bucks and born to doe previously mating with bucks that had recovered from myxomatosis also demonstrated immunity to the myxoma virus in a research done by [Sobey and Conolly \(1986\)](#). This discovery was later proved by other researchers ([Parer et al., 1995](#); [Williams and Moore, 1991](#)).

The manifest of telegony was recently seen in insects as offspring body size has been reported to be affected by the female’s previous mate instead of the biological father ([Crean et al., 2014](#); [Pascoal et al., 2018](#)).

1.2. The possible mechanisms of telegony

1.2.1. Sperm infiltration into the somatic tissues of the female genital tract

The presence of sperm in the uterine mucosa and uterine tube of the bat, mouse, and rabbit was reported by [Kohlbrugge](#) in the early 1910s ([Kohlbrugge, 1910, 1912](#)). He suggested that sperm-mediated uterine cell modification, which affects the embryo and lasts from one pregnancy to the next, might be one of the telegony processes ([Kohlbrugge, 1910, 1912](#)). In this regard, in 1959–60, [Austin et al.](#) ([Austin, 1959, 1960](#); [Austin and Bishop, 1959](#)) published three original papers regarding the presence of sperm in the uterine of two species of bat suggesting that sperm penetrates into the mucosa of the uterine and possibly alters the genetic structure. [Bendich et al. \(1974\)](#) found that mouse sperm could be taken up by Chinese hamster fibroblasts, resulting in the transfer of DNA from the sperm to the nucleus of the somatic cell. [Brodsky and Ivanov \(2009\)](#) proposed in 2009 that sperm may produce viable chimera cells after piercing somatic cells in vivo, which might live indefinitely in the body.

1.2.2. The incorporation of exogenous DNA into somatic cells

In modern biology, DNA may infiltrate into the somatic cells/tissues as documented in vitro and in vivo studies where penetrated sperm is deposited in the uterine and is spread to other tissues, such as adrenal, ovary, vagina, embryos, and tumor cells via blood or lymphatic system ([Bendich et al., 1974](#); [Ledoux and Charles, 1972](#); [Watson et al., 1983](#); [Wolff et al., 1990](#)).

Another interesting approach to this topic was provided by [Holmgren et al. \(1999\)](#) who posed the question if DNA might be transported among cells through the phagocytosis of apoptotic bodies. They found that genomic DNA transfer from apoptotic corpses to the nuclei of phagocytosing cells was sustained throughout time. As a result, phagocytic maternal cells may take up sperm-derived apoptotic bodies. It makes sense to assume that, the female reproductive tract absorbs those sperm which do not participate in the fertilization from the huge amount of DNA-including sperm that are stored during copulation. If this sperm-derived foreign DNA can affect the oocytes by incorporating it into somatic cells, then the next progeny may display this effect in their genetic structure, thus reinforcing the basis of telegony ([Liu, 2011, 2018a](#)).

1.2.3. The role of fetal genes in mother’s blood

[Lo et al. \(1997\)](#) firstly reported the presence of fetal DNA in maternal circulation which rises by increasing gestational age and shows a dramatic increase during the last two months of pregnancy ([Lo et al., 1997, 1998](#)). A pregnant mother’s blood contains a combination of her own DNA and fetal DNA, which originates from apoptotic cells in the placenta and accounts for 10% of total circulatory DNA in maternal plasma ([Tsui and Lo, 2012](#)). Circulatory fetal cells and cell-free fetal DNA are increasingly being discovered in the majority of pregnant women even decades after delivery. ([Bianchi et al., 1996](#); [Invernizzi et al., 2002](#); [Lissauer et al., 2007](#)). Therefore, the identification of fetal DNA in the maternal bloodstream paved the way to determine the entire fetal genome using the blood of pregnant mothers ([Fan et al., 2012](#)), and cast new light on telegony.

The possible integration of fetal DNA stemmed from the mother’s previous partner into the genome of the mother’s future fetus by a different male may influence the personality of the subsequent progeny. Male cells have been found in women with no history of male children or abortion, suggesting that these cells were transmitted from female sexual partners during sexual intercourse ([Lissauer et al., 2007](#)).

Regarding the period of time during which oocytes may have received genetic information from a previous partner, the course of pregnancy, accompanied by the ongoing release of fetal DNA into the mother’s blood, is regarded as a favorable opportunity for oocytes to receive this information and become transfected or transformed. If the transfection of oocytes happens which is subsequently fertilized with sperm from a different partner, the future children may bear some resemblance to the former male ([Liu, 2013](#)). In a general sense, transfection capability is low under normal circumstances. However, there are information indicating that the injected DNA into mouse oocytes could be identified in a portion of mature mice and new transgenes comprise about 20% of mouse progeny ([Gordon and Ruddle, 1981](#)). Correspondingly, [Carballada et al. \(2000\)](#) declared that immature eggs were effortlessly transfected via plasmid DNA along with cationic liposomes. It was indicated that many transient DNA breaks within embryonic DNA may assume a role in the integration of foreign DNA ([Kiesling and Markoulaki, 2000](#)). This evidence may explain the occasional happening of telegony.

Until now, we discussed the proposed mechanisms for telegony, but one important question remains yet to be answered. If telegony occurs through fetal DNA or integration of sperm into female somatic cells, we do not know how long it will take for the genetic information of the previous partner to be concealed someplace in the female reproductive tract and potentially contribute in a future conception. So, we need the packages to protect the genetic content of previous male and properly transferring it to future offspring. We will tell the story of uterine fluid-derived extracellular vesicles (uterosomes) as a possible destination of preceding male genetic information and describe how these vesicles may involve in telegony in the next sections.

The majority of existing information about the microchimerism generation comes from studies conducted on women who produced boys ([Brodsky and Ivanov, 2009](#)). It is likely that Y-chromosome-containing cells originate not just from fetal sources, but also through the interaction between sperm and somatic cells ([Brodsky and Ivanov, 2009](#)). [Brodsky et al. \(Brodsky and Ivanov, 2009\)](#) proposed that sperm could penetrate somatic cells in vivo, generating viable chimeric cells, which may endure and stable in the body for a long time. Although the presence of Y-chromosome is about one-half of sperm, the real number of chimeric cells could be higher than it is identified ([Brodsky and Ivanov, 2009](#)). [Brodsky et al. \(Brodsky and Ivanov, 2009\)](#) idea has yet to be tested and proven, particularly in terms of the stability and maintenance of live chimera cells and their nucleic acid contents over time. Future research should focus on this topic in depth.

2. Uterine fluid

Uterine fluid, uterine gland-derived histotroph, supplies key nutrients for successful embryo implantation and it is important during the first trimester ([Burton et al., 2002](#); [Hempstock et al., 2004](#); [Salamonsen et al., 2013](#)). Multiple sources have been introduced for the constituents of this fluid (carbohydrates, amino acids, lipids, nucleic acids especially extracellular vesicle (EV) miRNAs), including proteins exudation from endometrial epithelium and glands, evolving blastocyst, tubal fluid, and blood ([Salamonsen et al., 2009, 2013](#); [Simon et al., 2018](#)). Because of selective protein secretion in lieu of direct origination from blood and active transportation of amino acids, there is a distinct difference between the proteome and amino acid composition of blood and uterine fluid ([Leese et al., 2007](#); [Salamonsen et al., 1984](#)). The amino acid content of uterine fluid may be altered as a consequence of changes in women’s food quality, according to the data ([Kermack et al., 2015](#)). It is

important to note that uterine fluid contains information that reflects the mother's environmental exposure during early pregnancy and probably transmits that information to the embryo, afterward creating long-lasting epigenetic influences on the progeny through embryonic and placental programming (Simon et al., 2018; Zhang et al., 2017).

3. Uterine fluid in early pregnancy

It is believed that embryo-uterus crosstalk during early pregnancy is the key to successful embryo implantation and establishment of pregnancy as in excess of 50% of pregnancy losses occur in the course of early pregnancy (Cha et al., 2012; Chen et al., 2013). The disturbance of uterine fluid homeostasis in terms of volume and/or molecular components is one of the major causes of these failures (Lu et al., 2013; Zhang et al., 2015). The chaos of maternal circumstances before and after implantation, such as food fluctuations and stress, might reveal the major causes for errors in embryo development and adult-onset diseases, a concept known as the 'Developmental Origin of Health and Diseases.' (Barker and Osmond, 1986). According to this hypothesis, fetal programming may be affected by particular maternal lifestyle factors like environmental exposure and nutritional states, leading to metabolic and disease predispositions disorders in progeny (Bouret et al., 2015; Fleming et al., 2015). The fact that the epigenetic information conveyed by parental gametes could transmit acquired characteristics to offspring, has been strongly pointed out in the last few years (Chen et al., 2016b; Huypens et al., 2016; Lane et al., 2014; Radford et al., 2014). During the preimplantation phase, epigenetic control of the uterus and changes in its gene expression as a result of mothers' bad lifestyles may impair the developing embryo, with long-term consequences for offspring's health (Zhang et al., 2017). For instance, Kwong et al. (2000) have reported the incidence of postpartum hypertension in rats having undergone maternal nutritional stress during the preimplantation period. This *in vivo* study is reflected by data that *in vitro* growing embryo cultures may also cause postpartum complications in humans and mice, such as high blood pressure, defective glucose metabolism, and behavioral changes related to anxiety and spatial memory (Chen et al., 2014; Ecker et al., 2004; Watkins et al., 2007). Thus, these reports indicate that the unhealthy alteration in the environment of preimplantation embryos may engender a lasting impact on the health of the progeny, likely through epigenetic mechanisms during development. However, if we pose the question of how a growing embryo is influenced by maternally acquired environmental characteristics in the uterus, we can probably find the answer to our question in the uterine fluid environment because the growing embryo in the preimplantation stage is completely soaked in this fluid for a considerable period of time and may be affected or regulated via biological factors in this vital timeframe (Chen et al., 2013; Zhang et al., 2017). In recent years, the vulnerability of uterine fluid composition to maternal situations has been documented. As an exemplification, a maternal low protein diet limited to the preimplantation period changes the amino acids content of mouse uterine fluid, inducing adaptive responses to ensure adequate fetal growth, while such a compensatory response to a specific diet could finally provoke adult-onset diseases, such as high blood pressure and metabolic disease (Eckert et al., 2012; Kwong et al., 2000; Sun et al., 2014, 2015; Watkins et al., 2008). Similarly, Kermack et al. (2015) studied the amino acid composition of human uterine fluid and discovered that the concentrations of 18 amino acids were unaffected by age, BMI, various cycle stages, or benign gynecological disease; however, the amino acid content of human uterine fluid was altered by variations in the maternal diet.

Regarding the complexity of the molecular composition of uterine fluid, the mentioned changes in the amino acids content of human uterine fluid because of maternal dietary diversity may depict just the 'tip of the iceberg' while a broad spectrum of biological factors, such as proteins and non-coding RNAs (ncRNAs), could undergo significant modifications that might affect a developing embryo (Zhang et al.,

2017). The alterations in the content of uterine fluid may stem from the serum or blood/other body fluids-derived extracellular vesicles (EVs), reflecting maternal conditions not only dietary choice but also other harmful changes, in particular, stress, inflammation, and environmental pollutant exposure, may epigenetically affect embryo and fetal growth (Zhang et al., 2017). It was shown that the injection of sperm tRNA fragments (tRFs), obtained from high-fat-diet (HFD) model male mice, into normal oocytes resulted in appearing metabolic disorders and alteration in genes related to metabolic pathways in offspring similar to HFD father (Chen et al., 2016a). Similarly, acquired features are expected to be relayed into a developing embryo via uterine fluid EV non-coding RNAs and/or other epigenetic information transporters (Zhang et al., 2017). Recent studies provide insight into the novel types of embryo-maternal communication via uterine fluid EVs and RNAs (Zhang et al., 2017).

4. Uterosomes

The presence of EVs in uterine fluid (uterosomes), containing microvesicles (MVs) and exosomes (EXOs), has been reported in mice (Al-Dossary et al., 2013; Griffiths et al., 2008), sheep (Burns et al., 2014, 2016; Campoy et al., 2016; Ruiz-González et al., 2015), and humans (Ng et al., 2013; Vilella et al., 2015), including a wide range of biomolecules, such as proteins, and non-coding RNAs. Ng and colleagues (Ng et al., 2013) were the first group to confirm the existence of EVs in human uterine fluid and its related mucus. The movement of functional cargo from uterosomes to sperm is particularly intriguing. In this context, investigations show that during sperm transit through the female reproductive canal, the transfer of sperm adhesion molecule1 and plasma membrane Ca²⁺-ATPase4a, a key component of the capacitation process, occurs under neutral pH circumstances (Al-Dossary et al., 2013; Griffiths et al., 2008; Martin-DeLeon, 2016). Correspondingly, Burns et al. (2014) thoroughly surveyed the proteome and RNA content of uterosomes and found that there are significant differences in the proteome of pregnant and non-pregnant sheep (Burns et al., 2014). Furthermore, an abundance of non-coding RNAs was identified in cyclic and pregnant uterosomes which may be transferred to the cells *in vitro* (Burns et al., 2014). These results suggest that uterosomes may play a role in sperm maturation and may even transmit their own material to the embryo, which is important for embryonic development and embryo-endometrial interactions. A comprehensive discussion on the interactions of sperm with the uterosomes and other cells/tissues in the female reproductive tract is beyond the aim of this paper (see [(Martin-DeLeon, 2016; Saint-Dizier et al., 2020)] for an overview).

5. Uterosomes: the lost ring of telegony?

Sperm reach the uterus and may modify the genetic structure, as discussed in earlier sections. (Austin, 1959, 1960; Austin and Bishop, 1959; Kohlbrugge, 1910, 1912). We also noted Brodsky and Ivanov's findings (Brodsky and Ivanov, 2009), which suggested the creation of live chimera cells *in vivo* after piercing somatic cells, which may remain in the female body permanently. The word "permanently" we used is absolutely astonishing because the long-term storage of complex and unknown genetic information of sperm in the tissues of the female body, especially the uterus, can raise the question of whether this information can be passed on to next generations or, most especially, is it possible that epigenetic information within the uterus leftover from a previous parent to be transferred to another man's sperm and appear in the offspring after fertilization? In other words, could this long-term storage be the lost ring of telegony? If the answer to this question is yes, we can pose the question "how can this stored information participate in this process?" To address this issue and develop our own hypothesis, it is better to use the same processes which were proposed for the epididymis-derived extracellular vesicles, named epididymosomes.

It is highlighted that environmental stressors alter the content of the

circulatory EVs which may cross the Weismann barrier and achieve the paternal germ cells (Spadafora, 2018). Thereafter, the sperm takes up the RNA content of EVs and either reversely transcribes to cDNAs using LINE-1 retrotransposons or reserves as RNA packages (Spadafora, 2018). The ultimate destinations of cDNAs are thought to be the storage of cDNAs in sperm and, most likely, their transfer to oocytes during the fertilization process (Spadafora, 2018). Moreover, circulatory EVs may cooperate with epididymosomes, epididymis-derived EVs with a broad range of divergence in size and content and highly sensitive to environmental effectors, and unload their cargo (Nejabati et al., 2021). Afterward, epididymosomes could transfer their protein and RNA content to sperm in the course of sperm maturation and then deliver to the embryo during fertilization, succeeded by acquired by offspring (Bohacek and Rassoulzadegan, 2020). In the matter of ‘atavism’ (i.e. the reappearance of some ancestral genetic characteristics after having not been present in preceding generations) (Liu, 2018b), the central point is possibly the capacity of genetic and/or epigenetic dormancy, which sequentially may cause the vanishing of some acquired characteristics (ACs) in the immediate parents and their sudden recurring in the later generations (Liu, 2018b). In this context, epididymosomes may be a promising choice for preserving RNA content, modifying the epigenome of future generations, and allowing the revival of ancestral ACs. As a result, epididymosomes may disentangle parental life histories and show historical events that have an impact on parental life (Nejabati et al., 2021).

Based on the information obtained from the epididymosomes and their role in storing genetic information and transmitting it to sperm, a similar hypothesis can be given for uterosomes (Fig. 1). It can be said that after the previous male sperm entry into the female reproductive system, those sperm which do not participate in fertilization penetrate into the somatic cells of the uterus and store their genetic/epigenetic information, which may include previous partner’s sperm DNAs, mRNAs, and non-coding RNAs, which may subsequently be part of EVs, in particular uterosomes (Fig. 1A). Integration of prior partner’s genomic/epigenomic contents into uterosomes may also aid to shield them from degradation and preserve them for a longer period of time. It

is still questionable when this information may transfer to the next man’s sperm. But the mechanism of transmission of this information to the next male sperm can be related to uterosomes, which were shown to exchange information with sperm before fertilization (Fig. 1B). But at this point, the question that may arise is what kind of genetic/epigenetic information may be transferred by sperm to the somatic cells of the uterus and stored there. It was shown that the goldfish’s tail was transformed from double to single following injection of carp’s ovarian eggs-derived mRNA (Tung and Niu, 1973). Furthermore, the same findings were achieved by injecting various types of coding and non-coding RNAs into oocytes to create particular acquired traits (Bohacek and Rassoulzadegan, 2020; Liu, 2018a, 2018c). It is becoming increasingly clear that a considerable amount of effectors, such as food (Johnson, 1990; Love, 1909; Newberne and Young, 1973; Ng et al., 2010), acquired habits (Lindqvist et al., 2007; McDougall, 1927, 1930; Nätt et al., 2009; Pawlow, 1923), immunity (Guttmann and Aust, 1963; Lemke et al., 2004; Steele, 2009), light (Durken, 1923), chemicals (Akimoto et al., 2007; SANo, 2002; Spergel et al., 1975; Spergel et al., 1971), and age effects, (Dufton, 1932; Jablonka and Lamb, 1999; Liu et al., 2011; Redfield, 1917), may be inherited by the progeny. Regarding the mechanism underlying the RNA-mediated transfer of genetic information to offspring, Steele (1981) reported his own hypothesis named ‘somatic selection’, demonstrating the transmission of somatic genetic alterations to the germ cells in the form of RNA, which is reversely transcribed to DNA and subsequently merged into the germ-line DNA. Furthermore, the non-mendelian transfer of parental genetic material to future children is related to the action of sperm head transposable and/or repetitive elements, particularly LINE-1 (Spadafora, 2018), which make up the majority of circulating DNA (Bronkhorst et al., 2018; Grabuschnig et al., 2020). It was reported that a wide variety of non-coding RNAs, including miRNAs and tRFs, are involved in sperm biology along with transgenerational inheritance (Bohacek and Rassoulzadegan, 2020). In this regard (Sharma et al., 2016), evaluated the impacts of a parental low protein diet on the change in the content of sperm non-coding RNAs and metabolic outcomes in the following generations (Sharma et al., 2016).

Finally, we’d want to discuss one aspect of this idea that may be debatable. The duration between sexual encounters might be rather extensive, and it’s unclear how the RNA from the previous partner could be preserved in the absence of an RNA-dependent RNA polymerase. The answer to this question may underlie in “somatic selection” theory proposed by Steele et al. (Steele, 1981; Steele et al., 1998) and the historic and still unresolved and overlooked phenomenon termed “atavism”. We briefly discussed the importance of these theory in this section and also provided adaptive mechanism which proposed for epididymosomes, but the permeability and stability of the contents of EVs, which may be generated in a result of receiving previous partner(s) nucleic acid contents of sperm, is still questionable and needs to be examined and tested in the future well-designed studies.

6. Conclusions and perspectives

We offered a novel way to understand telegency in this review paper. Currently, two processes for telegency have been documented, one of which is connected to fetal DNA, which naturally includes the previous man’s genes and is released into the mother’s blood on a regular basis, after which it may be kept in the mother’s tissues for a long time. For this to happen, the woman must have had a child with the previous man. If the woman gets pregnant by another man, the genetic content of the previous man, which already exists in fetal DNA, may participate in the fertilization process and thereby telegency occurs. But another mechanism is defined based on the entry of sperm into the somatic cells of the uterus. The introduction of past male genetic contents into the uterus and other female bodily tissues may contribute in the future fertilization of the female by a different male in this technique. The goal of this work is to finish this process and provide a new window for telegency. In this

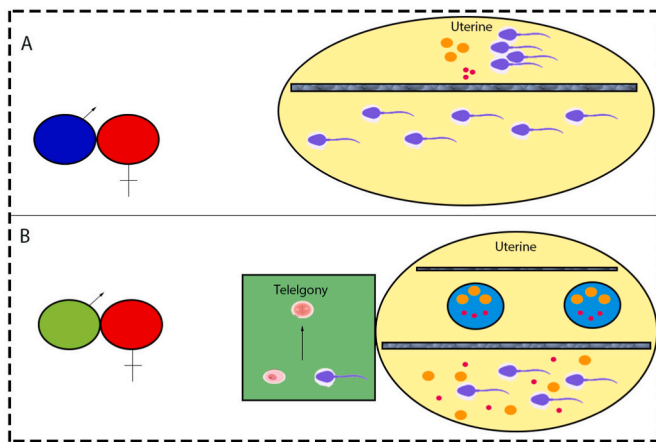


Fig. 1. The proposed mechanism for telegency. A. During the first partner (Navy Blue Circle) sperm entry into the female reproductive tract, those sperm which do not participate in fertilization penetrate into the somatic cells of the uterus and store their genetic/epigenetic information, including non-coding RNAs (Small Red Circles) and RNAs (Orange Circles). B. During the second partner’s sperm travel through the female reproductive tract, it reaches a point where it exchanges information with the uterosomes and receives the proteins and non-coding RNAs necessary for fertilization, embryogenesis, and, implantation. At this stage, specific non-coding RNAs (Small Red Circles), responsible for particular traits, left by the previous partner may participate in fertilization and subsequently, these traits appear in the offspring. Navy Blue Circle: first partner; Green Circle: second partner; Red Circle: the woman; Big Blue Circles: uterosomes; Orange Circles: RNAs; Small Red Circles: non-coding RNAs.

mechanism, for telegony to happen, the woman no longer needs to have children from the previous sexual partners. If a woman has sexual intercourse which has led to the entry of sperm into the female reproductive system, telegony would likely happen. But the question that remains unanswered is how the next man's sperm will receive the genetic information stored in the uterus. The answer may lie in uterosomes, which could contain a vast expanse of *genetic information, especially information from a woman's previous sexual partners*. The sperm of the next partner reaches a location in the female reproductive canal where it exchanges information with the uterosomes and obtains the proteins and non-coding RNAs required for fertilization, development, and implantation. Specific non-coding RNAs responsible for specific features left by the previous partner may engage in fertilization at this stage, and these traits will arise in the child as a result.

Therefore, testing this idea requires extensive research on uterosomes, including a variety of omics studies, which will add to our knowledge of these vesicles and open up new horizons in evolutionary biology as well as clinical research.

Declarations

Authors' roles

H.R.N. conception and design, drafting the article, acquisition of data, analysis and interpretation of data. L.R. and M.N. revising it critically for important intellectual content and final approval of the version to be published.

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