Speculation On Epigenetic Transference Occurring In Organ Transplant Recipients

Memory and personality transference are scientifically documented phenomenons. Cases occurring over the past fifty years have given rise to focused research within this field of psycho-social interaction and the cellular memory theory. Five cases conducted by Gary E. Schwartz, Professor of parapsychology at the University of Arizona, supports the transfer of memory and personality traits through known biological processes rather than abstract mediums. Professor of genetics at the University of Birmingham Medical School, Bryan M. Turner, theorizes that nucleosomes within cells attain the potential to act as the cell's memory bank, and can transmit epigenetic information from donor to host cells. The University of Freiburg's Professor of hematology, Maria Themeli, conducted empirical research of donor-DNA integration into host epithelium, resulting in genomic alterations occurring within the allogeneic organ transplant recipient. Themeli's work was supported by the experiments of the Polish Academy of Science's transplantology researcher Waldemar L. Olszewski, who produced evidence that allogeneic organ transplantation is not only followed by cellular microchimerism, but also integration of donor-DNA into recipient dendritic and graft cells. These, along with many other ongoing scientific studies in this field, have given rise to the credibility of the cellular memory theory and the transference of memory and personality genes from donor to host cells.

The accumulated research of studies done over the years have provided solid evidence that the nervous system, along with small parts of the immune system, are the primary organ systems that function in the role of retaining and storing memory within the human body. However, as organ transplantations are being utilized increasingly within the medical world, there is an unsolved enigma that arises from these allogeneic transplantations: if it is known that the nervous and immune systems are the main organ systems most directly involved with memory storage, why are organ transplant recipients, those of which are acquiring organs outside the peripheral nervous system, inheriting and experiencing the memories and personalities of their organ donors? Presently, from what many neurologists and psychologists understand about the non-genetic transfer of memory and psyche, the only legitimate scientific explanation they could offer behind this medical mystery would be the effects of the psycho-social stress and anxiety, immunosuppressive drugs and anti-rejection medications, and pre-existing medical conditions experienced by the organ-recipients.

Theories are being presented that may explain how this transfer of non-genetic material can occur in patients receiving allogeneic transplants (that is, transplants that involve tissues or organs from the same species; in this case, human-to-human). According to professors of hematology at the University of Freiburg, these organ transplant recipients receiving allogeneic transplantations would attain true biological chimeras, in which the transplanted organs attain a different genome than the other natural organs within the recipient's body (Themeli et al., 2011). As indicated by their research findings, some epithelial cells within transplant recipients reveal donor-derived genotypes and/or alterations in their genomes (Themeli et al., 2011). In response, Themeli et al. (2011) proposed the notion that "… the incessant charge of the transplant recipient with donor-DNA and its integration in host epithelium may indeed by operative in the generation of epithelial cells with donor derived genome" (p. 25). The incorporation of foreign DNA within the recipient's genome (DNA chimerism) may induce the

physical rearrangements of the host's DNA in the form of point mutations, deletions, chromosomal breakage and interruptions in coding sequences as the DNA undergoes replication (Themeli et. al., 2011, p.26). However, this observation, which suggests that distinct epithelial cells within transplant recipients contain donor-derived genomes, challenges the perception that the donor's cells are immediately cleaved and phagocytized by the recipient's passenger cells once transplantation occurs.

Furthermore, researchers at the department of surgical research and transplantology at the Polish Academy of Science have conducted experiments on mice to test how long donor DNA fragments remain within a recipient's dendritic cells (DCs), and if the donor DNA could enter into the nuclei of DCs, access and integrate itself into the recipient's genome (Olszewski et al., 2003). Transplanting allogeneic bone marrow cells, hearts, and skin grafts into 3 groups comprising of 3-5 rats each, Olszewski et al. (2003) concluded that donor DNA fragments could be identified within the recipient's tissue at high values for a period of approximately 30 days. Along with the observations of Themeli et al. (2011), the findings of Olszewski et al. (2003) also challenges the perception that the donor's cells are immediately cleaved and phagocytized by the recipient's passenger cells post-transplantation. Instead, the donor's cells may access and integrate themselves into the recipient's genome via dendritic cells, ultimately changing the host's genotype (Olszewski et al., 2003, p. 417).

Both the hypotheses of Themeli et al. (2011) and Olszewski et al. (2003) are supported and may be explained by the "cellular memory" theory, the pseudoscientific claim that "memories" can be stored individually in each body cell through the nucleosomal modification of histone tails, without the change in DNA sequence (Dodd et al., 2007, p. 813). University of Birmingham's Professor of Experimental Genetics, Bryan M. Turner, explains that all cells must have a mechanism for memory, as "a cell's identity is defined by its characteristic pattern of gene expression and silencing, so remembering who it is consists of maintaining that pattern of gene expression through the traumas of DNA replication, chromatin assembly, and the radical DNA repackaging that accompanies mitosis" (B.M. Turner, 2002, p. 285). Inside each cell's DNA-containing nucleus is the nucleosome core particle, which comprises of an octamer of the core histones: a pair of H2A, H2B, H3 and H4, which are coiled around 146 base pairs of DNA in 1 ¾ super helical turns (Luger et al., 1997). Despite histone-induced supercoiling having modest effects in the shortening of DNA length, it is the first step in the configuration of higher-order chromatin structures (B.M. Turner, 2011, p. 285). Until recently it has been discovered that the nucleosome has a crucial role in the regulation of gene expression, and therefore may transfer epigenetic information from one generation of cells to the next, attaining the characteristics of a "cell's memory bank" (B.M. Turner, 2011).

The DNA of eukaryotic cells is packed with histone proteins in a complex structure known as chromatin, which is the basic unit of a nucleosome. This chromatin structure consists of DNA coiled tightly around histone proteins. Each histone molecule has histone tails located within its N-terminus that protrude outward from the nucleosome. This compact structure of chromatin not only packs the cell's 2- meter strand of DNA densely inside the nucleus, but it also plays an essential role in gene expression (Zovkiv et al., 2017). Heterochromatin, which is defined as chromatin that has been highly-condensed, contains genes that are usually suppressed. Chemical modifications to the histone tails of chromatin influences both chromatin structure and gene expression through histone acetylation and methylation, which are catalyzed by certain enzymes (Imhof, 2006).

As the histone tails of each histone molecule in a nucleosome protrude outward, the tails are accessible to modifying enzymes that catalyze the addition or removal of certain acetyl or methyl groups. When the lysines (amino acids) in histone tails are attached to acetyl groups (-COCH), the lysines undergo acetylation, during which their positive charges neutralize and the histone tails not longer bind to their neighboring nucleosome. This results in the loosening of the chromatin structure. As the chromatin structure becomes less compact, the DNA strand within the nucleosome becomes accessible for gene transcription (Imhof, 2006, p. 4). When the lysines in histone tails are exposed to methyl groups (-CH), methylation of the lysines occurs and the chromatin structure condenses back into its compact form, preventing the transcription of genes. While certain enzymes are able to methylate the histone tails of the histone molecules, there are several enzymes that can methylate certain bases within the DNA strand itself, producing inactive DNA and unexpressed genes. The removal of these methyl groups can cause the chromatin to loosen, allowing the transcription of the DNA sequence for a certain gene (Verdone et al., 2006, p. 209).

The modification of chromatin previously described does not alter the DNA sequence, yet these modifications may be passed down from one generation of cells to the next. This is known as epigenetic inheritance, which is defined as the inheritance of traits transferred by mechanisms not entailing the nucleotide sequence (Zovkic et al., 2013, p. 61). While mutations to the DNA are permanent, irreversible changes, the modification of chromatin (acetylation and methylation) can be reversed.

Thus, cellular memory and epigenetic inheritance may be the causations behind the transfer of non-genetic material from one individual to another. The cellular memory theory states that every cell obtains a memory-storage mechanism through gene expression (acetylation) and silencing (methylation), and as these chromatin modifications are passed from one cell generation to the next, epigenetic inheritance occurs. The cells of donor-derived tissue is comprised of different DNA than that of the recipients, and the donated allogeneic tissue within the recipient is known as biological chimeras (Themeli et al., 2011). The research of Olszewski et al. (2003) challenges the notion that donor DNA is immediately cleaved and phagocytized by the host's passenger cells, and instead concludes that fragments of the donor-derived DNA can be detected in recipient tissue at high quantities for periods of approximately 30 days. According to the cellular memory theory, the cells within the donor-derived tissue still retain their "memory" (chromatin modifications) despite living in a different environment, and may exhibit the genes that were expressed when the cells existed within the donor (B.M. Turner, 2002). As the donor-derived cells replicate within the host's body, epigenetic transference may occur and these chromatin modifications can be passed to future generations of cells within the recipient. This may result in the expression or suppression of different genes within the transplant recipient, and the transfer of personality changes and memories that were incorporated into the donor's genome into the recipient's genome.

In a psychosocial experiment conducted by University of Arizona's Professor of parapsychology, Gary E. Schwartz, a number of heart-transplant patients were asked to disclose their observations about self-personality changes experienced post-transplantation (G.E. Schwartz, 2002). The patient's family and friends were also interviewed to convey any observations on the personality changes of the recipient. The donor's family and friends were interviewed separately, and prior to the procedure, the recipients were not told of whom they would receive the donor-organ from, and had no contact with the donor's family or friends. This would prevent the error that the recipient displayed personality changes similar to their donor

due to already knowing about their donor's personality. Reviewing the answers to the interview questions, Schwartz (2002) distinguished "statistically uncoincidental" and uncanny similarities between the donor's personality and the recipient's post-surgery (p. 9). The following are cases 4, 5, 6, 9 and 10 from the research article of Schwartz (2002) previously mentioned.

The donor was a 17 year old African American student, who was fatally shot during a drive-by shooting while walking to violin class. The donor's mother had reported to Schwartz: "He died right there on the street, hugging his violin case. He loved music and his teachers said he had a real thing for it. He would listen to music and play along with it" (G.E. Schwartz, 2002, p. 4). The recipient was a 47 year old white male who had been diagnosed with aortic stenosis. He reported to Schwartz: "I'm real sad and all for the guy who died and gave me his heart, but I really have trouble with the fact that he was black… I can tell you one thing though. I used to hate classical music, but now I love it. So I know it's not my new heart, because a black guy from the 'hood' wouldn't be into that. Now it calms my heart. I play it all the time. I more than like it. I didn't tell any of the guys on the line that I have a black heart, but I think about it a lot" (G. E. Schwartz, 2002, p.4). The recipient's wife reported: "… For the first time he's invited his black friends over from work. It's like he doesn't see colour any more, even though he still talks about it sometimes. He seems more comfortable and at ease with these black guys, but he's not aware of it. And one more thing I should say. He's driving me nuts with the classical music… He even whistles classical music songs that he could never know. How does he know them? You'd think he'd like rap music or something because of his black heart" (G.E. Schwartz, 2002, p. 5).

The donor was a 19 year old woman killed in an automobile accident. The donor's mother described her daughter to Schwartz: "My Sara was the most loving girl. She owned and operated her own health food restaurant and scolded me constantly about not being a vegetarian. She was a great kid. Wild, but great. She was into the free-love thing and had a different man in her life every few months. She was man crazy when she was a little girl and it never stopped. She was able to write some notes to me when she was dying… She kept saying how she could feel the impact of the car hitting them… She said she could feel it going through her body" (G.E. Schwartz, 2002, p. 5). The recipient was a 29 year old woman diagnosed with cardiomyopathy induced by endocarditis. She reported: "When I got my new heart, two things happened to me. First, almost every night, and still sometimes now, I actually feel the accident my donor had. I can feel the impact in my chest. It slams into me, but my doctor said everything looks fine. Also, I hate meat now… Actually, when I even smell it my heart starts to race. But that's not the big deal. My doctor said that's just due to my medicines" (G.E. Schwartz, 2002, p. 5). The recipient's brother reported a change in the recipient's sexual orientation: "Susie's straight now… She was gay and now her new heart made her straight… She holds hands and cuddles with Steven just like my girlfriend does with me. She girl-talks with my girlfriend, where before she would be lecturing about the evils of sexist men. And my sister, the queen of the Big Mac, hates meat. She won't even have it in the house" (G.E. Schwartz, 2002, p. 5).

As stated in the introduction of this article, it is believed by scientists, psychologists, and physicians alike that these differences in personality traits and memories are the symptoms of immunosuppressive drugs and anti-rejection medications taken by organ transplant recipients post-surgery. However, this assumption arises from doubt; there is not yet any evidence or clinical research that may prove or suggest that these changes are the direct consequences of medication and drugs (G.E. Schwartz, 2002, p. 8). Additionally, the reports of the recipient are uncannily similar to the experiences of the donor, and the possibility that the drugs produced

this effect is statistically uncoincidental (G.E. Schwartz, 2002, p. 8).

As seen in case 4, when a recipient (white male) was given a heart from the young donor (black male), he assumed that this change of heart would cause him to enjoy “rap music”. Because of this stereotypical assumption, he did not believe that his sudden interest in classical music was due to his heart transplant, when in actuality the donor loved classical music, even “hugging his violin case” at the time of his death (G.E Schwartz, 2002, p. 4). This is an example of personality transference occurring in the recipient post-surgery; the interest and passion of classical music was transferred from the donor to the unbeknownst recipient via heart transplantation.

In case 5, the recipient inherited not only the donor’s strong dislike for meat and a sexual orientation that was similar to the donor’s, but she also experiences nightmares that reflect the last moments of the donor; she reported to Swartz that she can feel the “impact of the car hitting them” every night (G.E. Schwartz, 2002. p.5). This is an example of both memory and personality transference, as the recipient developed a change in diet, sexual orientation (homosexual to heterosexual), and experiences the last physical sensation the donor had felt at the time of her death.

In case 6, the recipient, a middle age man, inherits both the youthful spirit and “giddiness” of his heart donor. Though this may be spawned from the recipient’s prior knowledge of his donor’s youth, the recipient also developed early symptoms of anorexia- the eating disorder that the donor was diagnosed during the period nearing the time of her death. The recipient, who prior to his surgery “loved food”, developed a sudden disinterest in food that prompted him to vomit after meals; his physician had also noted that this behavioral change “wasn’t anything to do with his new heart,” and only offers the possibility that it was a “reaction to something in the meal” (G.E. Schwartz, 2002, p. 6). Though this isn’t particularly memory transference, it is a transference of disinterests and disorders occurring between the recipient and the donor.

In case 9, the recipient, a 3 year old boy, can uncannily recall the name of his 2 year old donor, the incident leading up to the donor’s death, and can recognize the faces of the donor’s parents, without having any prior contact with the donor’s family or friends. The recipient also developed a strange disinterest in his Power Rangers action figures for no reason immediately post-surgery; considering that the donor died trying to catch his Power Ranger toys as they fell from a window, there is a possibility that the memory of the incident lingers in the recipient’s newly-transplanted heart cells.