REVIEW ARTICLE

The Narratives vs Biological Evidence in Understanding Early Human Embryo Development: The Example of Homunculus in the Sperm

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Abstract

The societal controversies addressing the human embryo and its features classify the embryo as a bio-object, where biological facts blend with the societal contexts. Here we consider a narrative of homunculus in the sperm based on the iconic image from 1694 by one of the first microscopists, Nicolaas Hartsoeker, as an example of male-derived deterministic understanding of embryo development. The narrative was confronted with the biological evidence of variability of the sexual reproduction and adaptive nature of human embryo development. The relations between narratives and biological evidence can contribute to the understanding of the societal perception of biological phenomena.

Keywords: Embryo, Fertilization, Gastrulation, Narrative, Organogenesis.

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Human Embryo as a Bio-object

The human embryo represents a source of controversies exemplified by a universal question of when human life began.[1] However, this is not the only controversy surrounding the human embryo, as the current technological achievements allow embryo manipulations in the experimental laboratory and during clinical procedures. *In vitro* fertilization or other assisted reproductive technologies represent routine clinical procedures and contribute to an estimated 2% of births in the United States of America in 2019.[2] The embryo and fetus are considered an important source of valuable stem cells, and the experimental procedures used in developmental biology research aim not only to understand the underlying mechanisms but as well to envisage novel therapeutic interventions for the adults contributing to the regenerative medicine. The ethical aspects of all these activities are carefully considered, however, the multitude of perspectives and rapid technological advancements make public consensus difficult. The human embryo represents a classical example of a bio-object—it escapes the traditional classifications and definitions and through the process of bio-objectification, it is a topic of societal controversies.[3,4] The biological facts are only a part of these controversies as they involve diverse societal concepts, which extend beyond biology.

The process of bio-objectification is highly dynamic and ever-changing because it integrates an understanding of biology and societal contexts.[5] Here we emphasize the power of narratives when discussing embryo development. A narrative created by microscopy observations, which origin is the biological evidence, was used as an example. Although the biological conclusions drawn were accepted as historical misconceptions, the very narrative based on the corresponding study is lively and continues to influence the current opinions about fertilization and human embryo development.

Intentionally, we avoided any religious aspects and related narratives as our competences in the field of religious studies are weak if nonexistent. Therefore, the generalization of our example could be criticized as an exaggeration. However, we

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would like to suggest that the transformation of biological evidence in the societal narratives could help to link societal discussions closer to the biological essence of the phenomenon.

Homunculus from the Microscope

The invention of the microscope enabled an unprecedented insight into the minute details previously invisible to the human eye. The microscopists were the first to see the cells subsequently accepted as key elements of living organisms. Seeing things allowed them immediately to speculate on their nature and microscopy indeed proved to be a window into the unknown. Human semen was of immediate interest and one of the first microscopists Antonie Van Leeuwenhoek examined the semen from humans and animals. Leeuwenhoek was claimed to be the first to see sperm, which he interpreted as independent lively creatures. He was unsure if they were of human origin or parasites. His observations were greatly extended by another Dutch microscopist, Nicolaas Hartsoeker, who presented in 1694 in his Essai de Dioptrique[6] a drawing of human sperm according to his observations. This drawing became iconic as he depicted a tiny human inside the sperm, referred to as a homunculus (Fig. 1). The drawing represented biological evidence for the theory of preformationism, that humans and animals develop from miniature versions of themselves.[7] The very theory was disproved by the onset of cell theory and further cellular and molecular evidence. The competing theory of epigenesis prevailed indicating the development from the undifferentiated stage toward gradual differentiation and formation of the structures leading to organogenesis.

However, the narrative of providing a miniature self to establish the next generation remains alive as well today. The propagation of the narrative was even aided by elucidating the genetic basis of heritage and public awareness of the importance of genes as building blocks of life. Every sperm indeed contains half of the genome representing half of the instructions for the future being. Therefore, although one accepts there is no homunculus in the sperm having a shape of the physical form, the imaginary visualization of the concept of the half of the genome being carried around in the sperm can easily be a virtual homunculus defined by the information software stored inside. The consequences of such a narrative are easy to follow. Every sperm starts to be important, and the virtual potential determines not only the biological features of the new being, but influences its destiny, virtues and flaws, possible diseases, and game-changing talents. In a world governed by men, the oocyte welcomes the male instruction software of the male-derived homunculus, and the females are there to assist in the fulfillment of the predetermined plans and father new generations.

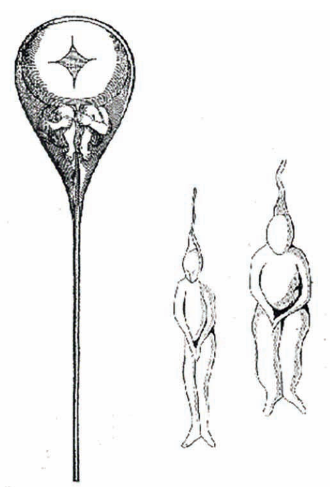

Fig. 1: Illustration of homunculi in sperm, drawn by Hartsoeker in 1695. Public Domain, https://commons.wikimedia.org/w/index.php?curid=635170

Homunculus vs Embryo

The sequence of events and biological mechanisms of fertilization and early development substantially differ from the above narrative. The sperm shape is determined by the father genome during the process of spermatogenesis, and not by the haploid genome (a random half of the father genes) within it. Many of these genes stored in the individual sperm did not actually contribute to the father phenotype, either being recessive or simply being non-used traits. At the moment of fertilization, they would encounter the analogous set of maternal genes, originating from the mother, but not mirroring the mother herself.[8]

The establishment of the diploid genome during fertilization results in two alleles for every gene locus, one coming from the mother, and another from the father. They represent a unique combination of randomly selected haploid sets contributed by the sperm and oocyte. These haploid sets, although they originate from the mother and father, represent a substantially different selection of genes. This is the crucial feature of sexual reproduction being different from asexual reproduction. The new generations host new combinations of genes from the population pool, which allow for necessary variability to withstand the unpredictable changes of the environment. Moreover, to avoid the competition between new and old combinations, the old ones being harbored by the fathers and mothers, death was introduced as a natural phenomenon, removing the previous combinations (i.e., previous generations), and allowing the new ones to thrive.[9]

The homunculus narrative of preformationism expects that the virtual image of the new being written in the genome is reproduced as its realization. However, the phenotype is not a printed image of the genotype. Moreover, the new combination of the genes created by fertilization is not at all activated immediately, but rather late in development. The first phase of embryo development, cleavage, relies completely on the maternal genome (i.e., the outcome could be assigned as "made by the mother's genome"). This is possible as the oocyte hosts an abundant amount of the mother's proteins supplemented by a collection of maternal messenger ribonucleic acid (mRNA), which serves to create even more maternal proteins. The cleavage as the first developmental phase is characterized by a series of rapid mitotic divisions, and it serves to produce equivalent copies of the newly formed genome. During the series of cleavage divisions, there is no time to untangle the chromosomes and make deoxyribonucleic acid ready for the transcription of mRNA. The zygote-derived gene expression and mRNA transcription are therefore delayed and initiate slowly during the compaction and blastocyst stage. Subsequently, it gradually replaces maternal mRNA, still using maternal ribosomes for translation. The maternal ribosomes would be later replaced by the synthesis of ribosomal ribonucleic acid from the new genome. The first concerted action of the new genome occurs during implantation, almost a week after fertilization. The outer layer of the blastocyst differentiates into the trophoblast, which afterwards segregates into two cell types, cytotrophoblast highly involved in cell mitosis (during which the chromosome structure does not allow for transcription), and syncytiotrophoblast being a multinuclear syncytium made by incorporation of cells originating from cytotrophoblast divisions. As syncytiotrophoblast itself does not divide, the genome could be used for high-rate transcription of new mRNAs using the genes located at various chromosomes. The orchestrated action of multiple genes (and chromosomes) establishes a connection with the mother and creates the placenta. The failure to do so regrettably causes spontaneous abortion. The successful implantation and production of human chorionic gonadotropin represent a major checkpoint for the presence of the adequate chromosomal and genetic set capable to govern the new being. However, although the formation of the placenta represents a key task for the new genome, the placenta is a temporary structure used only during intrauterine development.[10]

As the first two weeks of human embryo development provide enough cells to initiate the connection with the mother, the formation of the very body of the embryo is delayed for later stages. The embryo first secures its position in the uterus by the formation of the placenta, and when it is surrounded by the favorable environment, it executes in the next step the complex sequence of events resulting in the newborn child. The body plan formation starts with gastrulation followed by organogenesis, which shapes the embryo and forms its organ systems. Moreover, organogenesis is not a result of a predetermined cascade of events, but it is an adaptive process. Surprisingly, due to the increase in complexity of species being represented by humans as the most complex species, human development cannot be accomplished as a simple execution of the predetermined plan. Both, establishing the body plan (i.e., gastrulation), and shaping the organs according to this plan (i.e., organogenesis) require interactions among the cells through which they adapt to the situation and invoke the subsequent responses. This adaptive system allows the cells to activate various developmental pathways according to their positions and subsequent fates. Moreover, this as well serves to merge the environmental clues and despite their unpredictable influences adapt to them and accomplish a healthy child. The flexibility of the program implies that the potential coded by the genome can be adapted and altered during the development and the same genetic instructions can have variations of implementations, as exemplified by subtle differences between monozygotic twins.[11]

Subsequently, the imagined homunculus virtually conceived by the new genome does not represent a modified version of the parents, but a new being with a unique combination of features. Moreover, the underlying genetic plan is executed in an adaptive way as the best tactic to create healthy progeny.

Parents vs Children

The homunculus narrative can be as well related to the expectations parents have for their children. According to the homunculus narrative, it is surprising how children differ from their parents, how they do not follow the same reasonings and how it is possible that their life choices are so unpredictable. Eventually, new narratives could contribute to appreciating the abilities of new generations.[12] As futuristic views on the human future consider human cloning, perpetuating the specific genomes of to-be-perfect already existing persons, the narrative of children exploring new paths with their innovative gene combinations could be a welcoming alternative for present-day society.

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