My First Medical Writing

SECTION EDITOR

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Editorial

After a short break, I'm glad to be sharing the work of a rising star in the medical writing and science communication world. On this occasion, I had the pleasure of working with Valentina Torres Monserrat, who has a degree in biotechnology and a specialisation in human embryology. She is a dedicated health professional passionate about demystifying complex scientific concepts and making them relatable to everyday life. Over the past decade, she has devoted herself to human fertility, genetics, and assisted reproductive medicine. However, in recent years, she stepped away from the bench to undertake another mission: democratising scientific knowledge. Valentina is committed to bridging the gap between the scientific community and society. She is passionate about creating informative documents for patients that will empower them to make informed decisions about their reproductive health.

I hope you enjoy this inspiring read as much as I did!

Evguenia

Epigenetics unveiled: The Cinderella story in genetics

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In the grand ballroom of genetics, where we share 99.99% of the human genetic code, a hidden sister dwells in the shadows. The enigmatic Cinderella in this tale is epigenetics, a process regulating gene expression through biochemical mechanisms by altering the proteins that structure chromatin without tampering with the genetic code.

In 2003, when The Human Genome Project was completed and the Cinderella sisters resulted in disillusion, the fairy godmother of science brought epigenetics into the spotlight. Despite the wealth of information we had gained about the human gene code, mysteries persisted, especially in understanding the prevalence of disorders such as diabetes, heart disease, and infertility.[1]

Over the past three decades, exhaustive studies in both humans and animals have unravelled the unique characteristics and profound significance of epigenetics. This regulatory gene expression mechanism is responsible for an organism's phenotype and is not determined. Environmental conditions can shape epigenetics during critical developmental periods – preconception, prenatal, and early postnatal stages – collectively known as the first 1,000 days of a newborn's life.[2,3] These studies promoted the groundwork for the Developmental Origins of Health and Disease (DOHaD) hypothesis, putting forward that the early-life environment profoundly shapes the future health of the developing organism.[3]

Epigenetics is essential for setting cell diversity and permitting adaptation to different environmental conditions. This plasticity during the first 1,000 days of life is physiologically relevant, as it endows the developing organism with a mechanism to acclimate to the intrauterine environment, which reflects the external conditions. This kind of heritable mechanism has a unique characteristic that can be induced by endogenous and external signals, thus endowing the organism with additional complexity. Epigenetics modulation of gene expression can occur in four main ways: chemical modification of cytosine in the DNA molecule; posttranslational modification of chromatin structure through Histone proteins; genetic imprinting; and modulation via non-coding RNA.[4]

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Infertility is a multifactorial disease that affects both women and men equally. Today, this disease has a prevalence of 17.5% of the reproductive population, which means that 1 in 6 adults has this pathology.[5] Fertility in humans depends on a perfect interaction of the hypothalamic-pituitary-gonadal (HPG) axis. This neuroendocrine system involves aspects that are developed and fine-tuned during different developmental stages, especially during the embryological period. To date, within the area of reproductive medicine, the diagnostic capacity of infertility needs to be improved, having a decisive intervention on the symptoms but not on the origins.

In the last two decades, preclinical and clinical studies have consolidated the DOHaD hypothesis and its impact on reproductive development and function later in adulthood.[6,7] Just as Cinderella transforms from a maid to a princess due to the circumstances in her background, the intrauterine environment can modulate transgenerational effects via epigenetic mechanisms on the human precursors of gametes (oocytes and sperms). Gametogenesis and the development of the HPG axis occur during the gestational gastrulation phase. This is why environmental effects during the first 1,000 days of a newborn can explain numerous neuroendocrine deregulations adults suffer during their reproductive life. Clinical results have shown that maternal malnutrition during pregnancy and breastfeeding is a crucial factor influencing the offspring's reproductive health, impacting pubertal maturation, gonadotropic function, and gamete quality.[8]

Interestingly, the parental periconceptional environment has also proven to play a funda-

mental role in the determination of the reproductive phenotype of progeny.[9,10] Paternal and maternal malnutrition and stress previous to conception can induce changes in the oocyte and sperm, which modifies the heritable epigenome pattern that may enhance susceptibility to diseases in adulthood. In humans, it is challenging to address environmental conditions before and after conception separately. In animals, reciprocal embryo transfer allowed dissection of the impact of diet before versus during pregnancy on metabolic features in the offspring. It could be of scientific interest to do longitudinal studies on the life births of patients who received donated embryos.

Although the mechanism groundwork for the intergenerational transmission of non-genetic traits from parents to offspring is not yet fully elucidated, recent evidence suggests that epigenetic processes may be the primary agents. Gonadotropin-releasing hormone (GnRH) neurons in the hypothalamic area are the central regulatory mechanism leading the HPG axis. These neurons regulate the HPG axis at different developmental stages and play a fundamental role in controlling puberty onset and reproductive function.[11] During the last two decades, kisspeptin proteins have emerged as the master regulators of GnRH neurons.[12] Kiss1 neurons, also located in the hypothalamus, encode these regulatory peptides. Preclinical studies show that epigenetic regulation operates on these key neuronal populations, and adverse external conditions can affect various aspects of adulthood reproduction, such as puberty maturation, brain sex differentiation, and gametogenesis.[13]

The difficulties in setting the mechanistic basis of epigenetic phenomena have two main reasons: the difference in timing between the stressor and the physiological result and the tissue-dependent nature of this regulation. More epidemiological studies in different human populations, fertile and infertile, could bring more light to the crucial regulation program.

The Cinderella that is epigenetics is in the centre of the grand ballroom of genetics. However, the mystery behind her transformation is still to be elucidated. Epigenetics may be the clue to infertility diagnosis and also possible future neuroendocrine therapies. Today, evidence shows that the DOHaD hypothesis applies to both metabolic and adulthood fertility conditions.

Valentina Torres Monserrat

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