



REVIEW

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Epigenetics and male reproduction: the consequences of paternal lifestyle on fertility, embryo development, and children lifetime health

Liborio Stuppia^{1,2*}, Marica Franzago¹, Patrizia Ballerini², Valentina Gatta^{1,3} and Ivana Antonucci^{1,3}

Abstract

The correlation between epigenetics and human reproduction represents a very interesting field of study, mainly due to the possible transgenerational effects related to epigenetic modifications of male and female gametes. In the present review, we focused our attention to the role played by epigenetics on male reproduction, evidencing at least four different levels at which sperm epigenetic modifications could affect reproduction: (1) spermatogenesis failure; (2) embryo development; (3) outcome of assisted reproduction technique (ART) protocols, mainly as concerning genomic imprinting; and (4) long-term effects during the offspring lifetime. The environmental agents responsible for epigenetic modifications are also examined, suggesting that the control of paternal lifestyle prior to conception could represent in the next future a novel hot topic in the management of human reproduction.

Keywords: Male infertility, Gametogenesis, Epigenetics, DNA methylation, Transgenerational effect

Background

You shall not bow down to them or worship them; for I, the Lord your God, am a jealous God, punishing the children for the sin of the parents to the third and fourth generation of those who hate me (Exodus, 20.5)

Infertility represents a growing emergency in western countries, affecting about one out of seven couples who attempt to generate a child. In 2010, an estimated 48.5 million couples worldwide were infertile, against 42 million in 1990 [1]. In about 50 % of the cases, this condition is ascribable to the male partner, mainly due to a failure in the spermatogenesis process causing azoospermia or oligozoospermia at the sperm count [2]. Despite

the large number of tools available for the identification of the pathogenesis of male infertility, in many cases, no specific cause is detected and no personalized therapeutic protocol can be established. A large number of studies have investigated in the last decades the presence of genetic alterations responsible for the failure of spermatogenesis, which are nevertheless identified only in 15–30 % of infertile males, even when stringent selection criteria are used [3, 4]. Despite the identification of several rare genetic variants associated to disruption of spermatogenesis, so far, the only two categories of genetic alterations responsible for a significant portion of cases of male infertility, and thus commonly tested in the clinical practice, are represented by chromosomal alterations and Yq microdeletions [5–10]. The presence of other genetic mechanisms, such as partial Yq microdeletions [11–14], specific Y-chromosome haplogroups [15–18], and polymorphism in genes related to mitochondrial function [19–21] as risk factors for infertility have been suggested, but with inconclusive results. More recently, the presence of X-linked copy number variants (CNVs) in infertile males has been reported by several studies [22, 23], but the overall

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Lifetime Health Holt Rinehart and Winston, 2005

Childhood Adversity and Life-course Consequences Cheryl Zlotnick, Naixue Cui, Nadya Golfenshtein, Yang Li, 2022-08-05

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