Opinion

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Epididymal White Adipose Tissue: Endocrine Backbone of Spermatogonial Stem Cells Maintenance

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Opinion

White adipose tissue as the largest endocrine tissue of humans plays important roles in regulations of metabolic homeostasis due to secretion of numerous bioactive compounds [1,2]. In spite of well documentation in human females, the precise role of gonadal white adipose tissue in males reproductive functions including androgenesis and spermatogenesis is poorly understood [3,4]. Recently, experimental evidence revealed that epididymal white adipose tissue (EWAT) as a dynamic, endocrine repro-supporter structure regulates spermatogenesis through local nutritive and/or trophic factors production [5,6]. Confirming this fact, previous reports have shown that stimulation of epididymal fat pad androgen receptors lead to the increased accumulation of long-chain polyunsaturated fatty acids, suggesting the involvement of long-chain polyunsaturated fats in local functions of the epididymal adipose tissue [7]. Further, it has been suggested that epididymal fat pad can affect ipsilateral testis through a direct veno-arterial transfer [5]. Moreover, since adipocytes have the ability to express androgen receptors, androgens, particularly testosterone, have been attributed to local actions of the epididymal fat mass [8].

In line with that, previous reports have indicated that removal of epididymal white adipose tissue (EWATx) leads to spermatogenesis disruptions [9] as well as testicular damages [10]. Further, EWATx can result in epididymal sperms impairment along with their fertilizing potential reduction [11,12]. Recently, it has also been shown that EWATx disturbs mouse germline maintenance via glial cell line-derived neurotropic factor (GDNF) expression reduction **(Figure 1)**, [13]. A growing body of evidence has indicated that Sertoli cell-derived GDNF, the ligand for GFRα1, is an essential factor for the in vivo and in vitro regulation of self-renewal and differentiation of spermatogonial stem cells [14]. Additionally, recent findings have suggested that testosterone triggers GDNF secretion by peritubular myoid cells to regulate the level of GDNF in the testis niche to optimize renewal of the undifferentiated spermatogonial pool, representing a novel direct endocrine role in the regulation of spermatogonial cell development [15].

Taken together, it seems that EWAT is essential for normal spermatogenesis as well as spermatogonial stem cells self-renewal and maintenance may be due to secretion of growth and/or nutritive factors such as androgens which directly act on the adjacent testis. Also, it is noteworthy to mention that due to possible reduction of epididymal adipose tissue following chemotherapy drugs administrations [16] as well as in physiological and pharmacological weight losses [17] and critical roles of EWAT in male fertility, the most caution should be considered to avoid undesirable male reproductive disorders.

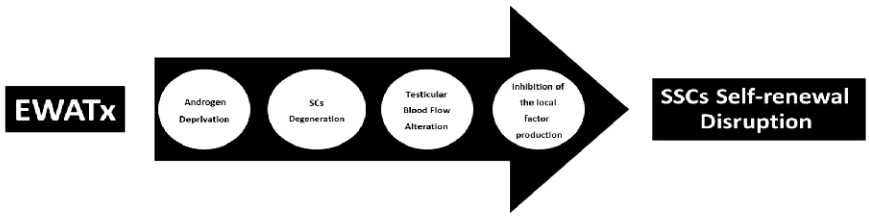

Figure 1 Possible effects of epididymal white adipose tissue removal (EWATx) on spermatogonial stem cells (SSCs), Self-renewal (SCS), Sertoli cells.

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