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INVITED COMMENTARY

Sperm Biology

Commentary on "Altered *PIWI-LIKE 1* and *PIWI-LIKE 2* mRNA expression in ejaculated spermatozoa of men with impaired sperm characteristics"

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Infertility affects approximately 15% of couples who have regular intercourse with male partners for over 12-month periods, without using any contraceptives. Among these infertile couples, the male factor accounts approximately 40%–50%. A significant proportion of male infertility is due to idiopathic azoospermia, severe oligozoospermia, and teratozoospermia. While some severe male infertility is associated with possible genetic alterations in germ cell lines or spermatogenesis, the cause of severe male infertility is still largely unknown.[1,2]

Although today the majority of severe male infertility can be treated by assisted reproductive technology (such as *in vitro* fertilization [IVF] and particularly intracytoplasmic sperm injection ICSI), it is still very important to investigate the underlying cause of idiopathic male infertility.

In this issue of *Asian Journal of Andrology*, Giebler *et al*.[3] reported a very good study on the relationship between mRNA expression of the four human PIWI-LIKE orthologs (*PIWI-LIKE 1*/*HWI*, *PIWI-LIKE 2*/*HILI*, *PIWI-LIKE 3*/*HIWI3,* and *PIWI-LIKE 4*/*HIWI2*) and sperm characteristics in ejaculates of 90 men with normozoospermia ($n = 47$) or abnormal sperm characteristics ($n = 36$) according to the World Health Organization (WHO) manual 5th edition. The study design and data analysis were adequate despite the relatively small sample size. The authors clearly demonstrated that *PIWI-LIKE 1-4* mRNA was measurable in various proportions of ejaculated sperm samples: 9.6% for *PIWI-LIKE 3,* 15.7% for *PIWI-LIKE 4,* 49.4% for *PIWI-LIKE 2,* and 100% for *PIWI-LIKE 1*. As both PIWI-LIKE 3 and PIWI-LIKE 4 can be detected in about 10%–16% of sperm samples, the data of these two mRNAs were insufficient for statistical analysis. However, the authors found a positive correlation between *PIWI-LIKE 2* mRNA expression and sperm concentration or the total number of spermatozoa/ejaculate. On the other hand, *PIWI-LIKE 1* mRNA expression was negatively correlated with the percentage of total motility or progressive motility. Furthermore, *PIWI-LIKE 1* mRNA expression is also negatively correlated with the proportion of nonviable spermatozoa of ejaculate from 49 men. It was interesting that both *PIWI-LIKE 1* and *PIWI-LIKE 2 mRNA* expressions were positively correlated with male age.

In literature, it is reported that *PIWI* genes play an essential role in spermatogenesis, and the PIWI subfamily of genes is also involved in spermatogenesis for the maintenance and meiosis of germ line stem cells. Thus, genetic variation in *PIWI* genes may be potential to affect normal spermatogenesis. Mice bearing targeted mutations in *PIWI* genes (*Miwi*, *Mili,* and *Miwi2*) are sterile with distinct defects in spermatogenesis.[4] In humans, it has been demonstrated that genetic variants in PIWI-interacting RNA pathway genes confer susceptibility to spermatogenic failure which has been demonstrated in Chinese men.[5] Genetic variants in piRNA pathway genes may contribute to the risk of spermatogenesis impairment. Although the human ejaculate sperm is generally considered to contain a very small amount of mRNA, the current article by Giebler *et al*.[3] has clearly shown to be able to extract sufficient mRNA from ejaculated sperm.

The authors have to be congratulated for their interesting study on the association of *PIWI-LIKE* 1 and *PIWI-LIKE* 2 mRNA expression of human ejaculated sperm and sperm characteristics. A limitation of this study is the small sample size which affects the ability to analyze the relationship between sperm characteristics and *PIWI-LIKE 3* and *PIWI-LIKE 4;* as these two mRNAs can be detected in only 10%–16% of sperm samples. Also, a more detailed analysis could be performed for *PIWI-LIKE 2* as it was only detected in about 50% of samples. Indeed, further study with a larger sample size is required to confirm the findings and to explore the insight of the cause of impaired sperm characteristics in infertile men.

COMPETING INTERESTS

The author declares no competing interests.

REFERENCES

1 Cram DS, O'Bryan MK, de Kretser DM. Male infertility genetics – the future. *J Androl* 2001; 22: 738–46.
2 Huynh T, Mollard R, Trounson A. Selected genetic factors associated with male infertility. *Hum Reprod Update* 2002; 8: 183–98.
3 Giebler M, Greither T, Müller L, Mösinger C, Behre H. Altered *PIWI-LIKE 1* and *PIWI-LIKE 2* mRNA expression in ejaculated spermatozoa of men with impaired sperm characteristics. *Asian J Androl* 2017; doi: 10.4103/aja.aja_58_17. [Epub ahead of print].
4 Deng W, Lin H. miwi, a murine homolog of piwi, encodes a cytoplasmic protein 342 essential for spermatogenesis. *Dev Cell* 2002; 2: 819–30.
5 Gu A, Ji G, Shi X, Long Y, Xia Y, *et al*. Genetic variants in Piwi-interacting RNA pathway genes confer susceptibility to spermatogenic failure in a Chinese population. *Hum Reprod* 2010; 25: 2955–61.

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