www.asiaandro.com; www.ajandrology.com

Open Access

INVITED COMMENTARY

Sperm Biology

New insights into SET protein during mouse spermatogenesis

Marc Yeste

Asian Journal of Andrology (2014) **16**, 783; doi: 10.4103/1008-682X.131065; published online: 13 June 2014

Spermatogenesis is a complex, unique process that takes place in the testis. It consists of a set of events including mitotic (from spermatogonia to primary spermatocytes) and meiotic divisions (from primary spermatocytes to early round spermatids), and spermiogenesis, a differentiation step from early round spermatids to testicular spermatozoa.[1] Although spermatogenesis is known as a well autocrine- and paracrine-regulated process, some proteins involved in its regulation remain to be determined. Related to this, the recent study conducted by Dai *et al.*[2] have shed light on the relevant function of SET protein, a protein phosphatase 2A (PP2A) inhibitor, also known as I2PP2A, or TAF-Ib. This protein, identified for the first time in 1992, has been described to be involved in multiple cell functions, such as control of cell cycle and apoptosis, gene transcription, epigenetic regulation, and nucleosome assembly. Apart from these functions, it is worth noting that SET has been found in theca cells, where appears to be involved in the regulation of androgen biosynthesis, and in mature oocytes, where plays a key role in the segregation of sister chromatids during the second meiotic division.[3] SET protein inhibits PP2A by enhancing lyase activity of P450c17, a substrate for PP2A when it is Ser- and Thr-phosphorylated. PP2A function in reproductive physiology is not restricted to gamete production (i.e. spermatogenesis and oogenesis), but this protein is also involved in human sperm capacitation.[4]

Using mouse as a model, Dai *et al.*[2] have conducted an excellent study as they have evaluated the localization of SET protein in seminiferous tubules (i.e. spermatogenic and Sertoli cells) and Leydig cells, and have also examined the levels of this protein in testicular tissues through western blot and quantitative real-time reverse transcription polymerase chain reaction (PCR). In addition, these authors have compared four animal groups of different ages (infant, prepubertal, postpubertal, and ageing), and have observed that SET protein is mainly located in spermatogonia and spermatocytes in prepubertal and postpubertal group, and in Leydig cells of postpubertal group, rather than in Sertoli cells. This higher content of SET protein in prepubertal and postpubertal groups has been confirmed through western blotting and quantitative real-time reverse transcription PCR. In contrast, testicular spermatozoa and testicular tissues from infant and ageing groups present lower levels of SET protein. As SET protein is highly expressed in Leydig cells, Dai *et al.*[2] suggest this protein is involved in the regulation of androgen biosynthesis. In addition, the authors also hypothesize the high content of SET protein in spermatogonia and spermatocytes may be related to the role of this protein in deoxyribonucleic acid (DNA) repair and chromatin remodeling because, as aforementioned, previous studies have demonstrated this SET protein is involved in DNA replication and transcription.[5]

CONCLUSION

Dai *et al.*[2] have conducted an excellent study and have reported, for the first time, localization of SET protein in testicular tissue at different developmental ages. This work contributes to our understanding about production of mammalian spermatozoa and warrants more research on the role of this protein in testicular stereidogenesis.

COMPETING INTERESTS

The author declares no competing interests.

REFERENCES

1 Bonet S, Garcia-Bonavila E, Sepúlveda L. The boar reproductive system. In: Bonet S, Casas I, Holt WV, Yeste M, editors. Boar Reproduction. Berlin: Springer-Verlag; 2013. p. 65–108.
2 Dai XN, Liu S, Shao L, Gao C, Gao L, *et al*. Expression of the SET protein in testes of mice at different developmental stages. *Asian J Androl* 2014; 16: 689–93.
3 Gao LL, Liu XQ, Xu BQ, Jiang SW, Cui YG, *et al*. SET/PP2A system regulates androgen production in ovarian follicles *in vitro*. *Mol Cell Endocrinol* 2013; 374: 108–16.
4 Signorelli JR, Díaz ES, Fara K, Barón L, Morales P. Protein phosphatases decrease their activity during capacitation: a new requirement for this event. *PLoS One* 2013; 8: e81286.
5 Gamble MJ, Erdjument-Bromage H, Tempst P, Freedman LP, Fisher RP. The histone chaperone TAF-I/SET/INHAT is required for transcription *in vitro* of chromatin templates. *Mol Cell Biol* 2005; 25: 797–807.

Department of Animal Medicine and Surgery, Autonomous University of Barcelona, Bellaterra, Spain.
Correspondence: Dr. M Yeste (marc.yeste@uab.cat)

Re: New insights into SET protein during mouse spermatogenesis

Yu-Gui Cui

Asian Journal of Andrology (2014) **16**, 783; doi: 10.4103/1008-682X.131708; published online: 13 June 2014

We are thankful to Dr. Yeste for the encouraging comments.[1] In the previous study, we revealed a specific, SET-initiated, PP2A-mediated, pathway that leads to the increased lyase activity of P450c17 in ovarian theca cells, by which SET regulates testosterone biosynthesis. How to work SET protein in Leydig cells is our new research interesting. Secondly, SET protein is a multifunctional protein involved in histone binding, transcription control, nucleosome assembly, and cell apoptosis. Very interestingly, we found the changing SET expression in the seminiferous epithelium at different stages in this manuscript. The highest level of SET protein was mainly in haploid and tetraploid cells of the prepubertal and adult mice, suggesting that SET is involved in the regulation of the complex, unique process of spermatogenesis. Our group is working on this role of SET protein as you proposed. It will contribute our understanding about molecular mechanism of spermatogenesis.

REFERENCE

1 Yeste M. New insights into SET protein during mouse spermatogenesis. *Asian J Androl* 2014; 16: 783.

The State Key Laboratory of Reproductive Medicine, Clinical Center of Reproductive Medicine, First Affiliated Hospital, Nanjing Medical University, Nanjing, China.
Correspondence: Dr. YG Cui (cuiygnj@njmu.edu.cn)