

RNA Binding Motif Y (RBM Y) and Human Spermatogenesis - An Overview

Shadaan Abid*

Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, Texas, USA

***Corresponding author:** Shadaan Abid, Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, Texas, USA. Tel: +12143567294; Email: Shadaan.Abid@UTSouthwestern.edu

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Overview

Genetic studies of men with infertility and subfertility have led to identification of genes that are vital for spermatogenesis. Amongst these, is the Y-chromosome-encoded gene RBMY (RNA-binding motif on Y), which is present in multiple copies and distributed throughout the Y-chromosome. Complete or partial deletions of the Y-chromosome regions encompassing the RBMY genes are observed in infertile men [1]; partial deletion of the *Rbmy* gene family in the mouse is associated with sperm abnormalities [2], emphasizing a critical requirement of RBMY in male fertility.

The sequence and cellular distribution of RBMY protein are consistent with their function in nuclear RNA processing. RBMY co-localizes and interacts with pre-mRNA splicing factors [3]. The murine and the human RBMY- RNA interactome has been reported [4]; as well as the NMR structure of RBMY complexed with RNA has also been solved [5]. These results are strong evidences to support the function of RBMY in splicing and its involvement in regulation of transcription and translational control in the male germline.

RBMY is a RNA splicing factor, it is possible that it may play a crucial role in spermatogenesis in the early stages. However, human males who harbor deletions of the AZFb locus (encompassing the RBMY genes) generally suffer from arrest of spermatogenesis at post-meiotic stages [1,6,7]; mice knockout for *Rbmy* also have normal spermatogenesis but develop structurally defective spermatozoa [2]. These observations suggest that beyond RNA editing and splicing in the pre-meiotic and meiotic germ cells, RBMY might have additional functions in the post-meiotic gametes.

Abid et al. [8] have demonstrated that RBMY is expressed in all the germ cell types of the testis and also in the ejaculated spermatozoa. In the pre-meiotic and meiotic germ cells, RBMY has distinct spatial pattern of staining depending on the stage of

differentiation; in the post-meiotic cells, RBMY is retained and expressed in the mid-piece and the tail of the testicular and ejaculated spermatozoa. Functional studies have revealed that RBMY may play a role in sperm motility. The Y-chromosome has been thought to have evolved from an ancient autosomal homologous chromosome and in the course, has lost most of its genes except those involved in male germ cell development. The genes left on the Y-chromosome such as RBMY have male-specific functions and are important for male fertility. Human males with deletions of the AZFb locus that harbor the RBMY genes have failure of spermatogenesis and are infertile [1,6]. Thus, highlighting the potential importance of the RBMY gene for maintenance of male fertility.

RBMY is not only present in the spermatogonia and the spermatocytes but the subcellular distribution differs significantly [8]. Considering the major role of RBMY is RNA editing and splicing, it is predicted that the expression of RBMY would be reduced or absent in the post-meiotic germ cells. In the mouse, *Rbmy* mRNA is not detected in the meiotic and post-meiotic cells [9], however human RBMY continues to express in post-meiotic cells, where protein is divided to the base of the elongating spermatids and condensed in the cytoplasmic droplet. Subsequently, in the mature testicular and ejaculated sperm, RBMY is retained in the mid-piece region and in the tail. The apparent variation in the mouse and the human RBMY expression profiles suggest fundamental differences in the mechanisms by which RBMY may regulate spermatogenesis. Alternately, it is possible that RBMY protein requirements in the germ cells differ between the mouse and man. The fact that the elongating spermatids and sperm are transcriptionally inert and the presence of RBMY in the cytoplasm but not in the nucleus suggest that it may not function as a splicing factor.

Conclusion

Subcellular distribution of RBMY in the male gametes might be essential in deciphering the regulation of spermatogen-

esis, spermiogenesis and sperm functions, and would be of clinical relevance in determining the molecular basis of male infertility.

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