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Review

Role of non-receptor protein tyrosine kinases in spermatid transport during spermatogenesis☆

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ABSTRACT

Non-receptor protein tyrosine kinases are cytoplasmic kinases that activate proteins by phosphorylating tyrosine residues, which in turn affect multiple functions in eukaryotic cells. Herein, we focus on the role of non-receptor protein tyrosine kinases, most notably, FAK, c-Yes and c-Src, in the transport of spermatids across the seminiferous epithelium during spermatogenesis. Since spermatids, which are formed from spermatocytes via meiosis, are immotile haploid cells, they must be transported by Sertoli cells across the seminiferous epithelium during the epithelial cycle of spermatogenesis. Without the timely transport of spermatids across the epithelium, the release of sperms at spermiation fails to occur, leading to infertility. Thus, the molecular event pertinent to spermatid transport is crucial to spermatogenesis. We provide a critical discussion based on recent findings in this review. We also provide a hypothetical model on spermatid transport, and the role of non-receptor protein tyrosine kinases in this event. We also highlight areas of research that deserve attention by investigators in the field.

Contents

1. Introduction

Production of spermatozoa is one of the two major functions of the mammalian testes besides sex steroids testosterone and estradiol-17β [1–5]. Testosterone is produced exclusively by Leydig cells found in the interstitial space between seminiferous tubules [5–7], whereas estradiol-17β is the product of Leydig cells, Sertoli cells and spermatozoa in adult mammals including rodents and humans [3,4,8] (Fig. 1). Besides regulating secondary sexual characteristics of the male such as, accessory glands like the prostate and seminal vesicles, and regulating other organ and body

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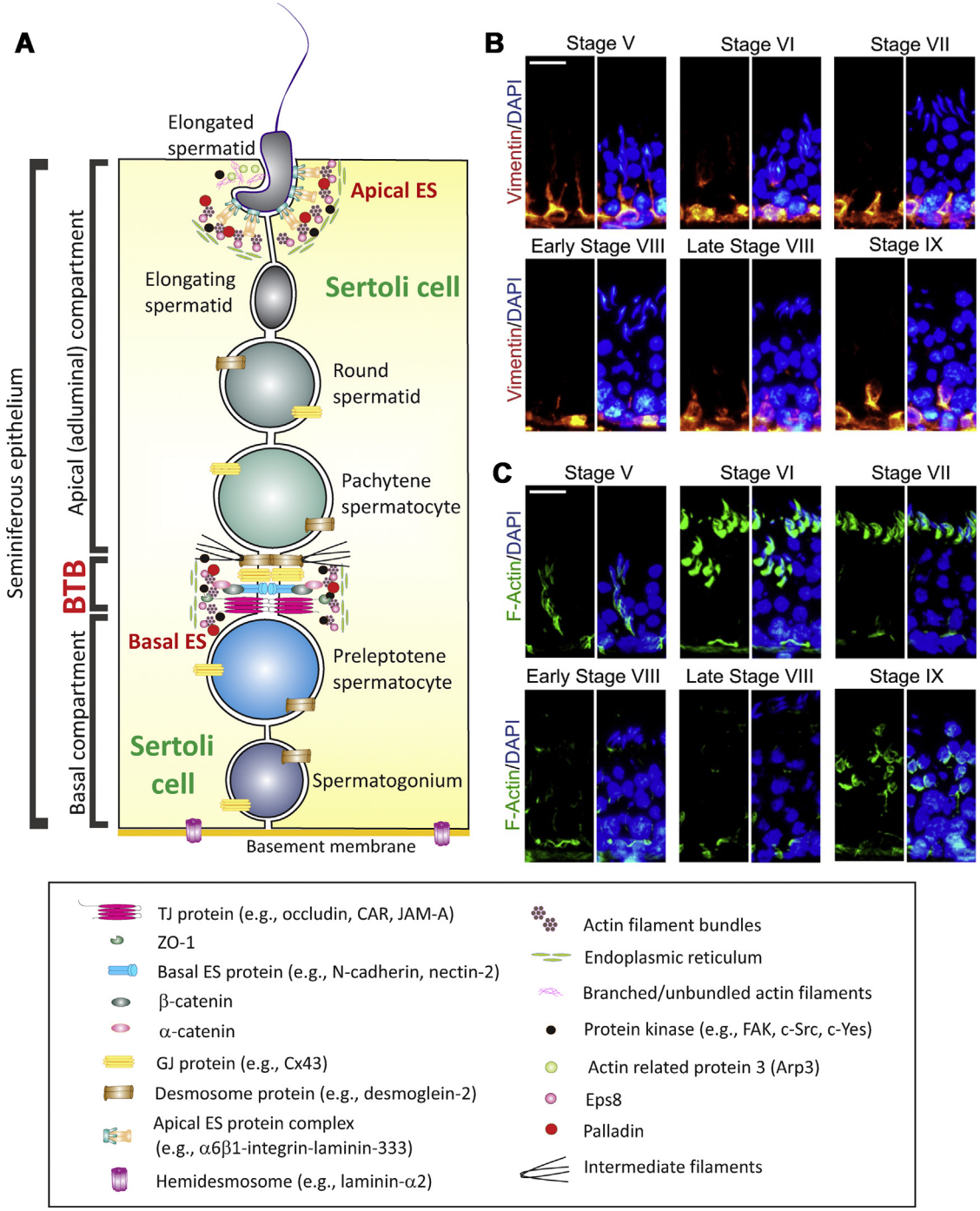

Fig. 1. A schematic drawing illustrating the relative location of the F-actin-rich ectoplasmic specialization (ES) at the Sertoli–spermatid (apical ES) and the Sertoli cell–cell (basal ES) interfaces, and the spatiotemporal expression of vimentin and F-actin in the seminiferous epithelium that support the ES. (A) A schematic drawing that illustrates the cross-section of a seminiferous tubule at stage VII of the epithelial cycle in the rat testis, showing intact apical ES and basal ES and other junctions in the seminiferous epithelium. (B and C) The relative localization of vimentin (red fluorescence) and F-actin (green fluorescence) at the apical and/or basal ES at stage V–IX of the epithelial cycle in adult rat testes are shown. Vimentin-based intermediate filaments are restricted to the basal compartment or at the BTB where desmosomes (an intermediate filament-based cell-cell anchoring junction) are present, most notably surrounding the Sertoli cell nucleus, but virtually undetectable at the apical ES (B). On the other hand, F-actin is localized to both the basal and apical ES except at stage VIII, when F-actin is considerably diminished (C) to facilitate the release of sperms at spermiation in which actin microfilaments no longer assume a "bundled" configuration via degeneration of the apical ES. Scale bar, 50 μm, which applies to other micrographs in the same panel.

functions (e.g., bone metabolism and blood pressure), steroids also contribute significantly to the production of spermatozoa via these effects on spermatogenesis that takes place exclusively in the seminiferous epithelium, which is composed of only Sertoli and germ cells [3,7,9–12]. Spermatogenesis is a complex, but tightly regulated series of cellular events which involve the formation of spermatozoa (haploid, 1n) from spermatogonial stem cells and spermatogonia (diploid, 2n) in the seminiferous epithelium [2,13,14] (Fig. 1). This process is comprised of four discrete cellular events: (i) renewal of spermatogonial stem cells (SSC) and spermatogonia via mitosis and differentiation of type B spermatogonia to pachytene spermatocytes, (ii) meiosis, (iii) spermiogenesis, and (iv) spermiation, the eventual release of spermatozoa transformed from step 19 spermatids.

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