Seminars in Cell & Developmental Biology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Seminars in Cell & Developmental Biology

journal homepage: www.elsevier.com/locate/semcdb

Review

Src family kinases (SFKs) and cell polarity in the testis

Xiang Xiao[a,b,*], Ya Ni[a], Chenhuan Yu[a], Linxi Li[b,c], Baiping Mao[b,c], Yue Yang[a], Dongwang Zheng[a], Bruno Silvestrini[d], C. Yan Cheng[b,**]

[a] Zhejiang Academy of Medical Sciences, Hangzhou, Zhejiang 310013, China
[b] The Mary M. Wohlford Laboratory for Male Contraceptive Research, Center for Biomedical Research, Population Council, 1230 York Ave, New York, New York, 10065, United States
[c] The Second Affiliated Hospital and Yuying Children's Hospital, Wenzhou Medical University, Wenzhou, Zhejiang 325035, China
[d] SBM S.r.l. Pharmaceuticals, Rome, Italy

ARTICLE INFO

Article history:
Received 20 November 2017
Accepted 20 November 2017
Available online xxx

Keywords:
Src family kinases
c-Src
c-Yes
Testis
Spermatogenesis
Spermatids
Sertoli cells
Cell polarity

ABSTRACT

Non-receptor Src family kinases (SFKs), most notably c-Src and c-Yes, are recently shown to be expressed by Sertoli and/or germ cells in adult rat testes. Studies have shown that SFKs are involved in modulating the cell cytoskeletal function, and involved in endocytic vesicle-mediated protein endocytosis, transcytosis and/or recycling as well as intracellular protein degradation events. Furthermore, a knockdown to SFKs, in particular c-Yes, has shown to induce defects in spermatid polarity. These findings, coupled with emerging evidence in the field, thus prompt us to critically evaluate them to put forth a developing concept regarding the role of SFKs and cell polarity, which will become a basis to design experiments for future investigations.

Contents

1. Introduction

In a typical cross-section of an adult mammalian testis, cell polarity across the seminiferous epithelium is readily notable (Fig. 1) [1]. For instance, Sertoli cell nuclei are located mostly near the basement membrane of the tunica propria. Furthermore, peritubular myoid cells are restrictively localized to the myoid cell layer behind the acellular zone of the tunica propria namely the basement membrane (also known as basal lamina) and the type I collagen layer (Fig. 1). On the other hand, elongating/elongated spermatids are mostly found in the adluminal compartment until these cells are line up near the tubule lumen, with their heads all pointing to the basement membrane and their tails to the tubule lumen (Fig. 1). This morphological setting of cell polarity is being used to support spermatogenesis. It is envisioned that the robust cellular output of spermatozoa in the tens of millions daily in the seminiferous tubules from an adult male (including rodents and

* Corresponding author at: Department of Reproductive Physiology, Zhejiang Academy of Medical Sciences, Hangzhou, Zhejiang 310013, China.
** Corresponding author at: The Mary M. Wohlford Laboratory for Male Contraceptive Research, Center for Biomedical Research, Population Council, 1230 York Ave, New York, 10065–6307, New York.
E-mail address: Y-Cheng@popcbr.rockefeller.edu (C.Y. Cheng).

https://doi.org/10.1016/j.semcdb.2017.11.024
1084-9521/

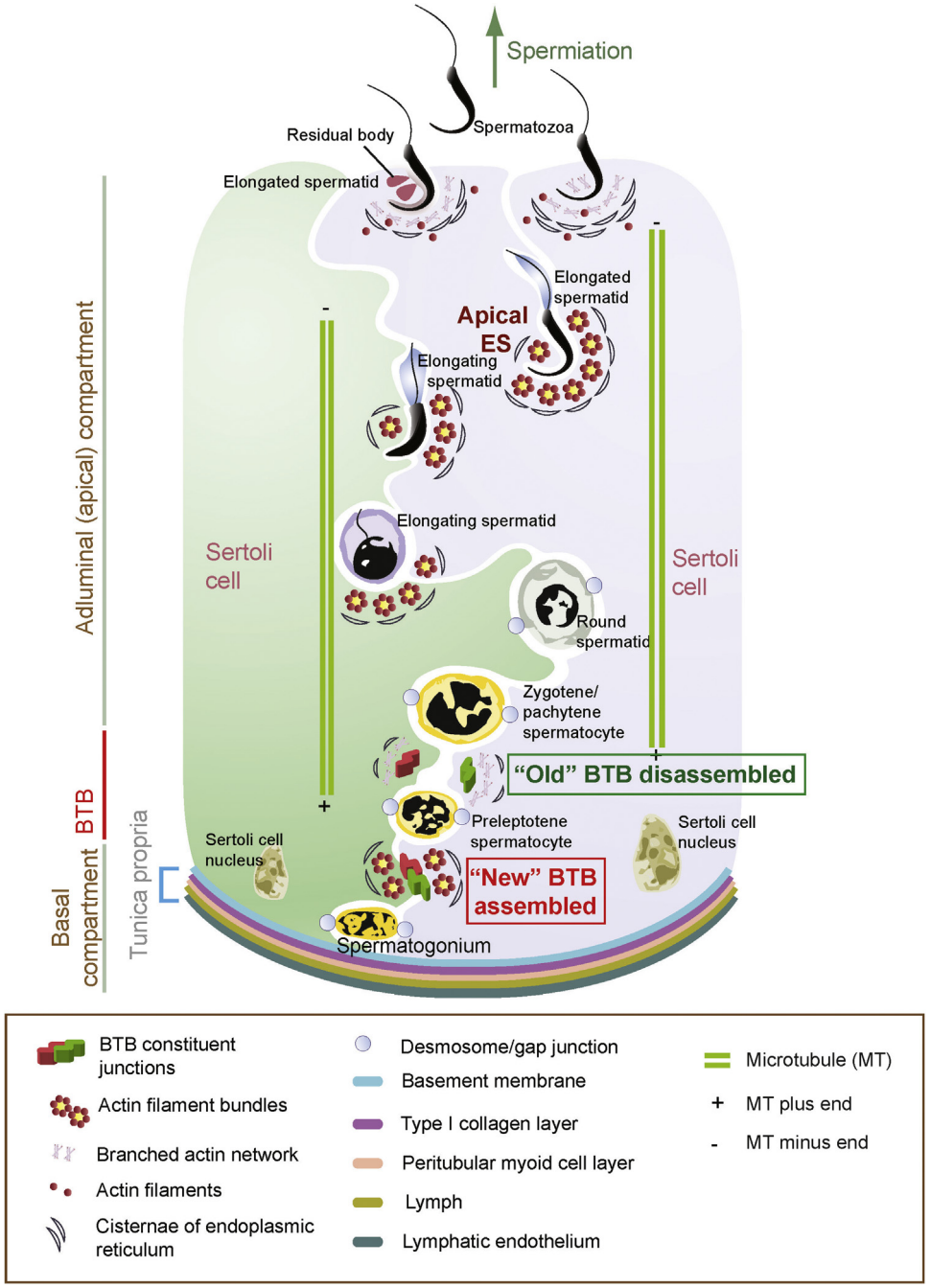

Fig. 1. A schematic drawing that illustrates the general morphological features of Sertoli and germ cells in the epithelium of the seminiferous tubule. The blood-testis barrier (BTB) physically divides the seminiferous epithelium into the adluminal (apical) compartment and the basal compartment, which in turn lays on the basement membrane of the tunica propria. Undifferentiated and differentiated spermatogonia are found in the basal compartment. Type B spermatogonia differentiate into preleptotene spermatocytes, which are the germ cells that are being transported across BTB while transforming to leptotene spermatocytes to enter the adluminal compartment to form zygotene and pachytene spermatocytes to prepare for meiosis I/II. The most notable anchoring junction in the testis is the actin-rich adherens junction (AJ) type called ectoplasmic specialization (ES), which is typified by the presence of an array of actin filament bundles found in the Sertoli cell near the plasma membrane and these bundles are sandwiched between the cisternae of endoplasmic reticulum and the apposing Sertoli cell-cell or Sertoli-spermatid plasma membranes. ES is either found at the Sertoli cell-cell interface called basal ES. The basal ES together with the tight junction (TJ) and gap junction all utilize F-actin for attachment. These actin-based junctions together with the intermediate filament-based desmosome constitute the BTB. At the Sertoli cell-spermatid (step 8–19 spermatids in the rat testis) interface, the ES is designated apical ES. The ES is an important structure to support Sertoli cell adhesion at the BTB and also spermatid adhesion. However, the ES is also an important cellular structure to support Sertoli cell and spermatid polarity, and also spermatid PCP (planar cell polarity) during spermatogenesis.

humans) is analogous to a car manufacturing plant. This requires highly orchestration of developing germ cells (i.e., vehicles) that move through the assembly line (conferred by actin and/or microtubule (MT)-based tracks) with well aligned machineries (e.g., endocytic vesicles aided by GTPases) that support the assembly of different components (e.g., various integral membrane proteins, adaptor proteins) onto the developing germ cells, and the removal of some necessary wastes (e.g., residual bodies). Nonetheless, the concept of cell polarity in particular the involving molecules and the signaling pathways that confer cell polarity in the testis have not been carefully investigated. For instance, it was first reported in 2008 that the Par (partitioning defective)-based polarity com-

Please cite this article in press as: X. Xiao, et al., Src family kinases (SFKs) and cell polarity in the testis, Semin Cell Dev Biol (2017), https://doi.org/10.1016/j.semcdb.2017.11.024