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Rat and mouse testicular testin is different from the human tumor suppressor gene TESTIN (*Tes*)

Authors' response to the letter of Dr. S. Kapoor

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In response to the Letter to the Editor from Dr. Shailendra Kapoor with regard to a paper previously published on testin in *Spermatogenesis*,[1] we wish to clarify some misinformation on this protein in the literature. In the late 1980s, two papers were published, reporting a new testicular protein purified from rat Sertoli cell-enriched culture media. It was designated testin based on its unique N-terminal amino acid sequence.[2,3] Specifically, testin is a testis-specific protein,[4] composed of two isoforms of testin I (35 kDa) and testin II (37 kDa) where testin II has three extra N-terminal amino acids of Thr-Ala-Pro.[3] The full-length cDNA encoding rat testicular testin was cloned, sequenced and published shortly thereafter (GenBank™ Accession Numbers: U16858; NM_173132, NP_775155).[5] Testin was subsequently cloned and sequenced in the mouse (GenBank™ Accession Numbers: NM_178098, NP_835199) and shown to display 90.1% similarity with rat testin.[6] Testin is also a gonad-specific protein,[4] with its expression restricted largely to the testis and ovary in adult rats.[7,8] Interestingly, its expression is upregulated during disruption of the testis-specific anchoring junction known as the apical ectoplasmic specialization (ES).[8-10] The recent report published in *Spermatogenesis* has shown that testin is also an actin-binding protein at the ES.[1] While the rat testin primary amino acid sequence contains an apparent His- and Asn-active site, a characteristic feature of cysteine proteases, and is ~60% homologous with human cathepsin L (NP_666023; NM-145918), testin does not possess protease nor protease inhibitor activity.[11] Equally important, Sertoli cell testin originally identified in the rat testis is entirely different from a tumor suppressor gene called TESTIN (gene name *Tes*) (GenBank™ Accession Numbers: NM_015641, NP_056456), which was identified and cloned around the same time rat Sertoli cell testin was identified.[12-14] The tumor suppressor TESTIN[14] shares no significant homology in its amino acid sequence (only ~1–3%) with rat Sertoli cell testin. Moreover, Sertoli cell testin does not contain any characteristic LIM domains or zinc finger motifs, which are found in the tumor suppressor TESTIN, illustrating that these two proteins are distinctly different and evolutionarily unrelated. A mouse genetic model is available for the tumor suppressor TESTIN, and its deletion was found to associate with hematopoietic malignancies and epithelial tumors.[15] However, findings from this genetic model are not applicable to Sertoli cell testin since they are two entirely different proteins.

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