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Zyxin, Axin, and Wiskott-Aldrich Syndrome Protein Are Adaptors That Link the Cadherin/Catenin Protein Complex to the Cytoskeleton at Adherens Junctions in the Seminiferous Epithelium of the Rat Testis

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During spermatogenesis, the movement of germ cells across the seminiferous epithelium is associated with extensive junction restructuring. Yet the underlying mechanism (or mechanisms) that regulates these events is largely unknown. If the molecular architecture of the cell-cell actin-based adherens junction (AJ), such as ectoplasmic specialization (ES) and tubulobulbar complex— two testis-specific AJ types, is known, many functional mechanistic studies can be designed. We thus undertook an investigation to study 3 adaptors in the seminiferous epithelium: zyxin, axin, and Wiskott-Aldrich syndrome protein (WASP). All 3 adaptors were shown to be products of Sertoli and germ cells. Zyxin was shown to be a stage-specific protein that was most prominent during stages V–VII and restricted mostly to pachytene spermatocytes, but it could also be detected at the site of basal and apical ectoplasmic specialization (ES). Zyxin, axin, and WASP were shown to be structurally linked to the N-cadherin/ß-catenin/α-actinin/actin complex but not to the nectin-3/afadin or the ß1-integrin–mediated protein complexes. Interestingly, zyxin, axin, and WASP are also structurally linked to vimentin (an intermediate filament protein) and α-tubulin (the subunit of a microtubule), which suggests that they have a role (or roles) in the regulation of the dynamics of the desmosome-like junction and microtubule. These results illustrate that zyxin, axin, and WASP are adaptors in both AJs and intermediate filament-based desmosome-like junctions. This raises the possibility that classic cadherins are also associated with vimentin-based intermediate filaments via these adaptors in the testis. While virtually no N-cadherin was found to associate with vimentin in the seminiferous tubules, it did associate with vimentin when testis lysates were used. Interestingly, about 5% of the E-cadherin associated with vimentin in isolated seminiferous tubules, and about 50% of the E-cadherin in the testis used vimentin as its attachment site. These data suggest that cadherins in the testis, unlike those in other epithelia, use different attachment sites to anchor the cadherin/catenin complex to the cytoskeleton. The levels of zyxin, axin, and WASP were also assessed during AF-2364–mediated AJ disruption of the testis, which illustrated a time-dependent protein reduction that was similar to the trends observed in nectin-3 and afadin but was the opposite of those observed for N-cadherin and ß-catenin, which were induced. Collectively, these results illustrate that while these adaptors are structurally associated with the cadherin/catenin complex in the testis, they are regulated differently.

Key words: Sertoli cells, testis, adaptors

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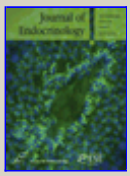

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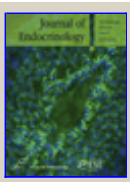

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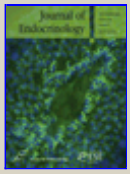

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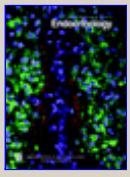

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[Abstract] [Full Text] [PDF]