Abstract


Long-term vitamin A deficiency induces alteration of adult mouse spermatogenesis and spermatogonial differentiation: direct effect on spermatogonial gene expression and indirect effects via somatic cells.

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OBJECTIVE: The objective of this study was to further understand the genetic mechanisms of vitamin A deficiency (VAD) induced arrest of spermatogonial stem-cell differentiation. Vitamin A and its derivatives (the retinoids) participate in many physiological processes including vision, cellular differentiation and reproduction. VAD affects spermatogenesis, the subject of our present study. Spermatogenesis is a highly regulated process of differentiation and complex morphologic alterations that leads to the formation of sperm in the seminiferous epithelium. VAD causes early cessation of spermatogenesis, characterized by degeneration of meiotic germ cells, leading to seminiferous tubules containing mostly type A spermatogonia and Sertoli cells. These observations led us to the hypothesis that VAD affects not only germ cells but also somatic cells.

METHODS AND RESULTS: To investigate the effects of VAD on spermatogenesis in mice we used adult Balb/C mice fed with Control or VAD diet for an extended period of time (6-28 weeks). We first observed the chronology, then the extent of the effects of VAD on the testes. Using microarray analysis of isolated pure populations of spermatogonia, Leydig and Sertoli cells from control and VAD 18- and 25-week mice, we examined the effects of VAD on gene expression and identified target genes involved in the arrest of spermatogonial differentiation and spermatogenesis.

CONCLUSION: Our results provide a more precise definition of the chronology and magnitude of the consequences of VAD on mouse testes than the previously available literature and highlight direct and indirect (via somatic cells) effects of VAD on germ cell differentiation.

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