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The *t* Complex Distorter 2 Candidate Gene, *Dnahc8*, Encodes at Least Two Testis-Specific Axonemal Dynein Heavy Chains That Differ Extensively at Their Amino and Carboxyl Termini

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Abstract

Homozygosity for the *t* haplotype allele of the testis-specifically expressed axonemal dynein heavy chain (axDHC) gene, *Dnahc8*, has been linked to male sterility resulting from aberrant sperm motility. However, the near absence of *Dnahc8* expression has been associated with male sterility resulting from an early breakdown in sperm flagellar development. Although axDHCs are integral participants in flagellar motility, a role in flagellar morphogenesis has never been attributed to a member of this highly conserved gene family. To gain a better understanding of this presumed novel role for *Dnahc8*, we have studied the organization and expression of full-length *Dnahc8*$^{+}$ *and Dnahc8*^{t} transcripts. Our results demonstrate the existence of at least two alternatively spliced, testis-specific *Dnahc8* mRNAs transcribed from both the + and *t* alleles. A highly expressed isoform encodes a protein with significant homology nearly throughout to the γ heavy chain of the *Chlamydomonas* axonemal outer arm dynein, while a more poorly expressed isoform codes for a protein whose sequence diverges significantly from that of other axDHCs at both its N and C termini. While *in situ* hybridization studies demonstrate that both mRNA species accumulate exclusively in mid to late spermatocytes, each isoform shows spatial independence. Additional experiments demonstrate the existence of a testis-expressed mRNA with no significant open reading frame, a portion of which is antisense to the 5′-untranslated region of the highly divergent *Dnahc8* isoform. The cumulative data imply that *Dnahc8* may have acquired functional plasticity in the testis through the tightly controlled expression of both typical and unusual isoforms.

Keywords

t complex; *t* haplotype; dynein heavy chain; stem domain; motor domain; sperm tail; flagellar motility; flagellar morphogenesis; axoneme; fibrous sheath

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