**Atm Inactivation Results in Aberrant Telomere Clustering during Meiotic Prophase**

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A-T (ataxia telangiectasia) individuals frequently display gonadal atrophy, and Atm<sup>−/−</sup> mice show spermatogenic failure due to arrest at prophase of meiosis I. Chromosomal movements take place during meiotic prophase, with telomeres congregating on the nuclear envelope to transiently form a cluster during the leptotene/zygote transition (bouquet arrangement). Since the ATM protein has been implicated in telomere metabolism of somatic cells, we have set out to investigate the effects of Atm inactivation on meiotic telomere behavior. Fluorescent in situ hybridization and synaptonemal complex (SC) immunostaining of structurally preserved spermatocytes I revealed that telomere clustering occurs aberrantly in Atm<sup>−/−</sup> mice. Numerous spermatocytes of Atm<sup>−/−</sup> mice displayed locally accumulated telomeres with stretches of SC near the clustered chromosome ends. This contrasted with spermatogenesis of normal mice, where only a few leptotene/zygote telomeres were detected. Pachyteni nuclei, which were much more abundant in normal mice, displayed telomeres scattered over the nuclear periphery. It appears that the timing and occurrence of chromosome polarization is altered in Atm<sup>−/−</sup> mice. When we examined telomere-nuclear matrix interactions in spermatocytes I, a significant difference was observed in the ratio of soluble versus matrix-associated telomeric DNA sequences between meiocytes of Atm<sup>−/−</sup> and control mice. We propose that the severe disruption of spermatogenesis during early prophase I in the absence of functional Atm may be partly due to altered interactions of telomeres with the nuclear matrix and distorted meiotic telomere clustering.

Ataxia telangiectasia (A-T) is an autosomal recessive disorder characterized by progressive neurological degeneration, premature aging, growth retardation, specific immunodeficiencies, telangiectasia, high sensitivity to ionizing radiation, genomic instability, cancer progression, and gonadal atrophy (9, 31). Cells derived from A-T individuals exhibit a variety of abnormalities in culture such as cytotoxic/skeletal defect, hypersensitivity to ionizing radiation, and higher requirement for serum growth factors (51, 78). They also show a prominent chromatin defect at chromosome ends in the form of chromosome end-to-end associations (also known as telomeric associations) seen at metaphase (38, 61, 63, 89). Chromosome end associations correlate with genomic instability and carcinogenicity (18, 61, 63) and involve telomeres (48, 55). Telomeres consist of repetitive (TTAGGG) DNA and proteins which protect chromosome ends from exonucleolytic attack, fusion, and incomplete replication (7, 98). Telomere erosion in a variety of cancers and cell lines has been found to lead to chromosome end associations that could contribute to genomic instability and gene amplification (18, 47, 60, 82).

It has been suggested that mammalian terminal (TTAGGG) <sub>G</sub><sup>4</sup>, repeat arrays interact with the nuclear matrix (19, 44). Whether ATM gene effectors influence the interaction of telomeres with the nuclear matrix is not yet known. The ATM protein exhibits the phosphatidylinositol (PI)-3 kinase signature of a growing family of proteins involved in the control of cell cycle progression, processing of DNA damage, and maintenance of genomic stability (32). The protein shows similarity to several yeast and mammalian proteins involved in meiotic recombination and cell cycle progression, e.g., the products of MECI in budding yeast and rad3<sup>−/−</sup> in fission yeast and the TOR proteins of yeast and mammals (35, 70, 71). In yeast, non telomeric DNA created by enzymatic cleavage leads to genomic instability and cell cycle arrest (69). Because of ATM homology to TEL1 and rad3<sup>−/−</sup> mutations of yeast, it has been suggested that mutations in ATM could lead to defective telomere maintenance (27). We have recently reported an alteration in both basal and radiation-induced telomeric associations and in mean telomere length in isogenic cells with aberrant ATM function, demonstrating a direct link between ATM function and telomere maintenance (27). A possible hypothesis explaining the defective telomere maintenance in A-T cells could be due to altered interactions between telomeres and the nuclear matrix. An altered interaction between telomeres and the nuclear matrix and nucleosomal periodicity in telomeric chromatin was found in somatic cells derived from A-T individuals (81).

Telomeres have also been considered key structures of meiotic chromosomes (1, 8, 20, 21, 53). Meiosis is a specialized cell division that ensures the proper segregation of genetic material and formation of viable haploid gametes. The most critical events of meiosis occur during prophase I, when homologous chromosomes become aligned (prealign), synapse (pair), and recombine with each other. During early meiotic prophase telomeres redistribute and accumulate at a limited sector of the nuclear envelope to form a chromosomal bouquet (for reviews, see references 21, 41, 73, and 94). A number of studies suggest that bouquet formation mediates prealignment of homologues and thereby facilitates synopsis (17, 41, 54, 67, 74, 88, 90, 91). The only known telomeric proteins that have been implicated in bouquet formation are the products of Taz1 of...
fission yeast (17, 58) and Ndi1/Tam1 of budding yeast (15, 16, 67).

ATM is a multifaceted protein and is part of a signaling pathway that responds to DNA damage. This pathway involves p53 as well as c-Abl, as A-T null cells are defective in activation of p53 and c-Abl (6, 33, 34, 47, 76). Accelerated shortening of telomeres in A-T cells and ATM-dependent telomere loss in aging human diploid fibroblasts have been reported (50, 61, 63, 80, 93). Abrogation of ATM function leads to telomereassociated deficiencies at metaphase (80) and to disruption of gametogenesis due to a meiotic prophase arrest (5, 65, 96). Immunocytochemical localization studies have indicated that the ATM protein is associated with sites along the synaptonemal complex (SC), which are thought to be involved in meiotic recombination (5, 34, 66).

Disruption of Atm in mice leads to severe defects in progression of first prophase and eventually to meiotic arrest and apoptosis (5, 65, 96). Since telomere clustering at meiosis is thought to bring about prealignment and pairing of homologues (see above) and the ATM mutation influences somatic telomere behavior (80), we investigated meiotic telomere distribution in isolated spermatocytes of mice disrupted in Atm function. Furthermore, we determined the interactions of telomere repeats with nuclear matrix, telomerase activity, and expression of TRF1 (telomere binding factor 1) and several other genes in spermatocytes I of Atm null and control mice. Our results suggest that Atm is required for the failure to disperse clustered telomeres in Atm null mice links with aberrant synthesis and arrest early during meiotic prophase.
The poly(A) RNA was treated with RNase-free DNase I (Boehringer Mannheim) and then used for cDNA synthesis and labeled with 32P. The labeled cDNA was hybridized to the Atlas arrays, followed by washing and exposure of the membrane in a PhosphorImager (Molecular Dynamics). The image analysis and quantification were done individually for each dot by using the Scion Image program.

RESULTS

Spermatogenesis is arrested in prophase I in Atm−/− spermatocytes. The progression of the meiotic cell cycle in Atm−/− and control mice was monitored in Giemsa-stained testicular touch preparations. All stages of meiotic prophase were present in preparations of testicles of 42-day-old control mice (Fig. 1a). In Atm−/− mice of the same age, spermatogenesis was arrested at the spermatocyte stage, and diplotene or dia- kinesis as well as spermatids were absent (Fig. 1b). In Atm−/− mice, the frequency of cells with leptotene Giemsa morphology was comparable to that in control mice, while the frequency of zygotene cells was significantly lower than in control mice (2% versus 13%) (Table 1). Cells with typical pachytene or diplotene morphology were largely absent.

It has been reported that Atm−/− spermatocytes arrest during prophase I and display aberrant synapsis (5, 65). To test whether this is also the case in our Atm−/−, we investigated SC formation by immunostaining of the SCP3 axial/lateral element proteins of the SC (40) in surface spread spermatocytes. Progression of synapsis in control mice appeared to be normal (not shown). In Atm−/− mice, however, a severe deviation from normal synapsis was apparent (Fig. 2; Table 1). The vast majority of spermatocytes of Atm−/− mice were aberrant in all aspects of SC formation and displayed large portions of un- paired axial cores, pairing partner switches, absence of sex vesicle formation (Fig. 2), and fragmented axial cores and SCs (not shown). In comparison to control, 94% of spread Atm−/− spermatocytes displayed these features of aberrant synapsis (Table 1), confirming the meiotic phenotype of this mutation.

Undisrupted Atm−/− spermatocytes I frequently display a bouquet arrangement. Since detergent spreading of spermatocytes I disrupts three-dimensional nuclear architecture like

<table>
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<tr>
<th>Prophase stage</th>
<th>Frequency (%)</th>
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<tr>
<td>Control</td>
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<td>Atm−/−</td>
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<tr>
<td>Leptotene</td>
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<td>Zygotene</td>
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<td>Pachytene</td>
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<td>Diplotene</td>
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<td>Aberrant spermatocytes</td>
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* One hundred spermatocytes were examined. Aberrant spermatocytes displayed fragmented SCs, pairing partner switches, absence of sex vesicle formation, SC fragments, and unpaired axial cores.
chromosome polarization, we investigated SC formation in undisrupted spermatocyte I nuclei from \textit{Atm}\textsuperscript{2/2} and control mice. In doing so, we wished to investigate the frequency of occurrence of spermatocytes at the bouquet stage, as nuclei with large chromocenters which were noted in the Giemsa analysis of \textit{Atm}\textsuperscript{2/2} testes suspensions (data not shown) suggested the association of proximal chromosome ends. In normal mouse meiosis, the transient formation of a chromosomal bouquet during leptotene/zygote discloses such nuclei at a low frequency, even in tissue sections (25, 75). In accordance with these observations, SCP3 staining of undisrupted control spermatocytes revealed that all of 226 nuclei showed chromosome ends scattered over the nuclear periphery. Accumulation of a considerable fraction of chromosome ends at a limited region of the nuclear periphery was seen in 2% of nuclei (Fig. 3a). These results are in agreement with earlier reports in female meiosis (85).

\textit{Atm}\textsuperscript{2/2} spermatocytes displayed a severe deviation from this pattern. Numerous spermatocyte I nuclei exhibited a single large chromocenter formed by DAPI bright heterochromatin, usually diagnostic for bouquet nuclei (75). SC immunostaining identified these nuclei as spermatocytes with partial synapsis (Fig. 3d), thereby excluding the possibility that these nuclei

<table>
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<th>Genotype</th>
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<td>Control</td>
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<tr>
<td>\textit{Atm}\textsuperscript{2/2}</td>
<td>24\textsuperscript{b}</td>
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\textsuperscript{a} Stages were assigned according to chromatin morphology (26). Pairing of the chromosome 8 subterminal region is reduced in \textit{Atm}\textsuperscript{2/2} mice.

\textsuperscript{b} Separated signals in \textit{Atm}\textsuperscript{2/2} mice are significantly different from those in control mice by chi-square analysis (\(P < 0.05\)).

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FIG. 3. SCP3 immunostaining (yellowish) to structurally preserved spermatocytes from normal (a to c) and \textit{Atm}\textsuperscript{2/2} (d to f) testicle suspensions. DAPI images (gray) are shown to the right. (a) Zygote nucleus with partial synapsis. (b and c) Pachytene nuclei with variously arranged SCs. (d) \textit{Atm}\textsuperscript{2/2} spermatocyte nucleus with a prominent chromocenter (seen as white mass in the DAPI image) and fragments of SC located at the chromocenter (compare with Fig. 3c and d). (e) \textit{Atm}\textsuperscript{2/2} spermatocyte with SCs looping out from the single chromocenter (bouquet arrangement). (f) Aberrant \textit{Atm}\textsuperscript{2/2} spermatocyte with long axial elements and few stretches of SCs.
represents aberrant spermatids, which also tend to contain a large chromocenter (10, 30). Furthermore, spermatocytes with a fair amount of synopsis and conspicuous polarization of chromosome ends were observed (Fig. 3e), giving rise to a bouquet arrangement during a late zygotene/pachytene equivalent stage. Hence, it appears that the timing and occurrence of chromosome polarization are altered in Atm−/− mice, since such an arrangement is rarely seen in pachytene spermatocytes of normal mice (Fig. 3b and c) (25).

**Pairing of a distal telomere region is reduced in Atm−/− spermatocytes.** It is believed that telomere clustering confers a spatial proximity to homologous chromosomes. Given the aberrant synopsis in Atm-defective spermatocytes, we wished to test whether this mutation influences homologue alignment and pairing. To address this question, we used a mouse chromosome 8 region-specific probe, which maps adjacent to the distal telomere. As shown in Fig. 4, we observed spatially separated, aligned, and fused chromosome-specific signals in early prophase spermatocytes of all mutant and normal mice (Table 2). Comparison of the frequency of cells with separated, aligned, and fused signals among Atm−/− and control mice, however, revealed that Atm−/− mice had significantly higher frequencies of cells with separated signals compared to control mice. These results suggest that the early prophase arrest seen in Atm−/− mice leads to a reduction of homologue pairing even at telomeric regions. Still, a considerable fraction of Atm−/− spermatocytes displayed paired signals, which could be mediated by the persisting bouquet arrangement.

**Sustained chromosome polarization occurs at high frequency in Atm−/− spermatocytes.** Since the above observations suggest a link between the Atm mutation and an altered telomere distribution at meiosis, we investigated the occurrence and frequency of telomere cluster formation in Atm−/− testes suspensions by telomere repeat FISH alone and in conjunction with SCP3 immunostaining. First, telomere distribution patterns were investigated in spermatocytes fixed with acetic acid-methanol (1:3) and counterstained with propidium iodide. This procedure detected various stages of telomere clustering and dispersion during prophase I (Fig. 5). In control mice (Fig. 5a and b), the frequency of spermatocytes with telomere clustering was about 0.7%, while cells with a pachytene chromatin morphology and dispersed telomeres were abundant (Fig. 5d to f). In contrast, a large number of Atm−/− spermatocytes had tightly clustered telomeres (Fig. 5c).

To be able to simultaneously stain telomeres and SCP3 proteins of the SC and to maintain nuclear structure, we performed FISH/immunostaining experiments on formaldehyde-fixed suspension nuclei. The distribution of DAPI bright chromocenters and the distribution mode of axial and lateral element proteins were used to identify cells at the various stages of prophase I. Premeiotic and preleptotene nuclei of Atm null mice showed a scattered telomere distribution similar to that of the wild-type mice (data not shown).

A regional accumulation of telomeres was generally seen in spermatocytes displaying a leptotene/zygotene-like arrangement of axial cores (Fig. 6a and b). The frequency of nuclei with a few large telomere cluster signals was observed in only 0.5% of nuclei from testis suspension of normal mice. These observations match earlier reports and the assumption that the bouquet is a transient stage during early mouse prophase (75, 85). Atm−/− spermatocytes with aberrant synopsis, on the other hand, often exhibited a bouquet arrangement (Fig. 6c and d), a three-dimensional organization motif rarely seen in spermatocytes of normal mice (see above and reference 25 and 75). The frequency of Atm−/− spermatocytes with extensive synopsis and locally accumulated telomeres was up to 50% in suspension slides (Fig. 6d; see also Fig. 3e), while this signal arrangement was encountered in only 7% of control spermatocytes. Many of the Atm−/− spermatocyte nuclei contained a large chromocenter and displayed short, strong SCP3 signals at and around the accumulated telomeres (Fig. 6c), as judged from the colocalization of FISH and SC signals. This distribution contrasts with extensive and scattered axial core and SC formation in the polarized spermatocytes of normal mice (Fig. 6b).

**Telomere nuclear matrix interactions are altered in Atm−/− spermatocytes.** Telomeres are attached to the nuclear matrix of somatic cells (19, 44, 81). Since such interactions may influence meiotic telomere mobility, we set out to characterize nuclear matrix-telomere interactions in spermatocytes derived from Atm null and control mice. To characterize the nature of telomere anchorage in spermatocytes obtained from Atm null and control mice, leptoneteygnotene cells were collected by elutriation and processed by the LIS procedure (22). The resulting halos were cleaved with Sty and probed with telomere TTAGGG repeats (Fig. 7). It was found that normal mice had about 50% of the telomeric DNA repeats associated with the nuclear matrix (P fraction), with 50% in the soluble (S) fraction. The summation of the P and S fractions was equal to the total telomeric DNA, suggesting that the telomeric DNA was retained during the extraction procedure. In contrast to normal mice, spermatocytes of Atm null mice had more than 99% of the telomeric DNA repeats associated with the nuclear matrix and only 11% in the S fraction. The ratio between the S and P fractions is about 1:8 in spermatocytes of Atm null mice, compared to 1:1 in normal mice. These results suggest that the major portion of telomere repeats in Atm null spermatocytes remain associated with the nuclear matrix and that Atm influences this attachment in some way.

**Telomerase activity in Atm−/− spermatocytes.** Whether the elevated interactions between telomeres and nuclear matrix could be attributed to telomerase or TRF is not known. It is
known that ATM function influences telomere metabolism (80). To determine whether inactivation of Atm influences germ line telomerase activity, we examined protein extracts from seminiferous tubules of mice of the different genotypes. Telomerase activities in Atm−/− and control mice were very similar (data not shown), which excludes a potential link between telomerase, Atm, and meiotic telomeres.

Expression of TRF1 and other genes in Atm−/− spermatocytes. The human TRF1 protein binds with telomeres and shows homology with the telomeric fission yeast Taz1-encoded protein (14, 17, 58). Recently, it has been demonstrated that fission yeast Taz1 is required for meiotic telomere clustering (17). In vitro studies demonstrated that human TRF1 promotes parallel pairing of TTAGGG arrays, and thus TRF1 may have an architectural role at telomeres (28). To determine whether the Atm gene has any influence on the expression of TRF1 in mouse testes, we used reverse transcription-PCR and a slot blot approach to quantitate the expression of TRF1 in testes. We found-similar levels of TRF1 expression at the transcriptional level in testis of Atm−/− and control mice (data not shown).

An attempt to further identify gene products that might be involved in defective meiosis in Atm null mice by Atlas cDNA microarray analysis, which monitors 588 genes, revealed similar expression of these genes in testes from Atm null and control mice (data not shown).

DISCUSSION

We have investigated the effects of inactivation of Atm on telomere clustering during male mouse meiosis. Our search was prompted by the observation that cells derived from A-T individuals show, among other features, an altered telomere metabolism and structure (61, 63, 80, 81). Telomere FISH to spermatocytes I of Atm null mice revealed that premeiotic and leptotene Atm−/− mice nuclei are similar in telomere distribution and signal number to control mice (74a). Spermatocytes I of Atm−/− mice, however, showed aberrant synopsis and telomere distribution, in that undisrupted spermatocyte nuclei frequently displayed clustered telomeres and a large chromosome. SC immunostaining in combination with telomere FISH to these nuclei revealed fragmentary, strong SCP3 signals at and around the clustered telomeres, with the SC protein signals often aberrantly extending between several chromosome ends. Such a distribution of SC proteins and telomeres was not observed in spermatocytes of normal mice, where synopsis has been shown to initiate more internally (references 29 and 75 and this investigation) and is usually delayed at the heterochromatic proximal ends of the acrocentric mouse chromosomes (2n = 40 [86]). In male mouse meiosis, a bouquet arrangement of chromosome ends resolves soon after the initiation of synopsis (early zygotene) (75) and renders only a very low percentage of bouquet nuclei readily detectable (25). The higher frequency of spermatocytes with locally clustered telomeres encountered in Atm−/− testis preparations suggest that the bouquet arrangement is maintained for a considerably longer period or is arrested in the absence of functional ATM protein. The prevalence of a bouquet arrangement could result from pairing partner switches, nonhomologous synopsis and/or illegitimate recombination events (4, 5) which interconnect accumulated chromosome ends at the cluster site, thereby preventing their dispersion during zygotene. Since telomere clustering occurs normally at the leptotene/zygotene transition (for a review, see reference 21), an elevated number of spermatocyte I nuclei showing a bouquet arrangement could also be a consequence of an arrest during leptotene/zygotene stages of meiotic prophase. This timing would be consistent with reports that the spermatogenic arrest in Atm−/− animals occurs as early as leptotene or zygotene (5, 96).

Cells derived from A-T individuals show a prominent defect at chromosome ends in the form of chromosome end-to-end associations seen at metaphase as well as prematurely condensed chromosomes of G1- and G2-phase cells. Frequency of cells with chromosome end associations decreases as cells pass

FIG. 5. Spermatocytes showing telomere clustering and subsequent separation of telomeres in postleptotene stage of meiosis prophase I as detected by the TTAGGG probe and propidium iodide used as counterstain. (a and b) Spermatocytes of control mice at leptotene/zygotene stage. (c) Spermatocyte of Atm−/− mice at leptotene/zygotene stage. Note that panels a to c have the fewest telomere signals but each signal is created by numerous closely spaced signals. Panels d to f show increased telomere signal numbers in cells from control mice with disperse telomere arrangement, as the clustered telomeres have organized in proper pairs. Such telomere dispersal at pachytene was rarely seen in Atm−/− spermatocytes.
from G1 phase to metaphase, suggesting that chromosome end associations are not permanent structures and probably do not involve covalent interactions. Whether the chromosome end associations are the cause for or the result of the accelerated loss of telomeres in A-T cells is unclear (50, 61, 63, 80, 93). Since the Atm gene has a PI-3 kinase domain, it is possible that the chromosome end associations defect are due to a defective kinase activity. Recently, we have reported that the ATM gene influences chromosome end associations as well as telomere length (80); however it is not clear how chromosome end associations are formed in cells derived from A-T individuals. We have recently shown that such cells have altered telomere chromatin and nuclear interactions (81). It is possible that altered telomere chromatin and nuclear matrix interactions influence telomere metabolism in somatic cells and telomere movement in meiotic cells, leading to a failure of normal telomere dispersion after bouquet formation and early prophase I.

ATM protein has been shown to be associated with chromatin (24), and ATM may be involved in the control of recombination (5, 65). The abrogation of Atm function results in meiotic prophase arrest associated with aberrant synapsis and fragmentation of SCs (references 5, 34, and 65 and this study). ATM also shows some homology to TEL1 and MEC1 genes of budding yeast, which are involved in telomere maintenance (27) and meiotic and mitotic cell cycle check point control (46). Since Atm- and Dmc1-deficient mice (64, 97) as well as many recombination mutants of budding yeast fail to form normal SCs (for a review see reference 68), it is possible that an absence of Atm function alters the progression of recombination. Consistent with this hypothesis, proteins involved in normal recombination processes, like Rad51, DMC1, and Atr (66), are mislocalized as early as leptotene in Atm-/- mice (64, 97) as well as many recombination mutants of budding yeast fail to form normal SCs (for a review see reference 68), it is possible that an absence of Atm function alters the progression of recombination. Consistent with this hypothesis, proteins involved in normal recombination processes, like Rad51, DMC1, and Atr (66), are mislocalized as early as leptotene in Atm-/- mice. Aberrant synapsis and failure to form normal SCs seems to induce apoptosis (59) and fragmentation of chromosomes in Atm-/- spermatocytes (65, 96). Given that telomere dispersion from the cluster site is delayed or prevented in Atm-/- bouquet cells, SC fragmentation could result from the physical stress building up between immobile meiotic telomeres and dynamic chromosomes with unrepaired double-strand breaks.

Recently, it was shown that a bouquet arrangement transiently forms during wild-type meiosis of budding yeast (91). The spo11 (13, 36) and rad50S recombination mutants of budding yeast (87), which fail to form normal SC (42, 95), form a chromosomal bouquet but fail to resolve this nuclear organization later at prophase, leading to elevated levels of bouquet nuclei (91). The timing and occurrence of a bouquet in yeast recombination mutants mirrors that in Atm-deficient sper-
matocytes, which also fail to resolve the bouquet arrangement. The observations that loss of all telomeres in fission yeast TEL1 rad3 double mutants prevents meiosis (57) and that telomeres support homologue search (67) strongly suggest that telomeres support homologue alignment. A persisting bouquet arrangement in Atm−/− spermatocytes could contribute to the high levels of chromosome pairing at a telomere associated chromosome 8 region, despite the widely aberrant synopsis in Atm−/− mice. This interpretation is consistent with the observation that recombination mutants of yeast form a bouquet (91) and undergo limited levels of homologue pairing (42, 56), which is elevated at telomeric regions (95).

Since ATM influences the organization of telomere chromatin in vegetative cells (80, 81) and telomeres have been shown to be tethered to the nuclear matrix in somatic cells (19, 44), we tested the interaction of telomeres with the nuclear matrix of spermatocytes from control and Atm null mice. This interpretation is consistent with the observation that recombination mutants of yeast form a bouquet (91) and undergo limited levels of homologue pairing (42, 56), which is elevated at telomeric regions (95).

We considered the possibility that aberrant telomere clustering in Atm null mice is due to defective telomerase activity. That is, telomerase may be required for the synthesis of the correct telomere termini without which telomere ends might have defective interactions with the nuclear matrix. We found no differences in the telomerase activity between testes of Atm null and control mouse cells.

ACKNOWLEDGMENTS

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Atm Inactivation Results in Aberrant Telomere Clustering during Meiotic Prophase

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Volume 19, no. 7, p. 5096–5105, 1999. Page 5103, Fig. 7 legend, line 4: Should read “Atm null (b) and control (a) mice.”