

Abstract 42

SHORTER TELOMERES IN YOUNGER MALE INDIVIDUALS WITH THE FRAGILE X PREMUTATION

Edmund Jenkins¹, Flora Tassone^{2,3}, Lingling Ye¹, W. Ted Brown¹, Randi Hagerman^{2,4}, and Paul Hagerman^{2,3}

Department of Human Genetics, New York State Institute for Basic Research in Developmental Disabilities, Staten Island, NY, USA¹

M.I.N.D. Institute, University of California Davis Medical Center, Sacramento, California, USA²
Department of Biochemistry and Molecular Medicine, UC Davis School of Medicine, Sacramento, California, USA³

Department of Pediatrics, UC Davis Health System, Sacramento, California, USA⁴

We have recently found that T lymphocytes from older men with premutation alleles of the fragile X mental Retardation 1 Gene exhibited shorter telomeres (that consist of highly conserved TTAGGG repeats) than controls. These findings were determined from ten premutation males ranging from 56-73 years of age with or without fragile X-associated tremor/ataxia syndrome (FXTAS) and/or dementia. Three of the ten have not [yet] exhibited any symptoms of FXTAS and/or dementia symptomatology. We have now observed shorter telomeres in six additional premutation males compared to age- and sex-matched controls ($p < .0002$). The carrier males did not present with FXTAS and/or dementia and ranged in age from 8.6-38.0 years. Subjects who were carriers of premutation alleles, documented by *FMR1* genotyping, were recruited through the Fragile X Research and Treatment Center at the University of California at Davis MIND Institute. Molecular and telomere length analyses were documented previously (Jenkins et al, 2008). PNA probes for telomeres and centromere 2 were used in the present study. Increased telomere shortening has also been observed in cellular senescence, neoplastic transformation, increased psychological stress, Alzheimer Disease, and Down Syndrome with dementia or mild cognitive impairment. Additional cross section as well as longitudinal studies are needed to determine whether three of the subjects included in our first study as well as any of the six people in our current study convert to FXTAS or FXTAS and/or dementia later on. Thus, shorter telomeres may become a biomarker for cellular dysregulation that may precede the development of symptoms of FXTAS/dementia.

Acknowledgements: This work was supported in-part by the NYS Office of Mental Retardation and Developmental Disabilities, NICHD grants HD 036071, HD02274, NINDS NS044299, and the NIH Roadmap Initiative (UL1 RR024922, NCRR: RL1 AG032119).