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Clinical studies and linkage analysis of a Central Illinois family with Autosomal Dominant Optic Atrophy *V.E. Kimonis[1], W.E. Franks[2], K. Herman[1], A. Avakian[3], J-P Lin[4].* [1]Dept. of Pediatrics, SIU School of Medicine, Springfield, IL. Division of Forensic Services and Identification, Illinois State Police, Springfield, IL, [3]SIU Eye Center, Springfield, IL., [4]Genetic Studies Section, Lab. of Skin Biology, NIAMS, NIH, Bethesda, MD.

Autosomal dominant optic atrophy of Kjer is one of the most common of the hereditary optic atrophies with a frequency rate of 1 in 50,000. It is characterized by insidious onset of vision loss in the first decade, atrophy of the optic nerve and typically blue-yellow color deficiency. Eiberg et al. (1994), Lunkes et al. (1995), and recently Johnson et al. (1997), and Brown et al. (1997) have reported linkage in different populations to a region on 3q28-qter using dinucleotide repeat polymorphisms. We report a 3 generation family with optic atrophy transmitted as an autosomal dominant disorder with some unusual features. Twenty-seven members of the family were evaluated for visual acuity, color vision, and optic disc appearance, 14 (10 males and 4 females) of whom were found to be clinically affected. There was considerable clinical variation in the visual acuity among adults in this family with age of onset of visual loss varying from 5 to over 30 years. There was evidence of earlier onset and increasing severity in each successive generation. Males were found to be more severely affected than females. Molecular linkage studies using microsatellite markers indicate that this family links to chromosome 3q28-29 (LOD score of 3.77 at zero recombination fraction with marker D3S1265). This is the second U.S family showing linkage to this locus suggesting that clinical variability in this disorder cannot be explained by genetic heterogeneity.