



**DGAP113: 46,XY,t(1;3)(q32.1;q13.2)**

**Revised:46,XY,t(1;3)(q31.3;q13.13)**

This male has bilateral congenital cataracts, mild developmental delay, a head circumference greater than the 95<sup>th</sup> percentile, and prominent extra-axial CSF spaces of uncertain significance. A BAC clone spanning the breakpoint on chromosome 1, RP11-401A10, was discovered and the breakpoint was further narrowed to ~1.4 kb using overlapping BAC clones and Southern blot analysis. The 1q32.1 breakpoint was cloned, contains a 4 bp insertion and also maps within an LTR. The 3q13.2 breakpoint was localized with FISH and suppression PCR, and localizes within a LINE element; the nearest gene maps ~515 kb downstream. The 1q32.1 breakpoint lies ~125 kb upstream of *NEK7*. We have chosen to focus our efforts on investigating the role of *NEK7* given the proximity of the gene to the chromosome 1 breakpoint. Our hypothesis is that the break on chromosome 1 exerts a position effect on *NEK7* and thus dysregulates expression of the gene. In order to address whether there is reduced or absent *NEK7* expression in our patient, we have generated somatic cell hybrids containing the derivative chromosome 3, and translocated *NEK7*, isolated away from the normal *NEK7* allele. RT-PCR analysis of *NEK7* expression in the human mouse somatic cell hybrids containing the translocated allele only demonstrates no expression from this allele. This finding suggests that the translocation exerts a position effect on the expression of *NEK7*.

The exact function of *NEK7* remains to be determined. *NEK7* is highly conserved and the mouse ortholog is expressed in the developing murine brain (Feige and Motro 2002). Whole mount *in situ* hybridization experiments using a *Nek7* probe hybridized to day 11.5 and 12.5 mouse embryos showed expression in the developing lens. These experiments support our hypothesis that *NEK7* plays a role in mammalian eye development. ES cells in which the coding region of *Nek7* is disrupted were obtained from the Sanger Institute (<http://www.sanger.ac.uk/PostGenomics/genetrap/>) and homozygous *Nek7* knock out mice were generated that appear to exhibit a partial loss of gene function. These mice are viable and have no obvious phenotype. This may be due to a redundancy in gene function between the *Nek6* and *Nek7* genes which are closely related and thought to represent a highly conserved subfamily of the NIMA-related kinases {Kandli, 2000 #225}. A double knock out mouse of both *Nek6* and *Nek7* could address this hypothesis.

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