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# Ophthalmic Manifestations of *KIF1A* Associated Neurological Disorder

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## INTRODUCTION

- *KIF1A* is part of the kinesin family that is responsible for the anterograde transport of organelles along neuronal axons. Mutations in *KIF1A* are associated with KIF1A Associated Neurological Disorder (KAND), an early onset neurodegenerative disorder.
- KAND is associated with developmental delay/intellectual disabilities, cognitive impairment, ataxia, cerebral atrophy, spastic paraparesis, optic nerve atrophy, peripheral neuropathy, and epilepsy. Different mutations are associated with different phenotypes and disease severity. One component of the phenotype that can have a significant impact on patient and family quality of life is ophthalmic manifestations.
- Previous research has shown there is an increased prevalence of ophthalmic manifestations, with optic nerve atrophy the most common. To date, there has not been a comprehensive review of the vision issues seen in KAND.

## METHODS & MATERIALS

- Written consent was obtained from 84 individuals with KAND, and studies were approved by the Columbia IRB. Data were collected by parental report, with primary record verification when available. Data collected included caregiver reported medical history, clinical genetic test reports, and Vineland Adaptive Behavior Scales-III.
- The Vineland Adaptive behavior scale is a measure of adaptive behavior that is widely used to assess individuals with intellectual, developmental, and other disabilities. The parent caregiver form assesses home and family-life behavior using a questionnaire completed by a parent or caregiver electronically. The ABC (adaptive behavior composite score) has three components: communication, daily living skills, and socialization. The score for each is expressed as a standard score with a mean of 100 and standard deviation of 15.
- ANOVA Single Factor analysis was run on the average ABC scores of the four different groups of ophthalmic diagnoses.

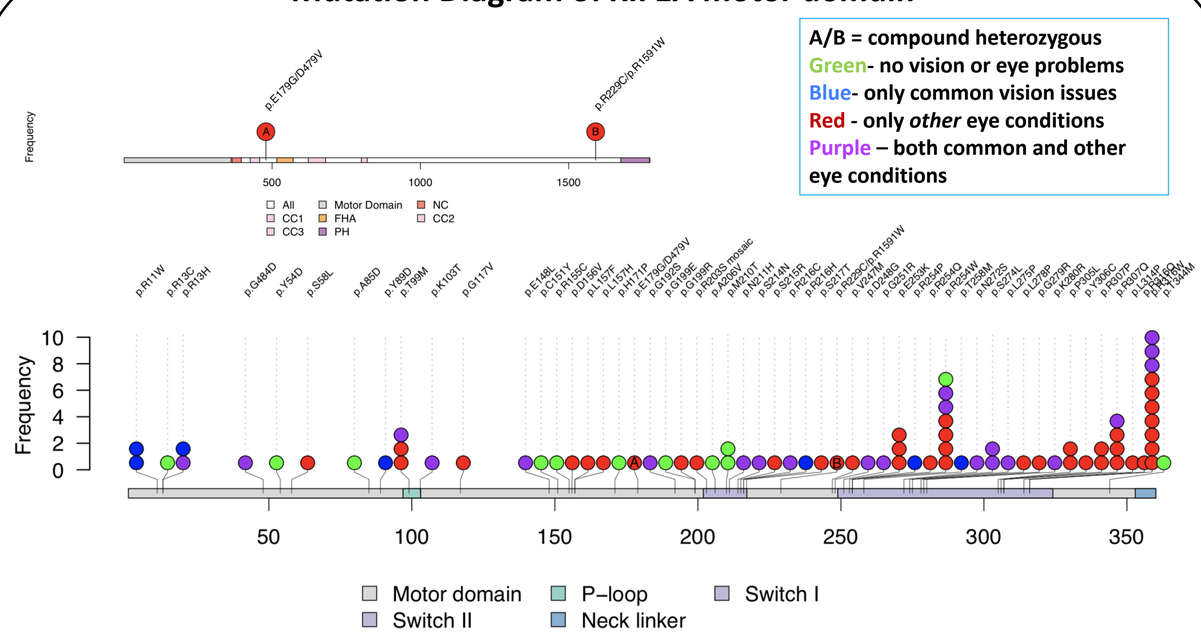
## COHORT

- 84 individuals with KAND were assessed
- 47 males (55.95%), 37 females (44.05%), age 1-29 years old (mean 9.9, SD =7.8)
- 82/84 individuals are heterozygous with a dominant form of the disorder, 2 with a recessively inherited form of KAND.

Divided into 4 subgroups:

**Group 1**: individuals whose eyes or vision are not affected
**Group 2**: individuals with only common vision issues (myopia, astigmatism)
**Group 3**: individuals with other eye conditions: *amblyopia, cataract, conjunctival abnormality, cortical blindness, depth perception problems, eye movement abnormalities, glaucoma, nystagmus, optic nerve atrophy, ptosis, retinal detachment, strabismus*, not including common vision issues
**Group 4**: individuals with both common vision issues and other eye conditions

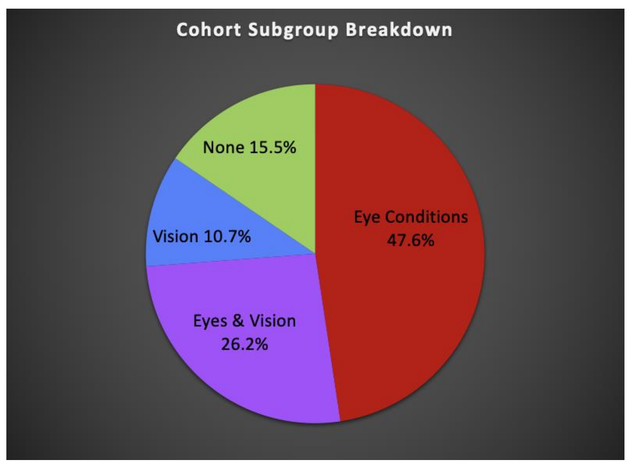
### Mutation Diagram of *KIF1A motor domain*




**A/B = compound heterozygous**
**Green- no vision or eye problems**
**Blue- only common vision issues**
**Red - only *other* eye conditions**
**Purple – both common and other eye conditions**

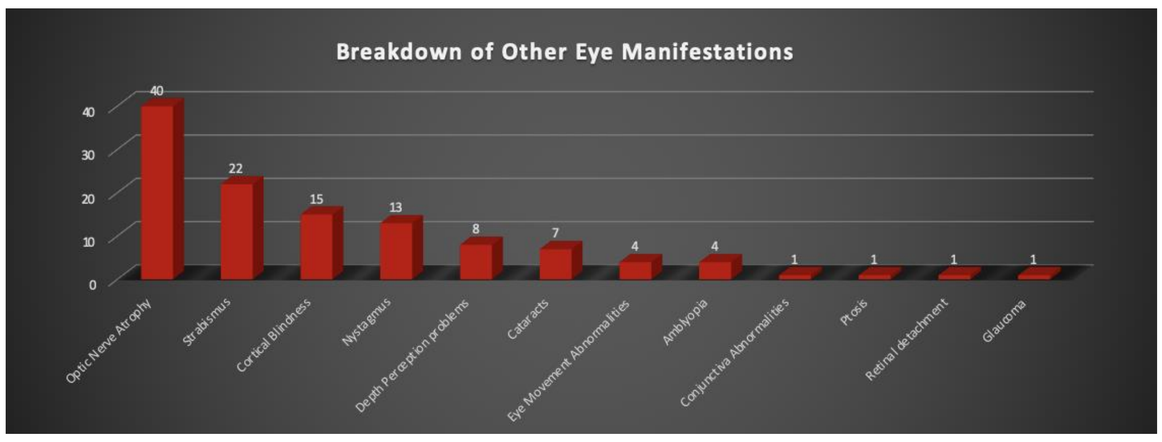
## RESULTS

**Group 1** - 13/84 (15.5%) individuals reported no visual or eye problems
**Group 2** – 9/84 (10.7%) individuals reported **ONLY** common vision issues (myopia, astigmatism)
**Group 3** - 40/84 (47.6%) individuals reported **ONLY** other eye conditions
**Group 4-** 22/84 (26.2%) individuals reported having **BOTH** common vision issues and additional eye problems

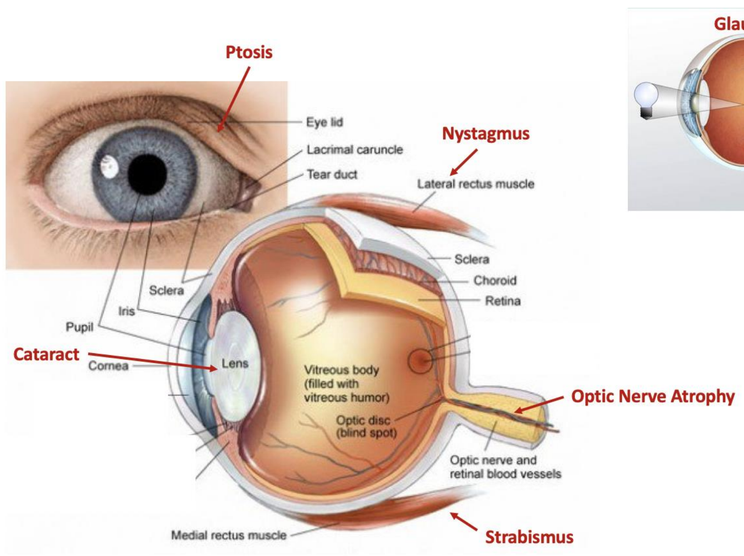



- Compared to the Center for Disease Control and Prevention percentage of children (ages 6-17) who have standard vision problems, our cohort is very comparable with a 35% prevalence.

### Breakdown of Those with Other Eye Manifestations (Group 3 & Group 4)



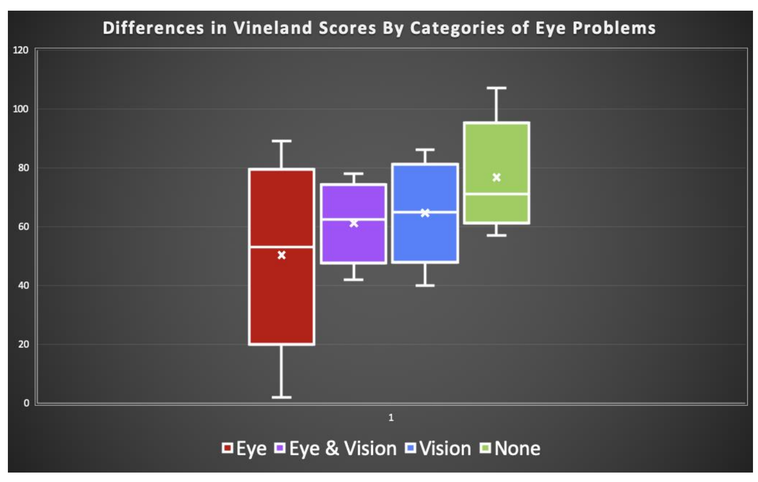

### Anatomical View of The Other Eye Conditions




### One-way ANOVA test results comparing the average ABC score for each subgroup

| F | P-value | F crit |
|---|---|---|
| 5.65 | 0.001 | 2.73 |

- Using the Vineland III ABC score as a proxy for disease severity, there was a statistically significant difference in severity of disease by ophthalmic manifestations (**p= .001**, F = 5.65, Fcrit = 2.73)




ABC score was normed to an average of = 100 w/ SD = 15

## DISCUSION/ CONCLUSIONS

- 13/84 (15.5%) reported no visual or eye problems, 9/84 (10.7%) individuals reported only common vision issues (myopia, astigmatism), 40/84 (47.6%) reported only other eye problems, and 22/84 (26.2%) reported having both common vision issues and additional eye problems.
- Compared to the CDC percentage of children (ages 6-17) who have common vision problems, our cohort is comparable to the general population.
- This suggests that *KIF1A* does not increase the prevalence of common vision problem but has a higher prevalence of other more serious eye conditions.
- There is an increased prevalence of ophthalmic manifestations in those who are more severely developmentally affected.
- There was a statistically significant difference (p=.001) in the average ABC score by ophthalmic manifestation groups.

## REFERENCES

- Cheon, C. K., Lim, S., Kim, Y., Kim, D., Lee, N., Yoon, T., … Lee, J. (2017). Autosomal dominant transmission of complicated hereditary spastic paraplegia due to a dominant negative mutation of KIF1A, SPG30 gene. *Scientific Reports*, *7*(1). doi:10.1038/s41598-017-12999-9
- QuickStats: Percentage of Children Aged 6?17 Years Who Wear Glasses or. (2019, April 8). Retrieved from https://www.cdc.gov/mmwr/volumes/66/wr/mm6634a7.htm