A. Specific Aims

The aim of the current proposal is to better understand the complex multifactorial etiology of developmental dyslexia, or reading disability (RD), by focusing on possible gene x environment and gene x gene interactions. The genetics of RD has advanced to the point of identifying candidate genes, but the identification of these genes is unlikely to answer all of the etiological questions about RD, unless interactions with the environment and other genes are considered. As such, this proposal has three specific aims:

1.) This project will test for gene x environment interactions using molecular genetic methods and measures of the home literacy environment. At present, there are two competing models that predict opposite directions for gene x environment interactions, the diathesis-stress model and the bioecological model. Importantly, there have been no previous studies of g x e interactions in RD using molecular genetic methods.

2.) Another neglected area in the RD genetics literature concerns the possibility of gene – gene additive and epistatic effects. RD is currently the leader among the complex behavioral disorders for replicated linkage peaks. Despite this evidence for multiple risk loci, there has been little research investigating how these loci may combine and interact to result in the RD phenotype. This project proposes novel methods to examine the phenotypic impact of additive genetic risk across loci and of two-locus interactions. Classification and Regression Tree (CART) analysis will be used to assess the impact of higher-order combinations of risk loci on RD status.

3.) Several lines of research indicate that RD is not a homogenous disorder. There is evidence for subtypes based on the reading profiles of the children and their comorbid disorders. Given this phenotypic heterogeneity, there is likely to be etiological heterogeneity as well. This project will consider the contribution of any detected gene x environment or gene x gene interactions to the development of RD subtypes.