

## **Admixture Analysis of Localized Aggressive Periodontitis**

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The search for the molecular basis of neutrophil abnormalities in Localized Aggressive Periodontitis, LAP, (previously known as Localized Juvenile Periodontitis, LJP) and the concomitant search for the genetic basis of inheritance of the clinical disease trait have revealed evidence supporting autosomal dominance, a gene or genes of major effect, and co-segregation of the neutrophil trait in specific affected populations. To understand the genetic basis of LAP, we have employed positional cloning approach. In our preliminary study, we have established a genetic linkage map of the LAP locus. Results from 4 families revealed that LAP is linked to D1S492 with a LOD score 3.48,  $r^2 = 0.00$  (see preliminary data, Section C).

The overall objective of this pilot project is to use the population bias found in aggressive forms of periodontitis to efficiently map the disease locus/ loci. This project will employ mapping by admixture linkage disequilibrium on sets of patient DNA samples collected at Boston University, Goldman School of Dental Medicine, Virginia Commonwealth University School of Dental Medicine and The Forsyth Institute. The samples will be formatted to meet the genotyping standards required at the MIT/Broad Institute where the admixture mapping techniques have been developed. Genotyping data will be returned to Boston University School of Dental Medicine, The Forsyth Institute, and Virginia Commonwealth University School of Dental Medicine for analysis. Positive results from the first genome wide scan will be considered a success of the pilot project and additional funding will then be sought to follow up with fine mapping of these regions with a denser set of markers. Other genomic regions implicated by functional or genetic data will also be fine mapped. Candidate genes from these regions will be sequenced in search of mutations that cause aggressive periodontitis. It is also expected that recruitment of patients will continue to increase the power of these studies to detect additional disease loci.