Inflammatory Bowel Disease Gene Discovery

Final Report
CRADA No. TC-1335-96

LLNL--99001313

Date: 9 September, 1997

Revision:

A. Parties

The project is a relationship between the Lawrence Livermore National Laboratory (LLNL) and gene/Networks, Inc.

University of California
Lawrence Livermore National Laboratory
P.O. Box 808, L-795
Livermore, CA 94550

gene/Networks, Inc.
1501 Harbor Bay Parkway
Alameda, CA 94502

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B. Project Scope

The ultimate goal of this project is to identify the human gene(s) responsible for the disorder known as IBD. As a first step towards this goal, the Parties agreed to carry out experiments to confirm and refine linkage of IBD to the chromosomal region(s) of interest identified by gene/Networks, Inc. If results confirmed association of these region(s) with the disease, the Parties planned to complete a physical map of the genetically defined region(s). The work was planned in two phases. The desired products resulting from Phase I were BAC clone(s) containing the genetic marker(s) identified by gene/Networks, Inc. as potentially linked to IBD, plasmid subclones of those BAC(s), and new genetic markers developed from these plasmid subclones. The newly developed markers would be genotyped by gene/Networks, Inc. to ascertain evidence for linkage or non-linkage of IBD to this region. If non-linkage was indicated, the project would move to investigation of other candidate chromosomal regions. Where linkage was indicated, the project would move to Phase II, in which a physical map of the candidate region(s) would be developed. The products of this phase would be contig(s) of BAC clones in the region exhibiting linkage to IBD, as well as plasmid subclones of the BACs and further genetic marker development. There would also be continued genotyping with new polymorphic markers during this phase. It was anticipated that clones identified and developed during these two phases would provide the physical resources for eventual disease gene discovery.

Phase I work completed during the abbreviated term of this CRADA included the identification of BACs positive for three genetic markers in a chromosomal region of interest, fluorescent in situ hybridization (FISH) analysis of BACs positive for two of the markers to confirm the chromosomal localization, subcloning of one of these BACs into both plasmid and M13 libraries, and preparation of colony filters of the M13 library for microsatellite screening to identify candidate clones for genetic marker development. At this point the CRADA was terminated by the gene/Networks, Inc.

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C. Technical

The first task of the project involved discussions between the PI at LLNL and scientists at gene/Networks, Inc. to plan specifics of the work to be done, as well as hiring a staff scientist to carry out the work. The scientist was hired and began work approximately four months after the initiation of the CRADA. Two months later, the CRADA was terminated by gene/Networks, Inc.

LLNL's technical accomplishments during the abbreviated term of the project were:

- 1) A human BAC library was screened with three genetic markers in the region of interest, and four positive BACs were identified.
- 2) DNA was isolated for BACs positive for two of the markers, and fluorescent in situ hybridization to metaphase chromosomes confirmed the correct chromosomal location for both.
- 3) DNA from one of these markers was sheared, and 1-2 kb inserts were subcloned into plasmid and M13 libraries.
- 4) Clones from the M13 library were spotted onto nylon filters for hybridization screening with microsatellite probes.
- 5) An additional 15 BAC DNA samples, isolated at gene/Networks, Inc. from other chromosomal regions of interest, were analyzed by FISH to determine the chromosomal location of each.

D. Partner Contribution

Linkage analysis for Inflammatory Bowel Disease (IBD) for a chromosome was provided to LLNL. The analysis included the multipoint linkage score and the pairwise association data for individual marker alleles and the trait in both the Jewish and Non-Jewish (Caucasian) populations. Markers under the primary linkage peak and markers showing some association between alleles and the IBD trait were used by staff at LLNL to select BACs containing these markers. gene/Networks, Inc. also provided DNA from other BACs and PACs which were used by LLNL to determine chimerism and location by FISH analysis.

No subject inventions were created during the CRADA project.

E. Documents/Reference List/Inventions

There were no publications or inventions during the CRADA project.

All biological materials generated by LLNL in the course of the CRADA were transferred to gene/Networks, Inc. on 9/9/97.

F. Acknowledgment

Participant's signature of the final report indicates the following:

- 1) The Participant has reviewed the final report and concurs with the statements made therein.
- 2) The Participant agrees that any modifications or changes from the initial proposal were discussed and agreed to during the term of the project.
- 3) The Participant certifies that all reports either completed or in process are listed and all subject inventions and the associated intellectual property protection measures attributable to the project have been disclosed or are included on a list attached to this report.
- 4) The Participant certifies that if real property was exchanged during the agreement, all has either been returned to the initial custodian or transferred permanently.
- 5) The Participant certifies that proprietary information has been returned or destroyed by LLNL.

Claire T. Wake Sept 29, 1997
Claire T. Wake Date
gene/Networks, Inc.

Anne S. Olsen 10/24/97
Anne S. Olsen Date
Lawrence Livermore National Laboratory