

Progress Report - 7/1/01 -- 6/30/02

Commonwealth Technology Research Fund Sponsored Project

Cancer Genomics and Development of Diagnostic Tools and Therapies (Grant # SE2002-02)

Virginia Commonwealth University

The Purpose of this Grant

Develop infrastructure and collaboration between two Virginia universities - Virginia Commonwealth University and George Mason University - and a major health care provider in Virginia – Inova to recruit extramural funding for research and develop new business opportunities for the Commonwealth of Virginia through creation of new diagnostic tools and therapies for use in patients with cancer.

Milestones and Progress To Date

A. Project Coordination and Management

- 1) Appoint Director - **Done** - Dr. Torr appointed Dr. Carleton T. Garrett, MD, PhD, Professor of Pathology at VCU as Interim Program Director for the CTRF Cancer Genomics project
- 2) Establish regular meetings of project leadership – **Done** – the project PIs meet monthly on the first non-holiday Monday of each month. Meetings are held simultaneously at VCU and Inova and are facilitated through televideo conferencing. Dr. Garrett alternates between the two sites on a monthly basis. Combined meetings between the three institutions have been held by the database design, data analysis and tissue bank focus groups over the past year. In addition, Dr. Garrett holds a regular meeting each Thursday morning with Focus Group leaders dealing with issues of tissue acquisition, clinical data sets, database design and QC/QA at VCU.
- 3) Initiate funding – **Completed in late September 2001**
- 4) Establish working groups to address task focused issues – **Done** (see Attachment#1)
- 5) Assemble required reports to CTRF
 - a. Annual Report – **Submitted 12/28/01** (<http://www.ctrf-cagenomics.vcu.edu/>)
 - b. 1st year Progress Report (**this report**)
- 6) Establish Listservs and Website to facilitate communication among members and focus groups – **Done** – (<http://www.ctrf-cagenomics.vcu.edu/>)

B. Project Milestones

- 1) Tissue Banking
 - a. Submit Tissue Acquisition System Protocol to IRB – **Done** (approved at VCU April 2002; approved at Inova June 2002).
 - b. Hire and train staff for tissue acquisition and primary data collection – **Ongoing** – one staff member hired (VCU) and a second staff person is actively being recruited (VCU). Inova has identified two existing research coordinators to support tissue acquisition at their institution.
 - b. Initiate tissue collection – **Ongoing** – tissue collection began at VCU in April 2002.
- 2) Clinical Data - Determine an appropriate data set of clinical and histopathological information to associate with each tissue sample – **In progress** – (A.2. above) the initial clinical data set will consist of information forwarded to the Virginia State Tumor Registry.
- 3) Database Design - Create a database(s) into which clinical, laboratory, tissue bank information, and expression microarray can be stored.
 - a. Database to hold Tissue Bank and Primary Clinical Data – **Done** – this database is currently being used at VCU and will be accessed via modem from Inova to enter their Tissue Bank and Primary Clinical Data.

- b. Database to hold microarray Data and tools for Data Analysis – **In progress** – currently efforts are underway to instantiate a version of the open source GeneX database (<http://genex.ncgr.org/>) at VCU and GMU, which permits entry of both Affymetrix and custom spotted array data.
- 4) QC/QA - Develop criteria for intralaboratory and interlaboratory assessment of quality using standard materials and shared specimens.
- a. Develop at least 1 standard material for intra- and inter-laboratory testing – **Done** – Both VCU and GMU investigators have agreed to perform QC analysis on their respective microarray platforms using a commercial preparation of human RNA provided by Stratagene.
 - b. Initiate intra- and interlaboratory testing comparisons – **In progress** – Each of the microarray laboratories is analyzing the human RNA preparation noted above. Data to be combined and analyzed jointly at the conclusion of the studies.
 - c. Study of microarray surface chemistries and blocking strategies -- VCU investigators have undertaken to evaluate different approaches with the view to evolving standards.
- 5) Data Analysis -
- a. Survey and enumerate data mining approaches and existing software tools to perform analysis of micro array data with clinical (including clinical laboratory) data. – **In progress** – Efforts prior to 12/31/01 are summarized in the annual report (<http://www.ctrf-cagenomics.vcu.edu/>). Subsequent efforts have focused on the use of the open source database and tools associated with GeneX (<http://genex.ncgr.org/>) and Teradata (<http://www.terdatalibrary.com/eb3025.pdf>)
 - b. Select software covering range of data mining approaches judged to be most statistically reliable and that will be compatible with anticipated CTRF SSDB structure. – **In progress** – (see above #5.a)
- 6) Chip Fabrication –
- a. GMU has begun fabrication of a 30k gene set cDNA microarray. VCU-C3B has begun fabrication of a 10k gene set oligo microarray. VCU-Microarray Core will begin fabrication of a 30k gene set cDNA microarray.
 - b. Appropriate controls, standards and protocols are being evaluated and developed for implementation by all three chip-fabrication laboratories. . – **In progress**

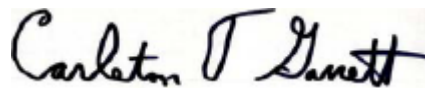
C. Specific Reportables (see Attachment #1)

D. Summary

The CTRF supported Cancer Genomics Project has completed or made significant progress in each of its objectives for FY01 of the Budget. Based on the ongoing level of cooperation among the partners and the degree to which infrastructure has been developed to date, continued excellent progress is expected in FY02 and FY03 of the grant.

Submitted by:

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Director, CTRF Cancer Genomics Project
 Dept. of Pathology
(for Dr. Marsha R. Torr)
(Vice President for Research)
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 (Signature)

Attachment #1

Focus Groups

Focus Group	GMU	VCU	Inova
TissueBank	Geraldine Grant	Suhail Nasim	Barrie Cook
Clinical and Laboratory Data	----	Lynne Penberthy Greg Miller	James Cooper Barrie Cook James Burgess
Database Design	Curtis Jamison	Greg Miller Lynne Penberthy	Mike Sheriden
Data Analysis	Vikas Chandhoke	Greg Buck	---
QA/QC	Alan Christensen	Andrea Ferreira-Gonzalez Suhail Nasim	---
Chip Fabrication	Curtis Jamison	Anthony Guiseppi-Elie	----

Specific Reportables

Publications and Presentations

- 1) Dumur CI, Ferreira-Gonzalez A, Wilkinson DS, Ware JL and Garrett CT. Use of Affymetrix single nucleotide polymorphism arrays (HuSNP™) for assessing loss-of-heterozygosity (LOH) in prostate cell lines. *J Mol Diag* 3:209, 2001.
- 2) Windle B and Guiseppi-Elie A. "Microarrays and Gene Expression Profiling Applied to Drug Research" In *Burger's Medicinal Chemistry*, 6th Edition, Donald J. Abraham, Ph.D., Editor, John Wiley & Sons, Inc. in press, 2002.
- 3) Dumur CI, Deshukhum, C, Ware JL, Wilkinson DS, Garrett CT and Ferreira-Gonzalez A. Genome-Wide detection of loss of heterozygosity (LOH) in prostate cancer using Affymetrix HuSNP™. Department of Pathology, Virginia Commonwealth University, Richmond, VA 23298. 22nd Annual Seminar of Cancer Researchers in Virginia Saturday, April 13, Virginia Tech Blacksburg, Virginia.
- 4) Taylor S, Gheorghe M, Bemeleit D, Blohm D, Böglér O, Broaddus W and Guiseppi-Elie A. "Detection of DNA hybridization by impedance and development of an impedimetric DNA microarray for clinical classification of brain tumors" 15th Annual Meeting of the Mid-Atlantic Biochemical Engineering Consortium, Drexel University, Philadelphia, PA 19104 March 22, 2002.
- 5) Guiseppi-Elie A. "Quality Issues In Microarrays: Surface Chemistry and Blocking Strategies for DNA Microarrays" Bioinformatics and Pharmacogenomics Symposium 2002, Richmond Virginia, USA. June 12-14, 2002.
- 6) Wen L-M, Mallonee D, Ozaki LS, Xu P, Carvalho MR, Zwierzynski TA, Alves J and Buck GA. Microarray analysis of gene expression in *Trypanosoma Cruzi*. Bioinformatics and Pharmacogenomics Symposium 2002, Richmond Virginia, USA. June 12-14, 2002
- 7) Torr MR⁽¹⁾, Garrett CT⁽¹⁾, Buck GA⁽¹⁾, Ginder GD⁽¹⁾, Guiseppi-Elie A⁽¹⁾, Abraham DJ⁽¹⁾, Chandhoke V⁽²⁾, Cooper JN⁽³⁾. Cancer Genomics and Development of Diagnostic Tools and Therapies. ⁽¹⁾Virginia Commonwealth University, ⁽²⁾George Mason University, ⁽³⁾Inova Health Systems, Bioinformatics and Pharmacogenomics Symposium 2002, Richmond Virginia, USA. June 12-14, 2002.
- 8) Penburthy, L. Considerations in developing a clinical informatics system. Bioinformatics and Pharmacogenomics Symposium 2002, Richmond Virginia, USA. June 14, 2002.
- 9) Garrett CT. Genomics – a medical perspective. Bioinformatics and Pharmacogenomics Symposium 2002, Richmond Virginia, USA. June 14, 2002.
- 10) Taylor S and Guiseppi-Elie A. "Surface Chemistries and Blocking Strategies for DNA Microarrays" Sensors for Biomedical Research and Medicine NIH Bioengineering Consortium BECON 2002 Symposium, National Institutes of Health, Bethesda, MD, USA. June 23 – 25, 2002.

New applications, identified

- 1) Dr. Lynne Penberthy has submitted on 5/21/02 a grant application (\$1,000,000 direct costs) entitled “A Multi-Institutional Project to Identify Biomarkers and Other Predictors of Smoking-related Cancers” to the Virginia Tobacco Settlement Foundation. Funding decision will be known in 2 mo. Dr. Penberthy expects to submit at least two applications based on this grant to the NIH for funding.
- 2) Dr. Karen Kurdziel submitted 6/13/02 a response to RFP-NIH-27018 “Early Clinical Trials of Imaging Agents”. This contract will permit the VCU Molecular Imaging Center to respond to subsequent specific RFPs for development of new imaging agents. 30 million dollars has been set aside to support applications in this programmatic area. Tissue acquisition and molecular diagnostic testing form critical components of the application.

Federal money leveraged – The CTRF Director has been approached by three NIH funded investigators with requests to assist them in procuring human residual samples for their research. These requests will be considered as the Tissue Banking efforts at VCU and Inova develop.