

CFFTI GeneChip[®] *P. aeruginosa* Genome Array Application

I. The Application

A. Description of the Program

(1) The Program

CFFTI is offering subsidies for the purchase of custom GeneChip[®] *Pseudomonas aeruginosa* Genome Arrays (“Arrays”) from Affymetrix, Inc. (“Affymetrix”) by academic, not-for-profit research laboratories (each a “Research Laboratory,” and, collectively, “Research Laboratories”) and discounts for the purchase of Arrays by certain research units of for-profit entities that have a preexisting relationship with the Cystic Fibrosis Foundation (each a “For-Profit Laboratory,” and, collectively, “For-Profit Laboratories”) for the purpose of conducting research related to cystic fibrosis (“CF”). Affymetrix has agreed to sell Arrays to Research Laboratories and For-Profit Laboratories selected by CFFTI (each, if selected, a “Qualified User”) beginning prior to the general commercial availability of the Arrays and at substantially discounted prices. Research Laboratories are eligible to receive a \$200 subsidy off of a reduced price of \$350 per Array that Affymetrix is offering only through this program. The expected market price for an Array is \$1000. For-Profit Laboratories are eligible to receive a discount of either 15% or 50% off of the expected market price, depending on whether the For-Profit Laboratory agrees to certain terms and conditions with Affymetrix. The \$200 subsidy is only available for the first 2000 Arrays (which number may be increased at CFFTI’s sole discretion) purchased by those Research Laboratories selected by CFFTI, with a minimum of 10 Arrays per order. CFFTI reserves the right to limit, at its sole discretion, the number of subsidized Arrays each Research Laboratory may order. In exchange for receiving the subsidy or the discount, Qualified Users will conduct CF-related experiments that utilize the Arrays and submit data from those experiments to a database managed by CFFTI and the University of North Carolina, Chapel Hill (“UNC,” and together with CFFTI, the “Program Administrator”). Each Qualified User will have access to this database for the purpose of data mining.

(2) Who may apply?

Research Laboratories and For-Profit Laboratories anywhere in the world may submit a GeneChip[®] *P. aeruginosa* Genome Array Application (an “Application”) to CFFTI through the Internet. This offer to apply is void where prohibited.

By submitting an Application to CFFTI, a Research Laboratory or For-Profit Laboratory agrees that, upon CFFTI’s approval of its Application, such Research Laboratory or For-Profit Laboratory will be contractually bound by the terms and conditions contained in the Application.

(3) What are CFFTI's criteria for selecting Research Laboratories to receive the subsidy and For-Profit Laboratories to receive discounted pre-commercialization access to the Arrays?

The main factors that CFFTI will consider in selecting Qualified Users from among the Research Laboratories and For-Profit Laboratories are:

- a. Will the Research Laboratory or For-Profit Laboratory utilize the Arrays to conduct important and relevant CF research?
- b. Does the Research Laboratory or For-Profit Laboratory have the facilities to conduct the research and compile the results or have a collaboration in place to accomplish the same?
- c. Will the Research Laboratory or For-Profit Laboratory guarantee that it will submit all data from each experiment conducted with the Arrays to certain databases, as described in detail in numbered section six (6) below?
- d. Has the Research Laboratory or For-Profit Laboratory provided sufficient detail in its description of its proposed CF-related experiments to be conducted with the Arrays?
- e. Will the Research Laboratory or For-Profit Laboratory use proper methods in conducting its proposed CF-related research to be conducted with the Arrays?
- f. Can the Research Laboratory or For-Profit Laboratory verify the results of its CF-related research?

(4) What happens if CFFTI approves my Application?

You will be notified by e-mail if you are selected as a Qualified User. The e-mail will include a PIN number that you will use to complete the Affymetrix Gene Chip Order Form and a registration form for the use of InforMax Inc.'s GenoMax[®] software, version 3.0.3 (the "GenoMax[®] Software"). Using your PIN, you will be able to download the Affymetrix Gene Chip Order Form for your review as a PDF file [<http://cfgenomics.unc.edu/GeneChipForm.pdf>]. After a Qualified User receives a PIN number, the UNC-based Cystic Fibrosis National Bioinformatics Center ("CFNBC") will contact such Qualified User about registering for and receiving access to the GenoMax[®] Software and the databases described in numbered section six (6) below.

(5) What is the process for ordering Arrays?

Upon notification that you are a Qualified User, you will order your Arrays directly from Affymetrix, using the Affymetrix Gene Chip Order Form, for the subsidized price of \$150 per

Array (or, in the case of for For-Profit Laboratories selected as Qualified Users, for the applicable discounted price). CFFTI will remit the corresponding subsidy payment of \$200 per Array to Affymetrix upon receipt from Affymetrix of proof that it has shipped the Arrays.

Affymetrix will assign a reference number to each Qualified User, which reference number must be included in all future orders for CFFTI-subsidized Arrays. Affymetrix will require each For-Profit Laboratory selected as a Qualified User to agree to its terms and conditions of sale, which terms and conditions shall be provided by Affymetrix. Research Laboratories will not be required to agree to those terms and conditions.

(6) What does CFFTI require of Qualified Users?

Each Qualified User, upon designation as such, will gain Internet access to GenoMax[®] Software from UNC, with which such Qualified User may conduct sophisticated analysis of the raw data from its experiments, including homology comparison and quantitative analysis. Qualified Users must agree to UNC's terms and conditions regarding the use of its services before gaining access to UNC's GenoMax[®] server. These terms and conditions are available for your review as PDF files at [UNC-CH ATN User Policy](#) and [UNC-CH Honor Code](#).

Each Qualified User will have six (6) months from the date it receives its Arrays from Affymetrix to conduct the experiments specified in its Application. Not later than six (6) months from the date that a Qualified User receives its Arrays from Affymetrix, the Qualified User will submit the data from its experiments to a database (the "Experiment Database") managed by the UNC-based Cystic Fibrosis National Bioinformatics Center ("CFNBC"). By submitting data to the Experiment Database, a Qualified User represents and warrants that all such data was generated in CFFTI-approved experiments conducted by such Qualified User. Data must be submitted in both (i) at the Qualified User's election, either AF or AF1 formats, and (ii) GATC formats. Each submission of data must be accompanied by (i) a record of the lot number(s) of the Array(s) used in the generation of that data, and (ii) an updated response to questions one (1) through five (5) of the "Methods" section of the Experimental Details portion of the application questions set forth below in this Application (the "Data Context"). If a Qualified User submits data to the Experiment Database earlier than six (6) months from the date that such Qualified User receives its Arrays from Affymetrix, such Qualified User shall receive exclusive access to that data for analysis purposes until that data is transferred to the Shared Database (as defined below). Not earlier than six (6) months from the date that a Qualified User receives its Arrays from Affymetrix, the data submitted to the Experiment Database shall be automatically released into a database (the "Shared Database") managed by CFNBC and made available to other Qualified Users for data analysis and data mining. The data in the Shared Database will be made available in GATC format, and therefore may be accessed with or without the use of GenoMax[®] Software. Upon the date that a Qualified User's data is transferred from the Experiment Database to the Shared Database, that Qualified User will gain access to the data submitted by other Qualified Users to the Shared Database. In case of extraordinary hardship, a Qualified User may request, and CFFTI, in its sole discretion, may grant, an extra thirty (30) day delay before the data is released into the Shared Database. Notwithstanding the six (6) month period during which a Qualified User is entitled to keep its data in the Experiment Database, a Qualified

User may instruct the CFNBC staff to accelerate the transfer of data submitted by such Qualified User from the Experiment Database to the Shared Database, in which case such Qualified User will gain access to the Shared Database as of the date of the accelerated transfer.

Each Qualified User must account for each of its subsidized or discounted Arrays not later than six (6) months from the date that such Qualified User receives each such Array, by either (i) submitting the data from successful experiments for deposit in the Experiment Database, (ii) submitting data from failed experiments for deposit in a trash database (the “Trash Database”) to be made available only to the Program Administrators, or (iii) submitting an explanation of any failed experiments that do not generate data for deposit in either the Experiment Database or the Trash Database.

(7) What kind of administrative support will the Program Administrators provide?

The website for this Program (the “Website”) will provide Qualified Users with options to obtain technical advice on the use of the Arrays and the preparation of material for analysis. The Website will link to standard protocols (applicable to the use of the Arrays) for isolation and labeling of *Pseudomonas* RNA and DNA. The Website will also provide links to other labs, allowing Qualified Users to access successful but non-standard protocols for these purposes.

Each Qualified User will also become part of a LISTSERV that will serve as a forum for discussing problems with or asking questions to the administrative staff at CFNBC. The staff will direct Qualified Users to the proper source of information (e.g. Affymetrix, Informax or CFFTI). If any comment or question is deemed useful to the whole group of participants, the LISTSERV will be used to notify all of the Qualified Users. Qualified Users will also be notified of group meetings and training sessions via the LISTSERV. Notifications of meetings and training sessions will also be posted on the web site for CFNBC.

(8) What happens if a Qualified User fails to comply with the requirements of this Application?

If a Qualified User has not submitted data to CFNBC within the applicable time period, CFFTI will suspend such Qualified User’s access to additional subsidized Arrays and will demand that a written explanation for the delay be submitted to the administrative staff of CFNBC. If the Program Administrators determine that the delay is unreasonable, the Qualified User will be required to reimburse CFFTI for each Array for which data has not been submitted in the amount of the market price at the time such Arrays were purchased (or, if such Arrays were purchased before commercialization, in the amount of the expected market price of \$1000) less the subsidized price of \$150 that such Qualified User originally paid for each such Array, plus CFFTI’s reasonable costs and expenses.

B. The Application Questions

ADMINISTRATIVE DETAILS

Are you applying as a Research Laboratory or For-Profit Laboratory?

Provide the following information:

Title of principal investigator
institution
mailing address
phone number
fax number
e-mail address
name of Institutional Financial Officer administering this award
PIN number (to be filled in by admin. after application is approved)

List individuals in your lab who will be using the Arrays (together with the principal investigator, the "Laboratory Investigators").

Number of GeneChip[®] *P. aeruginosa* Genome Arrays requested (must be in multiples of 10).

Will you register to use the GenoMax[®] Software provided by CFFTI? Alternatively, will you simply submit your data to the Website and not use the GenoMax[®] Software provided by CFFTI?

Are you using these GeneChip[®] *P. aeruginosa* Genome Arrays for hybridization with labeled DNA, RNA (cDNA) or both?

Do you have direct experience using any other Affymetrix GeneChip[®] Genome Array products? If so, which one? Have you used their GeneChip[®] *E. coli* Genome Array?

Can you hybridize and scan GeneChips[®] *P. aeruginosa* Genome Arrays in your own lab?

If not, have you secured access to a facility to do so? (NOTE : Following two paragraphs were changed on 05/09/01).

If you answered "yes" to the prior question, who will be doing this for you? Please fill in name and address of investigator performing this role and describe their equipment (make and model of hybridization chamber, scanner and software).

If you answered "no" to the prior question, you will still be eligible to receive the discounted arrays. CFFTI will make arrangements for you to have the arrays hybridized, processed and scanned. Please contact Dr. Melissa Ashlock at CFFTI (mashlock@cff.org) for details about this service.

What kind of computer software/resources do you have for data analysis and data mining?

~~Do you want a copy of Affymetrix data analysis software Micro Array Suite? Each Qualified User is entitled to this software free of charge. The Micro Array Suite (formerly GeneChip[®] Analysis Suite) provides systems operation, instrument control and data analysis for the entire GeneChip[®] platform. The software automatically acquires and processes hybridization data. Analysis algorithms allow review, comparison, graphing, filtration, analysis and reporting in different modes.~~

(NOTE: Above paragraph was deleted on 07/17/2002. As of July 16, 2002, at least 25 investigators have been approved under the CFFTI-Affymetrix Pseudomonas GeneChip[®] Genome Array program and the first 25 of them have each received a copy of Affymetrix Micro Array Suite software (MAS). Free copies of MAS are no longer available under this program).

EXPERIMENTAL DETAILS

Provide a brief (2-3 page) description of the proposed project you will perform with these arrays. Experiment designs should be simple and culture conditions should be well controlled.

If you are a recipient of a grant under the “CF Genome Analysis Programs,” you need not complete the “Background Hypothesis” section below. Instead, please indicate your grant number and please include the description of the study from that grant in which you will use the Arrays.

Organize the application to include the following points.

Background Hypothesis.

What scientific questions you are asking?

Describe the rationale for the experiments and why the array technology is appropriate.

Describe the relevance of the work for understanding mechanisms of disease and/or host defenses in CF; include the implications of the studies on antimicrobial drug discovery.

Methods (“Data Context”) (Include the following information:)

1. Source of the strain (PAO1 or a clinical isolate). If a clinical isolate will be used, describe how the strain was stored prior to use (e.g. frozen or lyophilized). Qualified Users who use a clinical isolate must store an aliquot of each such isolate for future reference, and will be asked to indicate the storage conditions of the isolate at the time of data deposit.
2. Bacterial culture methods (e.g. media type, physical conditions, stage of growth when RNA was harvested).

3. Will non-*P. aeruginosa* RNA be present in the sample (from other bacteria or from eukaryotic cells). What steps will be taken to separate the *P. aeruginosa* RNA?

4. Do you intend to follow Affymetrix RNA (DNA) extraction and labeling protocols (see Protocols on Website)? You are encouraged to follow the standard protocols provided by Affymetrix; however, if changes are necessary, please explain your rationale.

Data analysis:

How will be the data be organized and analyzed?

What comparison will be made to other type of work (cDNA microarrays, etc).

Verification of results:

Which analysis will be used to verify your findings from GeneChip[®] *P. aeruginosa* Genome Arrays (northern blot, quantitative RT-PCR, reporter gene fusions, etc.)?

As part of this program you are requested to provide a brief summary (by e-mail) of scientific findings to the CF National Bioinformatics Center, not later than 6 month after the delivery of Arrays.

Future plans or studies:

What do you plan to do as follow-up to your experiments?

C. The Application terms and conditions

By submitting an Application to CFFTI, you also agree that, upon CFFTI's approval of your Application, you will be contractually bound by the terms and conditions contained in this Application, including but not limited to Section A (1) – (8), above, and this Section C.

1. Electronic Signatures

The Program Administrators and you both agree that any document, including this Application, which is transmitted or received by electronic transmission by either party shall be treated in all manner and respects as an original signed document where sufficient indicia of acceptance by the respective party exists. Submitting an Application to the Program Administrators by means of the Website constitutes acceptance of the terms and conditions of this Application. The Program Administrators and you further agree that upon your submitting an application, all parties shall agree to accept electronic signatures or other reasonable electronic indicia as forms of acceptances. Such indicia of acceptance shall be considered for these purposes as an original signature and any such electronic transmission shall be considered to have the same binding legal effect as an original signed document. You agree that you shall not raise electronic transmission or electronic signatures as a defense to (i) this Application or (ii) any other matter related to this Application, or the binding nature of the documents referred to in (i) and (ii), and you agree to waive such defense.

2. Governing Law

This Application and any matter related to this Application shall be governed by and construed in accordance with the laws of the State of Maryland, exclusive of its choice of law rules and matters affecting copyrights, trademarks and patents under U.S. federal law.

3. Severability

In the event that one or more portions of this Application shall, for any reason, be held to be invalid, illegal or unenforceable in any respect, such validity, illegality or unenforceability shall not affect any other provision contained in this Application.

4. No Waiver

Any delay or failure by you or the Program Administrators, at any time or times, to require performance of any provision hereof shall in no manner affect your or the Program Administrators' right at a later time to enforce such provision. No delay or failure of you or the Program Administrators in exercising any right hereunder shall constitute a waiver of such right or any other rights hereunder.

5. Assignment

You may not assign your rights or delegate your responsibilities hereunder without the express written permission of CFFTI. CFFTI may, at any time, assign its rights or delegate its obligations hereunder without notice to you.

6. Third Party Beneficiary Rights

No person not a party to this Agreement is intended to be a beneficiary of this Agreement, and no person not a party to this Agreement shall have any right to enforce any term of this Agreement.

7. NO WARRANTIES, NO LIABILITY. THE PROGRAM ADMINISTRATORS DO NOT MAKE ANY EXPRESS OR IMPLIED WARRANTIES, REPRESENTATIONS OR ENDORSEMENTS WHATSOEVER (INCLUDING, BUT NOT LIMITED TO, THE IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE) WITH REGARD TO THE ARRAYS OR THE GENOMAX[®] SOFTWARE OR ANY INFORMATION OR SERVICE PROVIDED WITH RESPECT TO THE ARRAYS OR THE GENOMAX[®] SOFTWARE, AND THE PROGRAM ADMINISTRATORS SHALL NOT BE LIABLE FOR ANY COST OR DAMAGE ARISING EITHER DIRECTLY OR INDIRECTLY FROM THE USE OF MISUSE OF THE ARRAYS OR THE GENOMAX[®] SOFTWARE. NO ADVICE OR INFORMATION, WHETHER ORAL OR WRITTEN, OBTAINED BY ANY PERSON OR ENTITY FROM THE PROGRAM ADMINISTRATORS SHALL CREATE ANY WARRANTY NOT EXPRESSLY MADE HEREIN. THE PROGRAM ADMINISTRATORS MAKE NO WARRANTY THAT THE ARRAYS OR THE GENOMAX[®] SOFTWARE CONFORM TO THE MINIMUM QUALITY STANDARDS IMPOSED UNDER STATE AND/OR FEDERAL LAW.

8. Use of Arrays and GenoMax[®] Software

Qualified Users shall utilize the Arrays exclusively for the purpose of conducting the experiments described in, and submitted to CFFTI pursuant to, this Application and approved by CFFTI at its sole discretion, as such experiments may be amended upon the mutual consent of the applicable Qualified User and CFFTI. Only Laboratory Investigators employed by Qualified Users may, in strict accordance with the procedures and conditions set forth in this Application, use or access the Arrays and the GenoMax[®] Software. Such Laboratory Investigators shall not allow any third party to use or access the Arrays or the GenoMax[®] Software without the express written consent of CFFTI. Such Laboratory Investigators shall not alter, remove, adapt, reverse engineer or modify the Arrays or the GenoMax[®] Software or any part thereof. Such Laboratory Investigators shall not disclose any confidential and proprietary information and data contained in the Arrays or the GenoMax[®] Software to any third party, except consultants or auditors that sign a nondisclosure agreement which protects such confidential and proprietary information and data to at least the same extent as provided herein.

9. Use of Databases

You shall not use the GenoMax[®] Software or distribute, license, transfer or otherwise make available any data from the Shared Database, regardless of whether or not that data was originally submitted by you, for commercial purposes.

10. PIN Numbers

Qualified Users shall not disclose their PIN numbers to third parties. Qualified Users are responsible for all activities that occur under their PIN numbers. Each Qualified User agrees to immediately notify CFFTI in writing of any unauthorized use of such Qualified User's PIN number. Each Qualified User is solely responsible for ensuring that its PIN number is utilized only by the Laboratory Investigators to whom it is assigned.