MEMORANDUM OF UNDERSTANDING FOR DATA TRANSFER AND USE

Parties and Purpose

The signers of this Memorandum of Understanding ("**MOU**"), made effective as of September 10, 2012, establish a data sharing agreement affiliation between Children's Hospital & Research Center Oakland ("**CHRCO**") and the NIH Pharmacogenomics Research Network ("**PGRN**"). The goal of the affiliation is to advance research and discovery in genomics in order to enable safer and more effective drug therapies.

The Affiliation will focus primarily on developing statistical methods for analyses of large data sets containing different types of high throughput data as well as drug response phenotypes. The PGRN Systems Biology working group and the PSTAR Network Resource have developed a joint project using common data sets from different PGRN groups for use in developing novel statistical methods.

Background

CHORI has collected and/or developed the PARC Data (as defined below), under the PARC Collaborators Data Project (also defined below), which established a comprehensive clinical and cellular outcomes database of over 2,000 individuals from participating PARC centers, which aims to promote collaborative clinical research studies in cardiovascular disease by providing a comprehensive database that includes clinical, laboratory, and genetic de-identified information on all enrolled study subjects;

PGRN is a network of scientists focused on understanding how a person's genes affect his or her response to medicines, each scientist a "**PGRN Investigator**."

PGRN wishes to obtain the PARC Data for the purposes of a program of academic research to be carried out by PGRN Investigators.

CHRCO is willing to provide the PARC Data to the PGRN Investigator (as defined below) to carry out research on the terms set out herein,

Definitions

"Confidential Information" means confidential information relating to its business, scientific or other activities, including confidential information supplied hereunder in any form either as PARC Data or as information or data supporting, describing or otherwise relating to PARC Data or, including, but not limited to, data and data analysis, designs, datasets, plans, drawings, results of genotyping or other bioassays generated from individual or pooled samples of PARC Data and intellectual property rights in such confidential information or related invention disclosures.

"**PARC Data**" means the data sets described in Appendix 1attached hereto.

- **Expression Array Data:** Expression profiles of 480 paired lymphoblastoid cell lines (simvastatin or sham buffer treated, 24 hours) generated using the Illumina Ref8v3 beadchip. All 480 individuals were self-reported Caucasians from the Cholesterol and Pharmacogenetics (CAP) clinical trial.

- **RNAseq Data:** Expression profiles of 95 paired lymphoblastoid cell lines (simvastatin or sham buffer treated, 24 hours) generated by whole transcriptome paired-end sequencing of strand-specific libraries on the Illumina HiSeq. Cell lines were derived from donors comprising the tails self-reported Caucasian and self-reported African American LDL-cholesterol response distributions of CAP clinical trial.

- **Phenotype Data:** A variety of covariate and phenotype data for 587 self-reported Caucasian participants of the CAP clinical trial including clinical covariate information (sex, race, age, BMI, smoking status), cellular covariate information (simvastatin exposure data, cell count, RNA

hybridization batch, and array slide batch) for the expression array study described below, genotype array platform, and a variety of quantitative phenotypes measured in collected blood samples (Tg, TC, LDLC, HDLC, CRP, ApoAI, ApoB, ApoCIII, LDL subfractions, IDL subfractions, etc.).

- **Genotype Data:** Genome-wide genotypes collected in 583 Caucasian CAP participants. Genotypes at 317,503 SNPs are provided for 305 Caucasian individuals (self-reporting at least 3 Caucasian grandparents). Genotypes at 620,901 positions are provided for 282 additional Caucasians self-reporting at least 3 Caucasian grandparents.

"**PARC Collaborators Data Project**" means research project described as Grant Number: U19 HL069757-11, naming as Principal Investigator Dr. Ronald M. Krauss, M.D., and entitled "Pharmacogenomics and Risk of Cardiovascular Disease."

Terms:

1. Any PGRN Investigator can apply for access to the PARC Data for methods development projects by submitting a Data Use Request outlining brief proposal for such projects (each project a "**Project**") to the National Institute of Standards and Technology ("**PSTAR**")**.**

2. PGRN Investigators must state in the Data Use Request their intention to publish or otherwise broadly share any findings from his or her study with the scientific community.

3. PARC Data will be provided to a PGRN Investigator ("**Recipient**") upon approval of the Project and solely under the terms and conditions provided herein.

4. Recipients of the PARC Data will be expected to participate in conference calls or other activities related to the project.

5. Recipients shall whenever appropriate interact with the PARC investigators and include them in the data analysis and authorship should be decided based on investigator contributions. Such PARC Investigators will be made available by Ronald M. Krauss, MD of CHRCO. Such matters determined in accordance with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (http://www.icmje.org/)

6. Recipients who work with PSTAR or the PGRN Systems Biology working group members on their analysis of these PARC Data will be offered an opportunity to participate in projects utilizing PARC Data and share an authorship on the basis of their contributions. However, providing data only does not automatically lead to authorship.

7. The PARC Collaborators Data Project will be acknowledged in publications with individual grant numbers sited that supported the generation of data. Below is a statement that can be used in the acknowledgments.

   "This work was supported in part by U19 HL069757-11: Pharmacogenomics and Risk of Cardiovascular Disease. We acknowledge the PARC investigators and research team, supported by NHLBI, for collection of data from the Cholesterol and Pharmacogenetics clinical trial."

   The role of the PGRN PSTAR and the PGRN Systems Biology working group should be also acknowledged in publications.

8. Recipients of the PARC Data shall adhere to the following restrictions:

a. The PARC Data shall be used only for an approved Project covering pharmacogenetic studies designed to learn about, prevent, or treat health problems related to cardiovascular drug treatment response and not for any other purpose.

b. The Recipient shall not publish or otherwise disclose details regarding individuals from whom the PARC Data were derived (including but not limited to creating, publishing or disclosing photographic images or other information which may enable the identification of the individual involved by any means) without CHRCO's express written permission; shall not attempt to trace, contact or identify any individual from whom the PARC Data was derived; and shall not seek to recruit any such individual to take part in any other study or survey. Under no circumstances shall CHRCO have any obligation to supply the identity of, or any PARC Data or information that in its reasonable opinion could lead to the identification of the individual who was the source of that PARC Data. If the Recipient's use of the PARC Data requires the consent of the individual who was the source of the PARC Data, the Recipient shall ensure that the individual in question or their legal guardian has signed an appropriate consent form and that its use of the PARC Data is within the scope of that consent form.

c. Recipient shall not be publically post PARC Data on any web site, or submit PARC Data to any repository, or supply or transfer such PARC Data to any third party (or permit such supply or transfer), without the prior express written approval of CHRCO.

d. The Recipient shall use the PARC Data in accordance with good laboratory practice and with the highest standards of skill and care in full compliance with all applicable local, state, federal, government and international laws, regulations and guidelines relating to health and safety, data protection, conducting research and the transportation, storage, tracking, use and disposal of the PARC Data in force in the country, region or state where the PARC Data is used.

e. Wherever applicable, the Recipient shall not use, or permit the use of, the PARC Data in work where it has not first obtained full written approval from a properly constituted research ethics committee and holds all necessary consents from human participants or their legal guardians. If requested by CHRCO, the Recipient shall supply CHRCO with a copy of such ethical approval.

f. The Recipient shall not use the PARC Data for any commercial purpose, including but not limited to commercially-sponsored research or work that is subject to the granting of any rights to a commercial third party, and shall not use or permit the use of any products or processes containing, using or directly deriving from the PARC Data or which are further developments of the PARC Data for profit-making or commercial purposes without the prior written consent of CHRCO.

9. Any PARC Data delivered pursuant to this Agreement is understood to be experimental in nature. CHRCO and the PARC Collaborators MAKE NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESSED OR IMPLIED. THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR THAT THE USE OF THE PARC DATA WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK, OR OTHER PROPRIETARY RIGHTS.

10. Except to the extent prohibited by law, the Recipient assumes all liability for damages which may arise from its use, storage or disposal of the PARC Data. CHRCO and the PARC Collaborators will not be liable to the Recipient for any loss, claim or demand made by the Recipient, or made against the Recipient by any other party, due to or arising from the use of the PARC Data by the Recipient, except to the extent permitted by law when caused by the gross negligence or willful misconduct of the CHRCO or the PARC Collaborators.

11. This Memorandum of Understanding (MOU) shall be effective for an initial period of 3 years at which point it shall be reviewed for possible renewal. It is expected that each partner in the collaboration will participate in a manner consistent with the institutions' policies, programs, and available resources.

AGREED by the Parties through their authorized signatories:

For and on behalf of CHRCO	**For and on behalf of the Recipient**
Signature:	Signature:
Print name: Rajnesh Prasad, MBA	Print name:
Title: VP, Research Operations	Title:
Date:	Date: