International Consortium for Antihypertensive Pharmacogenomics Studies (ICAPS)
Memorandum of Understanding

Background

A number of pharmacogenomics research centers (the "consortium") are interested in discovering new genetic variants that are important for predicting response to antihypertensive drugs using candidate gene, genome wide association studies (GWAS), and other methods. In addition, large sample sizes provide the opportunity for various subgroup analyses to define in a more granular way various clinically-relevant phenotype-genotype associations. Most members of ICAPS have collected cohorts of individuals who have been treated with antihypertensive drugs and have obtained a variety of response phenotypes, including blood pressure response, adverse metabolic response, long-term cardiovascular outcomes, and long-term risk for metabolic adverse effects, including diabetes and have genotype data and/or DNA available from these individuals. Members of the consortium are willing to share these data for the purposes of replicating the findings of others, and for combined (meta) analysis. Other opportunities may present to the consortium based on the increased strengths that will arise from the collective efforts in hypertension pharmacogenomics. Based on the success of similar BP GWAS consortia, other disease genetics consortia and other pharmacogenetic consortia, ICAPS seeks to utilize this same approach to advance pharmacogenomics of antihypertensive drugs.

ICAPS has two main objectives:

1) Members will share information about the type of data they have available (including the sample size, drugs tested, response phenotypes, genetic data etc) for the purposes of facilitating collaboration and replication of genetic association findings. They agree to consider requests from others in the consortium to replicate findings using their datasets.
2) To undertake meta-analyses to increase the power to detect genetic associations. Those with GWAS data and relevant drug response phenotype data will be invited to participate in the GWAS meta-analysis; and those who do not have GWAS data but have relevant drug response data and DNA will be asked to participate in the replication efforts. These efforts are not expected/intended to preclude the primary publication of results from any research group.

Other opportunities may present to the consortium and the consortium members will evaluate at that time.

ICAPS is housed within an infrastructure based at the University of Florida (UF), in Gainesville, FL, under the direction of Rhonda Cooper-DeHoff, Pharm D, MS. Submission of genotype and phenotype data to a public resource is a desirable outcome and for GWAS may be mandatory for some grantees (e.g. from NIH or Wellcome Trust) and when possible UF will oversee submission of genotype information to public resources following ICAPS publications. For some

members, ICAPS recognizes that submission or sharing of data outside of the consortium may not be possible because of differences in international laws and practices.

Memorandum of Understanding

1. In order to be a participant in the consortium, a research group must agree to share information on the type of clinical and genetic data they have available on their dataset.

2. Consortium members agree to work with others in the consortium to replicate data. Likewise, they can engage other consortium members for replication of their own data. When asking for replication they will provide the other groups with clear guidance on the analysis they need to have conducted, and the manner in which they wish to receive the data. When collaborating for replication, all participating groups are expected to be included as authors on resulting manuscripts, and to respect the confidentiality of the data until it is published. Analysis plan and data output instructions will be shared on the ICAPS website.

3. Consortium members with GWAS data agree to consider participating with others with like phenotype and drug data on GWAS meta-analyses. Those agreeing to participation in GWAS meta-analyses will agree to imputation to a common genotypic dataset (e.g. 1000 genomes imputation). Assistance will be offered within the consortium for those needing assistance in achieving this imputation. Those who do not possess GWAS data agree to consider providing replication data for the GWAS meta-analyses. It is anticipated that an analysis plan will be developed, each research team will conduct their own analysis, and they will share essential data elements for the SNP-level data (e.g. beta value and p value) for the conduct of a meta-analysis. The data required for conduct of the meta-analysis will be provided via the ICAPS website, where it will be transferred to the ICAPS data analysis centers for meta-analysis.

4. Since there will likely be multiple analyses conducted on different phenotypes, and/or different drugs, it is expected that lead authorship (first and senior) will rotate between the groups, based on leadership within a specific effort, to insure equitable sharing of key authorship roles. Further, it is anticipated that there will be multiple authors designated as first and senior authors.

5. It is anticipated that larger GWAS meta-analyses might have smaller working groups, e.g. steering committee, analysis committee, manuscript writing committee, etc.

6. ICAPS has a dedicated website, where shared documents and data will be stored securely, with restricted access. This website is facilitated through the UF Health Science Center computing infrastructure. Consortium members will designate a primary contact person with whom ICAPS staff can work for each individual data set. This contact person should be very familiar with the details of the data sets, or have easy access to those who are.

7. Consortium members are free to write papers based on their own samples and data before, during, and after the activities associated with this memorandum and consortium.

8. Consortium members may not write papers based on the data of others, except with explicit permission of those who collected the data. If consortium members wish to propose an analysis that involves other members of the consortium, they will announce their intentions, so that all interested consortium members can participate.

9. Only consortium members who have submitted data will have access to the data set and agree to use these data only as a basis for conversation with the originators. Consortium members with access to the data agree that viewing these data is associated with responsibility for not publishing or disclosing it without approval of the consortium members.

10. Access to the consortium data sets and draft publications is limited to 1) consortium members that have contributed data; and 2) the ICAPS staff who also agree to the MOU.

11. In order to join the consortium, a participating investigator must sign page 4 of the MOU and send via email to Dr. Rhonda Cooper-DeHoff, Pharm D, MS, dehoff@cop.ufl.edu. By signing the MOU, an investigator is indicating acceptance of the terms of this MOU.

12. It is expected that within 6 weeks of acceptance of the MOU the research team will complete the ICAPS on-line data collection form, describing the data they have available.

International Consortium for Antihypertensive Pharmacogenomics Studies (ICAPS)

Commitment and Signatures

Study Name/Institution: _____ / _____

I agree to abide by the principals of this agreement.

Yes: ◯ , No: ◯

No intellectual property will be claimed by any of the investigators involved in discoveries made by the combined consortium using shared data.

Yes: ◯ , No: ◯

I agree that under no circumstance will results of analyses be presented prior to the final publication without the written consent of all groups who contributed data to the analyses.

Yes: ◯ , No: ◯

We will not conduct follow-up experiments based on consortium results prior to publication of the data without the disclosure of this activity and agreement by the members of the consortium.

Yes: ◯ , No: ◯

Name in print of Principal Investigator: _____

Name of co-investigators covered by this consortium MOU: _____,
_____, _____, _____

City, State, Country: _____ , _____ , _____

Date: _____ yyyy-mm-dd

Signature: _____

Please return signed copies by fax or email to:

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