The 17th International HLA & Immunogenetics Workshop

IHIWS CONNECTS

Issue № 3

Dear Colleagues,

Welcome to the third issue of IHIWS Connects, the newsletter for the 17th International Histocompatibility and Immunogenetics Workshop (IHIWS), to be held in Pacific Grove, California this September. We would like to provide a brief update on the status of the workshop components and projects as they stand today.

Currently, we have 127 unique laboratories/organizations registered to participate in the workshop. Progress has been made in the management and definition of requirements of all components and projects. In addition, several new projects have been added under the NGS of Full-length HLA genes component.

We are very excited to announce that registration is now open for the 17th International HLA & Immunogenetics Workshop (IHIWS) event. Register here: http://ihiws.org/event-registration.

NGS of full length HLA genes: Component Updates

Reference Cell Lines Project

The goal of this project is to sequence Cell Lines (collected historically by the previous workshops) with complete NGS sequence of HLA genes performed by multiple laboratories, the results of which will serve as an unambiguous reference of the evaluation of each reagent/platform used. If your laboratory is planning to submit NGS HLA typing data for the various projects of the 17th IHIWS, your participation in this project is required, as the results will be used for performance validation.

We have been working in coordination with the major NGS genotyping software platform vendors to integrate their output report with the 17th IHIWS NGS data collection system. This will allow a more effective and standardized transfer of NGS genotyping data that includes GL String, consensus and locus data and, ultimately, meeting the Minimum Information for Reporting Immunogenomic NGS Genotyping (MIRING) and Histoimmunogenetics Markup Language (HML) 1.0 data reporting standards. While some platforms have HML or XML reports ready, others are still

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Event Dates & Locations

17th International Histocompatibility and Immunogenetics Workshop and Workshop Conference

September 6–10, 2017
Asilomar Conference Grounds
800 Asilomar Ave
Pacific Grove, California 93950

Steering Committee

Contact

Website:
ihiws.org

Program Manager:
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About The Host

The Stanford Histocompatibility, Immunogenetics, and Disease Profiling Laboratory (HIDPL) performs state of the art and cutting edge histocompatibility and genetic testing for solid organ and bone marrow transplantation as well as for disease associations and drug resistance/susceptibility. The HIDPL offers a wide selection of testing services, has an active research and development program and houses and curates a bio-repository of patient specimens. It primarily services the Stanford Hospital and Clinics and the Lucile Packard Children's Hospital but also performs services for outside centers (e.g., Kaiser). It is accredited by the American Society for Histocompatibility and Immunogenetics (ASHI), CLIA, and the state of CA for high complexity testing. The HIDPL performs greater than 60,000 tests per year and employs a staff of more than 50 full-time employees.

Histocompatibility, Immunogenetics & Disease Profiling Laboratory

Stanford Blood Center

NGS of full length HLA genes: Component Updates (continued)

developing these reports. To facilitate this process, the IHIWS database held a Database Summit during the 42nd ASHI annual meeting. At this meeting, it was agreed that each vendor would assist the participants using their software and provide the necessary tools to facilitate the upload of NGS HLA typing of the Proficiency and Reference panels in GL String format.

We extended the deadline for uploading reference cell panel typing to the IHIWS database to November 30, 2016 for those who have ordered and received the panels. For those of you who have not ordered the panel and are planning to submit NGS HLA typing data, we have additional proficiency testing (PT) panels available for this purpose. Please contact tamara.vayntrub@stanford.edu to order additional panels. We will set a timeline for submission of results for this second batch on a later date.

A consensus report for the cells included in the proficiency testing (PT) panel was sent to the ASHI Commissioners. Laboratories that wish to include this report as part of their accreditation may submit the NGS HLA typing of the cells in the PT panel as blinded samples.

Three new exciting projects were added since our last newsletter:

T Cell Receptor (TCR)-HLA Interaction

Project leaders:
Sami Djoulah Ph.D., sami.djoulah@wiratech.com
Emmanuel Mignot M.D., Ph.D., mignot@stanford.edu

T cell receptors have immense diversity and are the next step in the adaptive immune response following HLA presentation of peptides. The aim is to combine the analysis of T cell receptor diversity and HLA typing by Next Generation Sequencing to better understand the rules of HLA-peptide-TCR interactions to evaluate TCR and HLA in the context of disease, vaccination/immune alterations and populations.

The following areas of interest will be included in this project:

- Disease Study: Meta-analysis of autoimmune disease disorders for the report of the workshop and Individual disease analysis (led by specific investigators). These may include case/control and longitudinal studies.
- TCR usage/HLA Study: Changes in TCR usage and Complementarity Determining Region (CDR) as a function of HLA types. The analysis will be performed in control samples for anthropological/environmental population studies, and could possibly be applied to specific disease.
- Transplantation Study: Analysis of the TCR repertoire in relation to HLA in transplantation.
- Technology and Nomenclature Normalization Study: Various commercially available techniques using the same samples will be tested and analyzed.
- GWAS-TCR Study: GWAS data, when available, will be submitted to study genome wide and TCR cis QTL effects on the TCR repertoire

For additional information regarding this project, please visit the IHIWS.org website, or contact the project leaders ihiws.org/t-cell-receptor-tcr-hla-interaction

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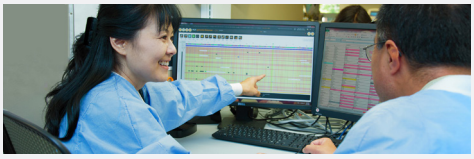

Informatics of Genomic Data: Component Update

The integration of the NGS genotyping software platforms currently in use by participants of the 17th International HLA and Immunogenetics Workshop is a big part of the process of completing the IHIWS database system, allowing a systematic and comprehensive collection and analysis of NGS data.

To this end, we held a Vendor Summit which was attended by representatives from GenDx, Illumina, Immucor/Sirona, Omixon, PacBio Systems, Scisco Genetics, Thermo Fisher/One Lambda, Anthony Nolan Research Institute as well as our own IHIWS Informatics and database team members.

Please visit the IHIWS website at ihiws.org/17th-ihiws-vendor-summit to read more about the presentation and conclusions from the Summit.

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Pharmacogenetics and HLA

Project leaders:
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Maria Bettinotti Ph.D., mbettinotti@jhmi.edu

Serious adverse reactions to some drugs are associated with certain HLA alleles in some ethnic groups, but have not been investigated in other populations. It is also likely that additional associations will be established for other drugs with increasing awareness of possible immunogenetic predisposition.

The overarching goal of the Pharmacogenetics project is to establish an ongoing registry for compilation of data on the incidence of associations of HLA alleles and/or other immunogenetic factors with adverse drug reactions in different populations. Specifically, this project will include a retrospective study of HLA alleles in patients of different ethnic groups who had adverse reactions to carbamazepine.

If you are interested in participating in this project, contact the project leaders or check out the www.IHIWS.org website for additional information.

Immunogenetics of Aging

Project leaders:
Elissaveta Naumova, Ph.D., immunology@abv.bg
Milena Ivanova, Ph.D., mivanova@intech.bg

The aging process is very complex and longevity is a multifactorial trait, which is determined by genetic and environmental factors. The aim of the component "Immunogenetics of Aging" is to identify new biomarkers for successful aging and an increased capacity to reach the extreme limits of life-span by analysis of immune response genes. In addition to classical HLA loci (HLA-A,-B,-C,-DRB1/3/4/5, -DQB1,-DQA1, -DPA1, -DPB1), genes in the extended MHC region such as MICA will be included in the analysis. Polymorphisms in pro- and anti-inflammatory cytokine genes (IL-2, IL-6, IL-10, IL-12, IFNγ, TNFα, TGFβ) with possible correlation to the level of gene expression, KIR, MBL, Toll-like receptor genes could also be analyzed.

The overarching goal of this project is to identify new biomarkers, including extended HLA haplotypes, cytokine genes, other MHC-encoded loci and innate immunity genes, for successful aging and an increased capacity to reach the extreme limits of life-span. The objectives of the project will include:

- Extended HLA haplotype analysis using NGS technology of samples collected during 14th, 15th and 16th IHIWS, including healthy randomly selected elderly individuals, young controls, and families with long-lived members. Additionally, new samples will be collected.
- Analysis of polymorphisms in regulatory and/or coding regions, with a possible impact on the level of gene expression of pro- and anti-inflammatory cytokines in elderly and young/middle age individuals.
- Analysis of innate immunity gene polymorphisms in elderly and young/middle age individuals.
- Perform linkage and association analysis in order to identify extended immunogenetic profiles that could be relevant to understand better the mechanisms of longevity and could be applied as new molecular targets for prevention, immunopharmacology and immunotherapy.

Learn more on our website: ihiws.org
Register to participate on our database: workshop.ihiws.org
Register to attend the 17th IHIWS: http://ihiws.org/event-registration

Mapping of Serologic Epitopes: Component Update

Dr. Dolly Tyan, Ph.D., **Component Chair**

Leaders: Marcelo Fernandez-Vina Ph.D., Robert Bray Ph.D., Peter Nickerson M.D., Frans Claas Ph.D., Ms. Rhonda Holdsworth

Liaison: Donna Phelan CHS

We continue to make progress in this component. Fourteen laboratories participated in the Epitopes Pilot Project by performing solid phase antibody testing on the same 5 samples. Testing included IgG SAB I, IgG SAB II, Bio-C1q SAB I, Bio-C1q SAB II using IHIWS SOPs, custom and commercial reagents provided by the Workshop organizers. The results are being analyzed and should be available by the end of the year 2016. An important part of this project includes data analysis to understand limitations and nuances for each protocol or reagent used, as well as the opportunity to evaluate algorithms for analysis and ways of capturing data. This latest task will rely on the use of a secure FTP server to house the raw data files, the IHIWS database that will include the sample's profiles, demographics and other pertinent information, as well as a program that will compile and analyze the data.

The goals of the Mapping Serologic Epitopes component can be summarized as follows:

1. To determine what HLA epitope mismatches are immunogenic
2. To determine what outcomes are related to immunogenic epitopes

The expectation is that all the participants will contribute data and or samples for the component, analysis will then be performed based on the specific project of interest.

Stay in Touch

Thank you for taking a moment to stay up-to-date on the status of the 17th IHIWS. We are thrilled to see so much progress being made, and look forward to our discussions in Pacific Grove, California beginning on September 6, 2017. For further information, please visit our website at ihiws.org, or contact Program Manager, Tami Vayntrub at tamara.vayntrub@stanford.edu. Reservations for the workshop and accommodations will be announced soon.