Intriguing Questions

- Could molecular taxonomy of SCAR provide better characterization and nomenclature?
- Why is there wide variation in degree of inflammation histopathologically?
- Why is skin reaction patchy?
- What is unique about stratified squamous epithelium that makes it susceptible to SJS/TEN?
- Why are many of the same HLA alleles implicated repeatedly?
- What can be learned from ethnic-specific associations?

Intriguing Questions

- What is impact of rare variation in HLA? Can we use sequencing and burden tests to look for common pathways to SJS/TEN?
- Why do such a small minority of HLA risk allele carriers actually develop the condition?
- Are drugs recognized same ways as viral antigens?

- Should Steve Leeder become a US citizen?

Innovative Studies

- Genetic variation in drug trials that were halted for SJS/TEN– was DNA stored?
- Include negative predictive value as well as positive in cost-effectiveness studies
- Step backward from identified risk allele to immuno-pathogenesis
- Move toward *in vitro* preclinical testing of drugs, if get to case-control studies we've failed
- Surveillance/research in burn units or with burn association

Innovative Studies

- Measure HLA expression levels and use as direct tests of association across HLA alleles
- Study risk allele carriers who don’t get disease to identify predictive co-factors, multiple timepoints even after acute phase

Major Challenges

- Difficulties in early diagnosis
- Lack of systematic reporting– mandate somehow?
- Practitioner education critical but may not suffice
- Balance individual utility vs. societal impact
- Animal models lacking but they lack HLA restriction, use in more narrow range to test specific pathways
- Basic landscape definition– don’t know burden of problem

Real Opportunities

- Compare and harmonize case-report forms/databases across RegiSCAR, iSAEC, others
- Work with patient advocates to encourage adoption of ADR reporting more broadly
- Provide research case reports directly to FDA electronically
- Get HLA typing done now when can actually use it before become potential organ donor

High Priority Research Needs

- Improved *in vitro* testing for causative drugs, bedside back to bench
- Electronic phenotyping
- Ethnicity information in surveillance data
- Long-term outcomes especially serious morbidity, “non-standard” sequelae such as arthralgias, myalgias
- Demonstrating value of screening to hospitals/systems
- Discriminate risk allele carriers who’ll react from vast majority (90%?) who won’t
- Better epidemiology (incidence, RR) to permit accurate economic assessments

High Priority Research – Consensus

- Collect good biosamples early in course to develop early diagnostic and prognostic biomarkers
- Large-scale international network for collection of early biosamples, harmonized phenotyping
- Race-ethnic breakdown in SJS/TEN in US
- Standardized case definition useful for both prospective and retrospective studies– aggregate what's currently available
- Engage burn units in research – 60 across US

Next Steps

- Caption and post webcast on NHGRI website
- Draft meeting summary and executive summary
- Draft white paper for publication authored by meeting speakers and moderators
- Consider possible research initiatives
- Work among federal partners (AHRQ, CDC, FDA, NIH, ONC, PCORI) to identify potential joint efforts in drug safety and research focused on SJS/TEN
- Facilitate comparison and harmonization of phenotyping and case report efforts
- Stimulate interest amongst home agencies in collaborative effort

NHGRI staff NIH + FDA +…? Your name here…

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Translational Strategies

- Put HLA type in EMR– but will clinicians know how to use it?
- Guideline development, need to engage multiple medical subspecialties prescribing causative drugs
- Recognize iatrogenic nature and moral obligation to reduce/prevent

High Priority Research – Basic Research

- Develop reliable confirmatory *in vitro* challenge tests
- Define cellular processes leading to development of neoantigens
- Characterize how specific culprit drugs activate immune response outside of HLA
- Identify co-factors that drive immunogenicity
- Look beyond T cells to NK cells, dendritic cells, checkpoint blockade molecules
- Association studies of other high-priority drugs and in varied ethnicities: oxicam NSAIDs, lamotrigine, cough meds

High Priority Research – Clinical Research

- Burden of SJS/TEN problem– HLA study in Asian Americans
- Patient preference survey: how people behave when faced with risk data– patients, relatives, population