Ciencia Básica

Dr. José Luis Pablos Álvarez
Hospital Universitario 12 de Octubre
Madrid
Resumen Sesiones Ciencia Básica

Abstracts: Innate Immunity 4:00 PM - 4:10 PM CET
- 2045, 2046

Abstracts: Genetics, Genomics & Proteomics
- Genome-wide Association Study of Sjögren’s Syndrome Identifies Ten New Risk Loci
- High-throughput Identification of Functional Regulatory SNPs Associated with Systemic Lupus Erythematosus
- Somatic Mutations in a Single Residue of UBA1 Cause VEXAS, a Severe Adult-Onset Rheumatic Disease Presenting as Relapsing Polychondritis, Polyarteritis Nodosa, or Giant Cell Arteritis

Abstracts: Osteoarthritis & Joint Biology – Basic Science
- Gut Microbiome Transplantation from MRL/MpJ Mice Prevents Post-Traumatic Osteoarthritis in C57BL6/J Mice
- The Dynamics of Macrophage Sub-Populations in the Inflammatory Phase Following Joint Trauma

Abstracts: Cytokines & Cell Trafficking
- Identification of Small Molecules with Efficacy as Steroid Sparing Suppression of Chemokine and Cytokine Production by Rheumatoid Arthritis Fibroblast-like Synoviocytes

Molecular Insights from the Accelerating Medicines Partnership (AMP): Rheumatoid Arthritis
Pathogenesis of Checkpoint-Induced Arthritis
Detailed immunophenotyping analyses highlighted a robust expansion of PD1^{hi} CD39^{hi} cells in CCP+ early RA patients.

In CCP+ individuals at risk of future RA, PD1^{hi} CD39^{hi} cells were not clearly increased in frequency, but expressed higher levels of PD-1 compared to CCP-controls and PD-1 levels were correlated with disease status.

These results suggest that alterations in T cell phenotypes may be detectable not only early in RA but even preceding clinical onset after CCP elevation.
CD8 TRM residuales
- Fenotipo
- Transfieren enfermedad a modelos animales
- Su depleción bloquea la transmisión
Christopher Lessard, PhD
Oklahoma Medical Research Foundation
6:00 PM - 6:10 PM CET (Mon, Nov 9)

1955. High-throughput Identification of Functional Regulatory SNPs Associated with Systemic Lupus Erythematosus
Qiang Wang
Brigham and Women's Hospital
6:00 PM - 6:10 PM CET (Mon, Nov 9)

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**87 Lead SNPs**

- Search criteria:
  - Data Set: 1000 genomes Phase 3
  - Population: EUR
  - \( r^2 \) threshold > 0.8
  - Distance limit = 1 Mb

**SNPs Summary**

<table>
<thead>
<tr>
<th>SNP ID</th>
<th>Associated gene</th>
<th>Candidate TF binding preference</th>
<th>EMSA Preferential binding</th>
<th>Luciferase assay activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs2297550</td>
<td>IKBKE</td>
<td>IKZF1 (G&gt;C)</td>
<td>G&gt;C</td>
<td>G&gt;C</td>
</tr>
<tr>
<td>rs9907966</td>
<td>IKZF3</td>
<td>YBX1 (C&gt;A)</td>
<td>C&gt;A</td>
<td>C&gt;A</td>
</tr>
</tbody>
</table>
Somatic Mutations in a Single Residue of UBA1 Cause VEXAS, a Severe Adult-Onset Rheumatic Disease Presenting as Relapsing Polychondritis, Polyarteritis Nodosa, or Giant Cell Arteritis

David B. Beck M.D. Ph.D.
Inflammatory Disease Section, National Human Genome Research Institute, National Institutes of Health

11/20
Bone Marrow-Resident Myeloid Cells in *UBA1* Patients Exhibit Striking Vacuoles

The Clinical Spectrum of 25 Patients with *UBA1* p.Met41 Somatic Mutations (2)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count (Percentage)</th>
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</thead>
<tbody>
<tr>
<td>Relapsing polychondritis</td>
<td>15 (60%)</td>
</tr>
<tr>
<td>Sweet syndrome</td>
<td>8 (32%)</td>
</tr>
<tr>
<td>Myelodysplastic syndrome</td>
<td>6 (24%)</td>
</tr>
<tr>
<td>Multiple myeloma (MGUS)</td>
<td>5 (20%)</td>
</tr>
<tr>
<td>Polyarteritis nodosa</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>Giant cell arteritis</td>
<td>1 (4%)</td>
</tr>
</tbody>
</table>

Varones (ChrX) 64 años VEXAS
Destabilization of the medial meniscus (DMM)
Collagenase-Induced Osteoarthritis (CIOA) is a mouse model of trauma-induced joint damage.

The macrophage niche in the joint synovium comprises at least 4 subpopulations.

The inflammatory response observed in CIOA differs from that in inflammatory arthritis.

The MA (synovial lining) population exhibits a distinct response from other populations.

AMP Synovial Biopsy
RA vs. OA Patients
Zhang et al 2019

Serum Transfer Induced Arthritis (STIA)
Unpublished Data
Cell-based high throughput screening using a FRET based NFκB reporter

HTS1: 155,452 compounds at 5 hours  
HTS2: LPS+ compounds at 12 hours

Conclusion

- We successfully identified novel anti-inflammatory compounds by an immune phenotype-based screening.
- The lead 1H-pyrazolo[3,4-d] pyrimidin-4-amine compound (1-1) had an IC50 at the micromolar level and showed synergistic anti-inflammatory effects with dexamethasone in primary RA FLS.
5M044. Molecular Insights from the Accelerating Medicines Partnership (AMP): Rheumatoid Arthritis

Insights Into Stromal Cells in the Synovium
Kevin Wei, MD PhD
Brigham and Women's Hospital
9:35 PM - 9:45 PM CET (Mon, Nov 9)

Insights Into Monocytes and Other Innate Cells in the Synovium
Laura Donlin, PhD
Hospital for Special Surgery
9:25 PM - 9:35 PM CET (Mon, Nov 9)

Integrated Analysis of the Adaptive and Innate Immune Response in the Synovium: What Have We Learned About RA from AMP?
Michael Brenner, MD
Brigham and Women's Hospital, Harvard Medical School
9:45 PM - 10:00 PM CET (Mon, Nov 9)
CD8 T cells

- They produced granzyme B, perforin, along with TNFα and IFNγ
- IFN signature of CI-A synovial fluid CD8 T cells