Autoantibody Standardizing Committee

Subcommittee for the IUIS Quality Assessment and Standardization Committee

Milan, August 25, 2013

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Chair
WHO/IUIS/AF
Autoantibody Standardizing Committee
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IUIS – International Society of Immunology Societies
WHO – World Health Organization
CDC – Centers for Disease Control
Historical landmarks

- **1980:** AF/CDC Reference Laboratory founded by
  - Eng M Tan (University of Colorado)
  - Frederic McDuffie (Arthritis Foundation) | 5 reference sera
  - J. Steven McDougal (Centers for Disease Control)

- **1982:** Dr. Ephraim Engleman ➔ internationalization of the ANA Standardizing Committee, which was recognized by
  - ILAR (International League Against Rheumatism)
  - IUIS (International society of Immunology Societies)
  - WHO (World Health Organization)
Mission

- Improve quality control to the field of immunodiagnostics in the rheumatic autoimmune diseases
- Uphold the highest standards of patient care by promoting accuracy in autoantibody testing.
- Establish and promote studies and research projects that enhance the quality of autoantibody testing.
- Develop and promote Clinical Practice Guidelines for Autoantibody Testing through:
  - educational activities
  - publication of key findings, recommendations, and critical reviews on the cost-effectiveness of autoantibody testing and new technology that impacts on the detection of autoantibodies in humans.
- Evaluate and undertake to provide index reference sera to appropriate individuals, industry, manufacturers, hospitals, and academic institutions.
- Promote and look over distribution of reference sera without charge to research laboratories, diagnostic laboratories, and commercial organizations developing autoantibody diagnostic kits.
Reference sera available

- Anti-native DNA
- Anti-SS-B/La
- Anti-Sm
- Anti-fibrillarin
- Anti-Scl-70 (DNA topoisomerase I)
- Anti-Jo-1 (histidyl tRNA synthetase)
- Anti-ribosomal P protein
- Anti-RNA polymerase III
- Anti-cardiolipin IgG
- Anti-MPO (pANCA)
- Anti-PM/Scl
- Anti-SS-A/Ro
- Anti-U1-RNP
- Anti-centromere
- Anti-cardiolipin IgM
- Anti-PR3 (cANCA)
Reference serum samples distribution

- Reference serum for 17 autoantibody specificities
- Survey in 1997 ➔ over 28,000 reference serum vials distributed
- Estimated rate: approximately 350 vials annually
- August 2012 to August 2013 ➔ 694 vials
Requirement rate for each serum standard
2012/213

<table>
<thead>
<tr>
<th>ANA #</th>
<th>Antigen</th>
<th>Vials</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1 (DNA)</td>
<td>ANA #10 (Jo-1)</td>
<td>47</td>
</tr>
<tr>
<td>#2 (SS-B)</td>
<td>ANA #11 (PM/Scl)</td>
<td>32</td>
</tr>
<tr>
<td>#3 (RNP)</td>
<td>ANA #12 (Ribo P)</td>
<td>34</td>
</tr>
<tr>
<td>#4 (RNP)</td>
<td>ANA #13 (IgM aCL)</td>
<td>28</td>
</tr>
<tr>
<td>#5 (Sm )</td>
<td>ANA #14 (IgG aCL)</td>
<td>28</td>
</tr>
<tr>
<td>#6 (U3-RNP)</td>
<td>ANA #15 (MPO-ANCA)</td>
<td>44</td>
</tr>
<tr>
<td>#7 (SS-A)</td>
<td>ANA #16 (PR3-ANCA)</td>
<td>44</td>
</tr>
<tr>
<td>#8 (Centr)</td>
<td>ANA #17 (ACPA)</td>
<td>14</td>
</tr>
<tr>
<td>#9 (Scl-70)</td>
<td>ANA #17 (ACPA)</td>
<td>50</td>
</tr>
</tbody>
</table>
Most frequent destinations of shipping of serum standards in 2012/2013
Current members

- Agmon-Levin Nancy **Israel**
- Andrade Luis E.C. (Chair) **Brazil**
- Block Donald B. **USA**
- Chan Edward K.L. (Treasurer/Secretary) **USA**
- Fritzler Marvin J. **Canada**
- García-De La Torre Ignacio (Vice-Chair) **Mexico**
- Hiepe Falk **Germany**
- Koike Takao **Japan**
- Konstantinov Konstantin **USA**
- Lahita Robert **USA**
- Lightfoote Marilyn **USA**

Reeves Westley H. **USA**
Rönnelid Johan **Sweden**
Sheldon J **United Kingdom**
Shoenfeld Yehuda **Israel**
Takasaki Yoshinari **Japan**
Tincani Angela **Italy**
Steiner Günter **Austria**
Vogt Robert F., Jr. **USA**
Meroni Pier Luigi **Italy**
Five-year strategic plan

• Replenish CDC standards that are projected to be depleted from the CDC stocks.
• Involve patient advocate organizations, such as Lupus Foundation of America, Lupus Research Institute, SjS Foundation, etc. to communicate the objectives and goals of ASC.
• Enhance communication/collaboration/affiliation with other relevant organizations: ACR, EULAR, AMLI, LF, LRI, AF, etc. Consider joint projects or initiatives of mutual interest.
• Recruitment of young faculty/investigators to the committee.
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Five-year strategic plan (cont’…)

- Publication of review and technical articles on critical aspects of autoantibody testing (on going)
- Generate guidelines for clinical diagnostic laboratories in reporting ANA and related autoantibodies (on going)
- Review, update and publish a glossary of terms used in autoantibody testing.
- Establish international consensus description on ANA IIF patterns (on going)
- Work with industry on specific collaborative projects involving autoantibody standardization
- Develop education modules and become the go to source for information on the ASC website and continue efforts in organizing Study Group at the ACR
Current operational tasks

Replenishment of current standards

• Anti-U1-RNP (to replenish ANA #4, U1-RNP, IS2075, 95-0055L )
• Anti-Sm (to replenish ANA #5, Sm, IS2076, 96-0005L)
• Anti-Scl-70 (to replenish ANA #9, Scl-70/topoi, IS2135, 84-0027L)
• Anti-Jo-1 (to replenish ANA#10, Jo1, IS2187, 88-0024L)

Novel standards

• Anti-Mi-2 Anti-RNA pol III Anti-LEDGF/p75
• Anti-Th/To Anti-SS-A/Ro 52kDa Anti-PCNA
Nuclear homogeneous pattern

Wiik AS et al, J autoimmunity 2010; 35:276-90
SS-A/Ro-specific nuclear fine speckled ANA pattern

Dellavance A, Alvarenga RR, Andrade LEC, J Immunol Mehtods in press
Non-specific nuclear fine speckled ANA pattern
Centromeric pattern

Wiik AS et al, J autoimmunity 2010; 35:276-90
Nuclear coarse speckled pattern

Wiik AS et al, J autoimmunity 2010; 35:276-90
Nuclear pleomorphic pattern

Clumpy nucleolar pattern

Two patterns ➔ multiple discrete nuclear dots & cytoplasmic linear dot array

Type NuMA-1 mitotic apparatus pattern

Andrade LEC; Arthritis Rheum 1996;39:1643
Brazilian Consensus for ANA-HEp-2 Nomenclature


- **IV Consensus (2012)** – manuscript in preparations
Impact of external quality assessment on antinuclear antibody detection performance

B-N Pham\textsuperscript{1*}, S Albarede\textsuperscript{2}, A Guyard\textsuperscript{2}, E Burg\textsuperscript{2} and P Maisonneuve\textsuperscript{2}

\textsuperscript{1}Service d’Hématologie et Immunologie, Hôpital Beaujon, 92 Clichy, France; and \textsuperscript{2}Agence Française de Sécurité Sanitaire des Produits de Santé, 93 Saint-Denis, France
Autoantibody Detection Using Indirect Immunofluorescence on HEP-2 Cells

Ulrich Sack, a Karsten Conrad, b Elena Csernok, c Ingrid Frank, d Falk Hiepe, e Thorsten Krieger, f Arno Kromminga, g Philipp von Landenberg, h Gerald Messer, i Torsten Witte, j and Rudolf Mierau k for the German EASI (European Autoimmunity Standardization Initiative)

Antinuclear antibodies: A contemporary nomenclature using HEP-2 cells

Allan S. Wiik\textsuperscript{a,*}, Mimi Høier-Madsen\textsuperscript{a}, Jan Forslid\textsuperscript{b}, Peter Charles\textsuperscript{c}, Jan Meyrowitsch\textsuperscript{d}

\textsuperscript{a}Department of Clinical Biochemistry and Immunology, Statens Serum Institut, Artillerivej 5, 2300 Copenhagen S, Denmark
\textsuperscript{b}Department of Clinical Immunology and Transfusion Medicine, Karolinska University Hospital, 171 76 Stockholm, Sweden
\textsuperscript{c}Translational Research, Kennedy Institute of Rheumatology, Imperial College London, 65 Aspenlea Road, London W6 8LH, United Kingdom
\textsuperscript{d}Perceptron Ltd., Rialtovej 12, 2300 Copenhagen S, Denmark
I Argentinean Consensus on ANA-HEp2

- 28 ANA experts
World Consensus of Antinuclear Antibody Nomenclature
12º International Workshop on Autoantibodies and Autoimmunity
28-30, August, 2014
São Paulo - Brazil

Speakers and Lectures

- ANA Pattern Nomenclature - an International Consensus
  Allan Wiik (Denmark) and Tsuneyo Mimori (Japan)

- Establishment of Autoantibody Standards
  Pier Luigi Meroni (Italy) and Johan Rönnelid (Sweden)

- Methodological Platforms Affecting Autoantibody Testing
  Marvin J. Fritzler (Canada) and Xavier Bossuyt (Belgium)

- Molecular and Cellular Biology of Autoantigens
  Ger J.M. Pruijn (The Netherlands) and Edward K.L. Chan (USA)

- Pathophysiologic Aspects of Autoantibodies
  K. Michael Pollard (USA) and Westley H. Reeves (USA)

- Clinical Relevance of Autoantibodies
  Minoru Satoh (Japan) and Ignacio Garcia de la Torre (Mexico)

- Autoantibodies and Immunobiologic Therapy
  Falk Hiepe (Germany)

Informations: iwaa.brazil@numeneventos.com.br