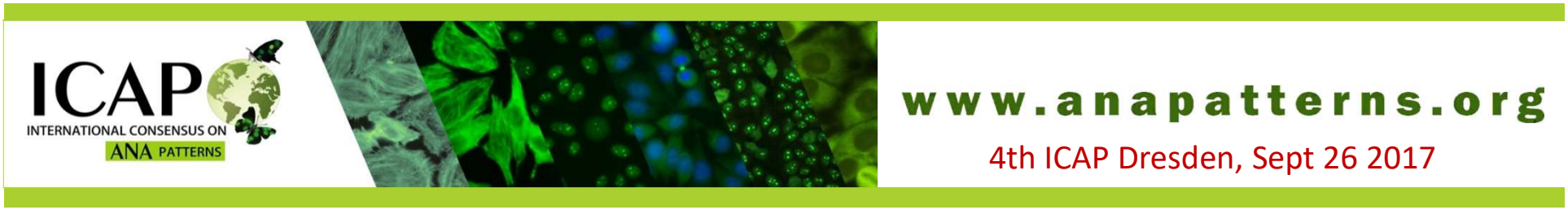


The International Consensus on Standardized Nomenclature of Antinuclear Antibody HEp-2 Cell Patterns (ICAP) – Overall Update

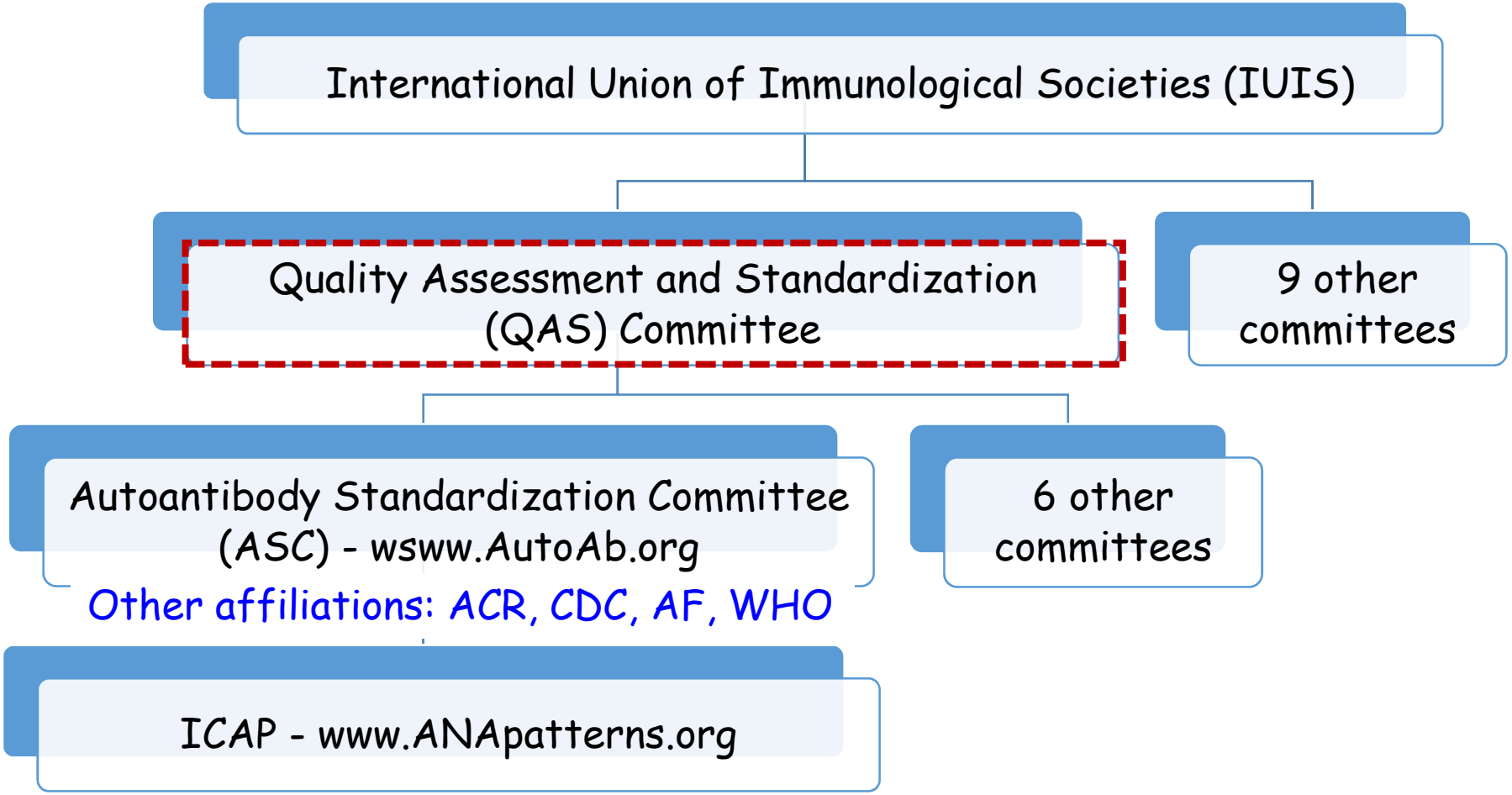
Edward K.L. Chan
Professor
Dept. Oral Biology
Dept. Anatomy & Cell Biology

UF | UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Chair, Autoantibody Standardization Committee:
www.autoab.org
Co-coordinator (with Luis Andrade), ICAP:
www.ANApatterns.org

- The first ICAP workshop in 2014 was initiated to discuss and promote consensus morphological patterns observed in the indirect immunofluorescence assay on HEp-2 cells. It was model after the Brazilian ANA Consensus which had already a 10-year history.
- ICAP was implemented during the 12th International Workshop on Autoantibodies and Autoimmunity (IWAA) in Sao Paulo by several members of the Autoantibody Standardization Committee (ASC) together with other founding members.

Committee Structure – the ICAP committee has been operating as an ASC subcommittee



Committees

Home

Committees

CIC - Clinical Immunology Committee

EDU - Education Committee

GEC - Gender Equality and Career Development Committee

ITH - Immunotherapy Committee

NOM - Nomenclature Committee

PID - Primary Immunodeficiency Expert Committee

PUB - Publication Committee

QAS - Quality Assessment and Standardization Committee

VAC - Vaccine Committee

VIC - Veterinary Immunology Committee

Quality Assessment and Standardization Committee (QAS)

What is the QAS?

The Quality Assessment and Standardization Committee (QAS) goals and objectives are the following:

1. **Keep the existing Sub-Committees supported**
2. **Make standardization activities public by organizing symposia during IUIS Meetings**
3. **Contribute overview articles for the IUIS journal** *Frontiers in Immunology*
4. **Attract sponsorship to increase Committee activities**

The next IUIS meeting will take place April 25-30, 2019, in Beijing, China, as part of the 17th International Congress of Immunology.

IUIS Immunology without Borders

International Union of Immunological Societies

Home | About IUIS | Member Benefits | Committees | News | Activities | Events | Resources | Contact

Home » QAS - Quality Assessment and Standardization Committee

Committees

- Home
- Committees
- CIC - Clinical Immunology Committee
- EDU - Education Committee
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- ITH - Immunotherapy Committee
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- PID - Primary Immunodeficiency Expert Committee
- PUB - Publication Committee
- **QAS - Quality Assessment and Standardization Committee**
- VAC - Vaccine Committee
- VIC - Veterinary Immunology Committee

Quality Assessment and Standardization Committee (QAS)

Sub-Committee for the Standardization of Autoantibodies in Rheumatic and Related Diseases

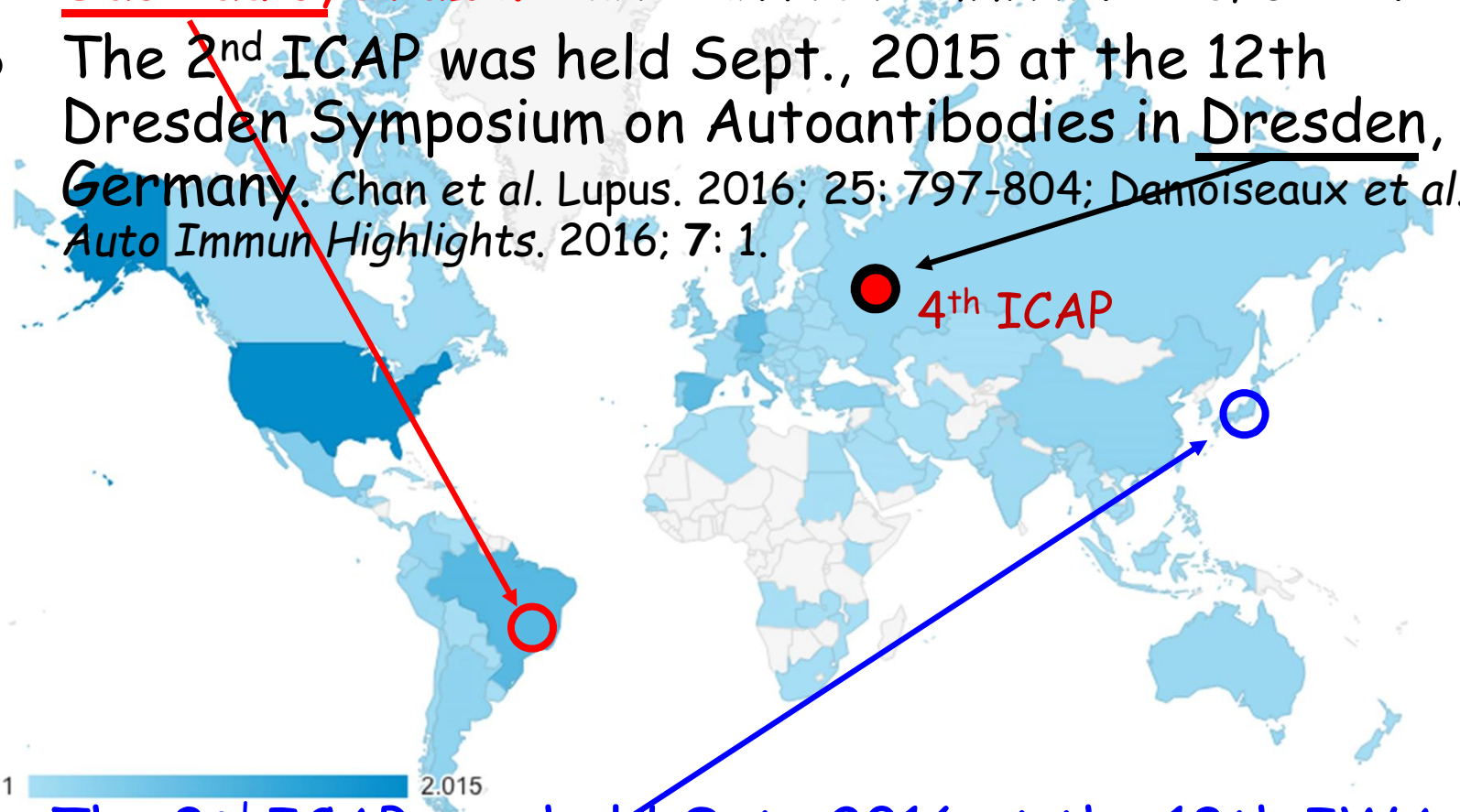
www.AutoAb.org *(aka. Autoantibody Standardization Committee)*

Chair: Edward K.L. Chan (USA)
echan@ufl.edu
Vice-Chair & Secretary: Minoru Satoh (Japan)

Current Members:

Agmon-Levin, Nancy (Israel)
Andrade, Luis, E.C. (Brazil) *(immediate past Chair)*
Arntsen, Kathleen A. (USA
Block, Donald B. (USA)
Cavazzana, Ilaria (Italy)
Fritzler, Marvin J. (Canada) *(past Chair)*
García-De La Torre, Ignacio (Mexico) *(past Vice-Chair)*
Hiepe, Falk (Germany)
Koike, Takao (Japan)
Konstantinov, Konstantin (USA)
Lahita, Robert (USA)
Lightfoote, Marilyn (USA)
Meroni, Pier Luigi (Italy)
Reeves, Westley H. (USA)
Rönnelid, Johan (Sweden)
Selmi, Carlo (Italy)
Sheldon, Joanna (UK)
Shoenfeld, Yehuda (Israel)
Steiner, Günter (Austria)
Takasaki, Yoshinari (Japan)
Tincani, Angela (Italy)
Vogt, Robert F., Jr. (USA)
Wener, Mark H. (USA)

- The 1st ICAP was held at the IWAA August 2014 in São Paulo, Brazil. Chan *et al. Front Immunol.* 2015; **6**: 412.
- The 2nd ICAP was held Sept., 2015 at the 12th Dresden Symposium on Autoantibodies in Dresden, Germany. Chan *et al.* Lupus. 2016; 25: 797-804; Damoiseaux *et al.* *Auto Immun Highlights.* 2016; **7**: 1.



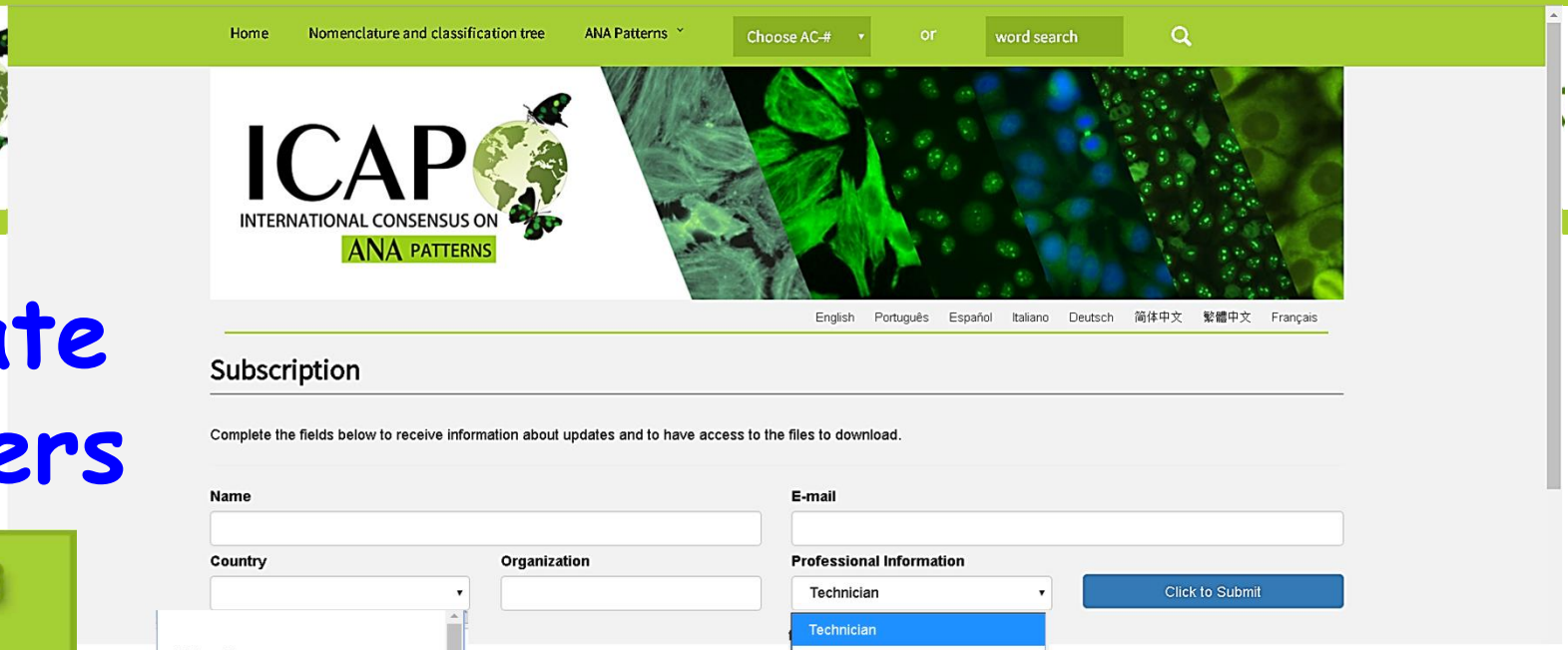
- The 3rd ICAP was held Oct., 2016 at the 13th IWAA meeting in Kyoto, Japan

ICAP Membership – Why?

Membership: Members are expected to provide input and feedback for the ICAP initiative, help report error, and promote the implementation of the ICAP classification. Membership benefits include important updates in ICAP committee activities and downloads of posters and other relevant files from the ICAP website.

- **Full Members** – includes membership of the ICAP Executive Committee and other members appointed from time to time by the Executive Committee.
- **Associate Members** – individuals participating in various activities to help construct, maintain, and advance ICAP initiatives.
- **Affiliate Members** – users of the ICAP community who have registered at the ICAP website.

Affiliate Members



	Professional	Affiliate	%
1	Physician	480	39.7
2	Technician	473	39.2
3	Researcher	193	16.0
4	Student	62	5.1
		1208	100

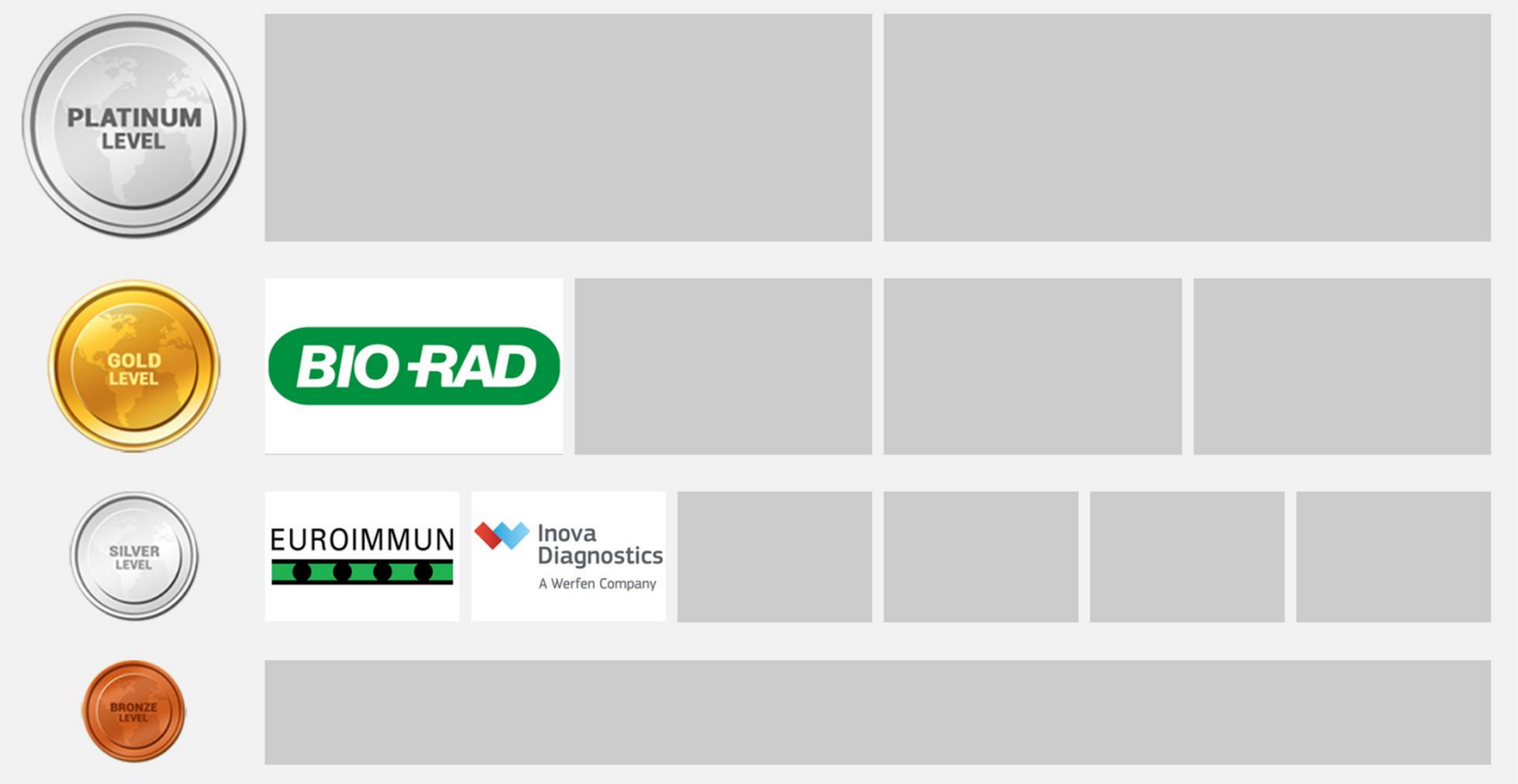
ICAP Membership

ICAP Executive Committee – currently Founding Members constitute this committee. The Executive Committee will include appointees from the Associate Membership who take on leadership roles. Nomination to ICAP Executive Committee will be an open process, conducted annually, and finalized by a simple majority vote on by members of the Executive Committee.

Sponsors – a sponsorship category has been established to facilitate donations of unrestricted educational grants to the Autoantibody Standardization Committee, of which ICAP Committee is operating as a sub-committee.

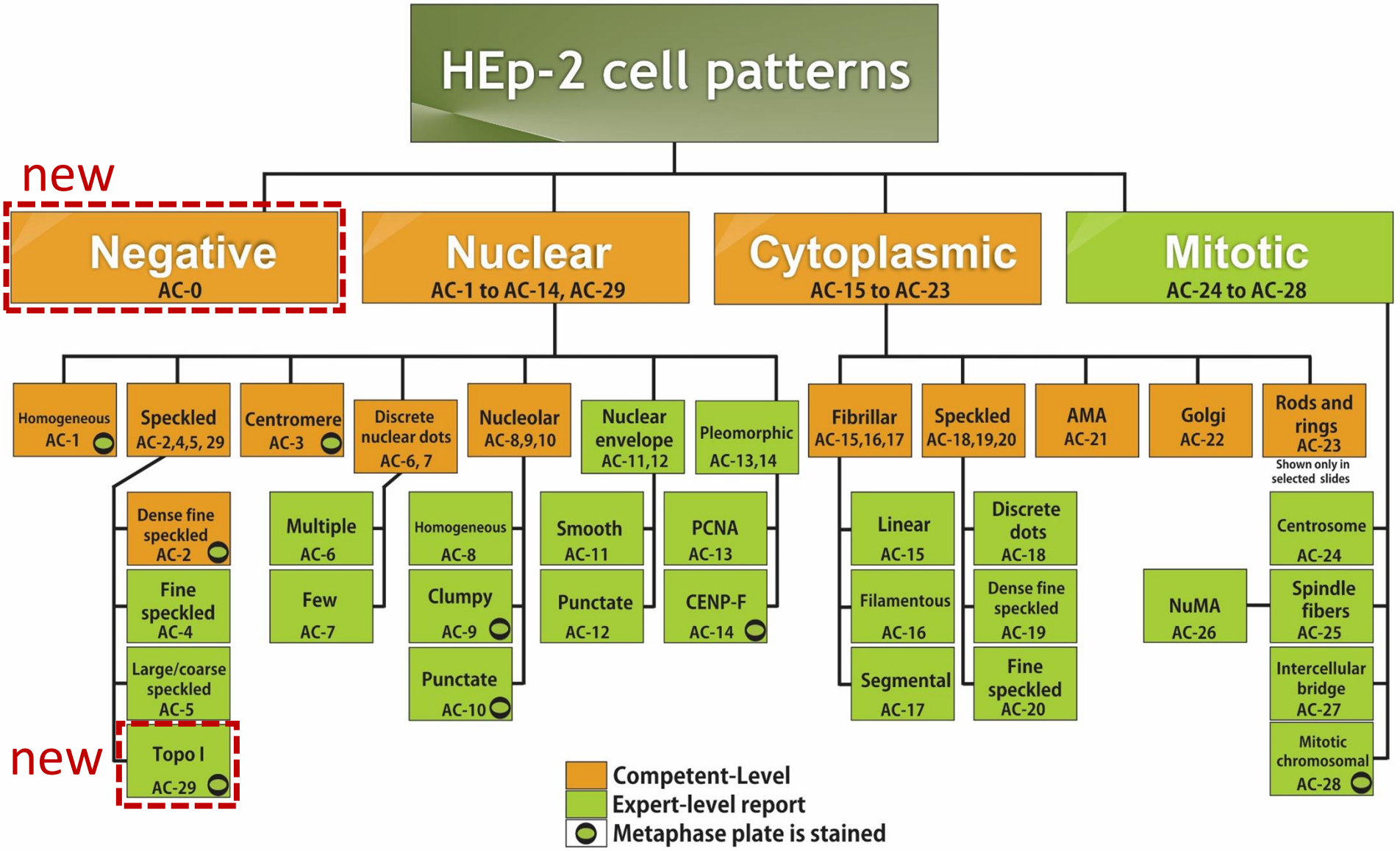
Unrestricted Educational Grant Support for the Autoantibody Standardization Committee - ASC/ICAP

https://www.anapatterns.org/sponsors.php



ICAP (International Consensus on ANA Patterns)

- Why do we need ICAP?
  - ACR ANA Task Force – ANA as Gold standard
  - There are much agreement AND disagreement in how ANA patterns are described in the literature.
- The ultimate goal of ICAP is to promote harmonization of autoantibody nomenclature, and thereby optimizing ANA usage in patient care.



- AC-0 + 3 divisions
- 2 levels
- 30 AC patterns

www.anapatterns.org

Competent- vs. expert-level patterns

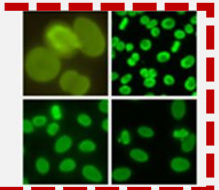
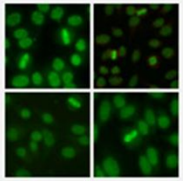
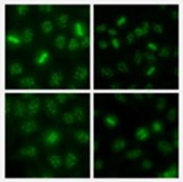
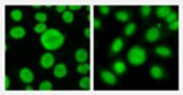
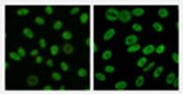
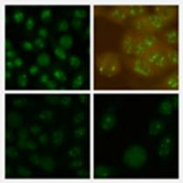
- The classification of patterns as competent level did not follow strict criteria, but took into consideration the clinical relevance and the morphological consistency of the patterns – *not necessary a permanent separation*
- For new/inexperience labs, they should focus on getting all the competent-level patterns identified accurately but should also move towards identifying the expert-level patterns
- For an established labs, they should make sure that all the competent-level patterns can be identified and reported as well as becoming comfortable to report expert-level patterns

ICAP

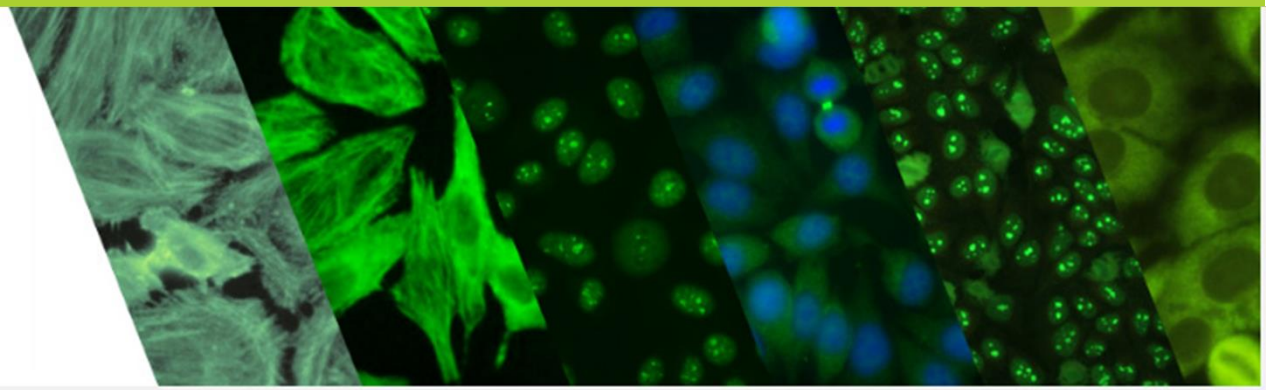
www.anapatterns.org

English Português Español Deutsch Italiano 简体中文 繁體中文 Français

ANA Patterns - Nuclear Patterns

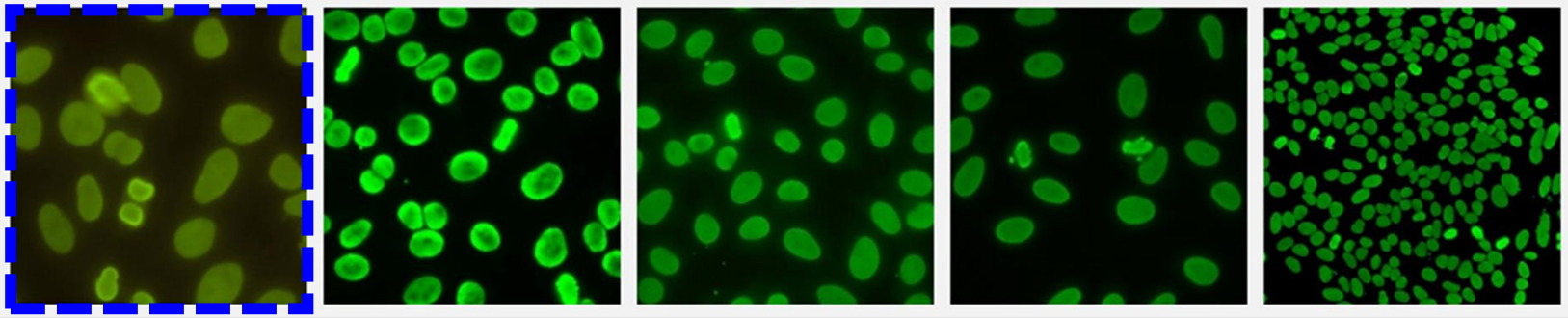
Code	Pattern	Synonym	Description	
AC-1	Nuclear homogeneous	Diffuse	Homogeneous and regular fluorescence across all nucleoplasm. The nucleoli maybe stained or not stained depending on cell substrate. Mitotic cells (metaphase, anaphase, and telophase) have the chromatin mass intensely stained in a homogeneous hyaline fashion.	
AC-2	Nuclear dense fine speckled	none	Speckled pattern distributed throughout the interphase nucleus with characteristic heterogeneity in the size, brightness and distribution of the speckles. Throughout the interphase nucleus, there are some denser and looser areas of speckles (very characteristic feature). The metaphase plate depicts strong speckled pattern with some coarse speckles standing out.	
AC-3	Centromere	kinetochore	Discrete coarse speckles (40-80/cell) scattered in interphase cells and aligned at the chromatin mass on mitotic cells. e.g. anti-CENP B	
AC-4	Nuclear fine speckled	fine granular	Fine tiny speckles across all nucleoplasm. The nucleoli may be stained or not stained. Mitotic cells (metaphase, anaphase, and telophase) have the chromatin mass not stained. e.g. anti-SS-A/Ro, anti-SS-B/La	
AC-5	Nuclear large/coarse speckled	spliceosome/nuclear matrix	Coarse speckles across all nucleoplasm. The nucleoli may be stained or not stained. Mitotic cells (metaphase, anaphase, and telophase) have the chromatin mass not stained. e.g. anti-Sm, anti-U1 RNP	
AC-6	Multiple nuclear dots	6-20 nuclear dots, NSpI, PML bodies	Countable discrete nuclear speckles (6 to 20 nuclear dots/cell). e.g. SP-100	

ICAP
INTERNATIONAL CONSENSUS ON
ANA PATTERNS



English Português Español Deutsch Italiano 简体中文 繁體中文 Français

AC-1 - Nuclear homogeneous



Synonym	Diffuse
Antigen Association	dsDNA, nucleosomes, histones
Disease Association	SLE, drug-induced lupus, juvenile idiopathic arthritis
Description	Homogeneous and regular fluorescence across all nucleoplasm. The nucleoli maybe stained or not stained depending on cell substrate. Mitotic cells (metaphase, anaphase, and telophase) have the chromatin mass intensely stained in a homogeneous hyaline fashion.

- Nuclear patterns - Jan Damoiseaux
- Cytoplasmic patterns - Carlos Alberto von Mühlen
- Mitotic patterns - Manfred Herold

Moving forward with internationalization – translation into other languages

- **Prioritize, establish contacts, <u>team efforts</u>**

Guidelines for ICAP translation

- For each language translation project, consider a responsible *team* rather than a single individual.
- Promote *inclusion* of more participants at different stages whenever possible. This may take a longer time but it helps to spread the message regarding the ICAP rationale.
- Further promotion is recommended. Plan for a *manuscript* in a regional/local journal to announce the translation work; target audience should be clinical immunology laboratory.

SPANISH

Aresio Plaza López (EASI member)
Hospital Universitario Puerta de Hierro. Majadahonda, Madrid, España.

Carlos A. Casiano
Facultad de Medicina y Centro Medico de la Universidad de Loma Linda, Loma Linda, California, Estados Unidos de America.

Ignacio García-De La Torre (Coordinator)
Hospital General de Occidente y Universidad de Guadalajara, Guadalajara, México.

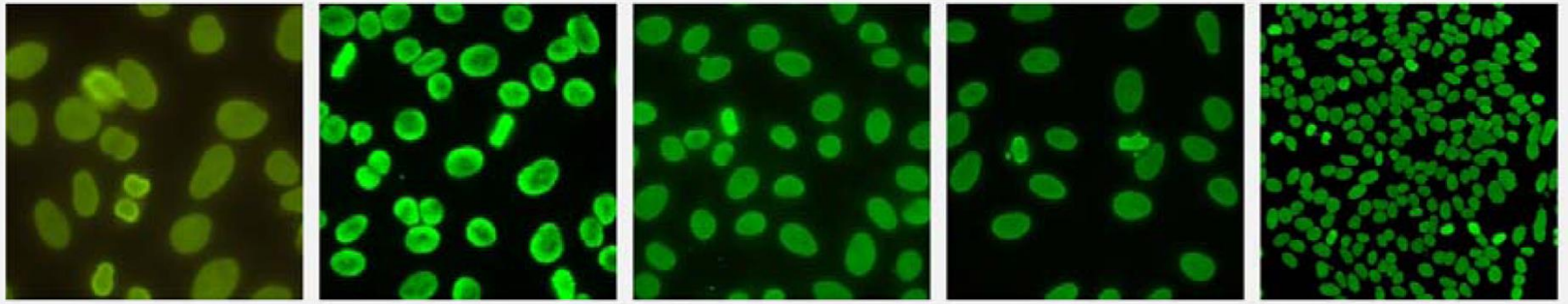
Orlando Gabriel Carballo
Hospital General de Agudos Carlos G Durand y Universidad del Hospital Italiano, Buenos Aires, Argentina.

Translations online

Translations example

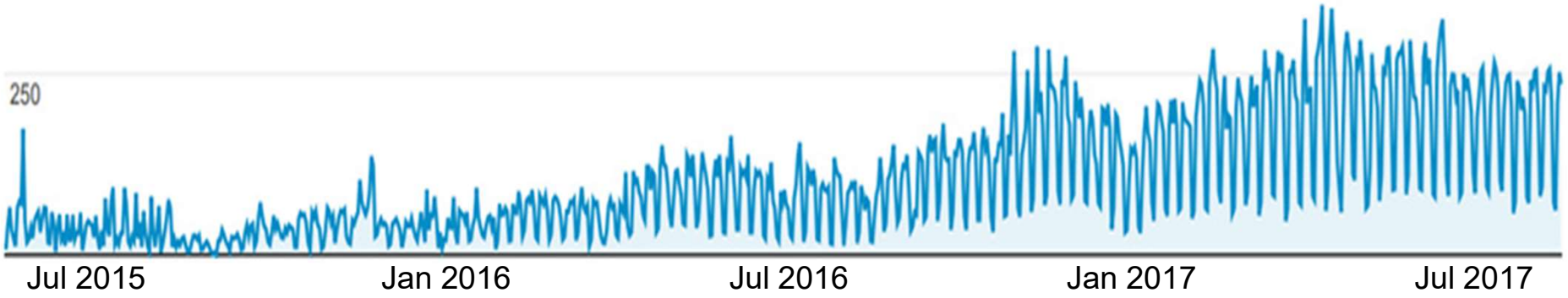
English Português Español Italiano Deutsch 简体中文 繁體中文 Français

AC-1 - 細胞核均勻着色

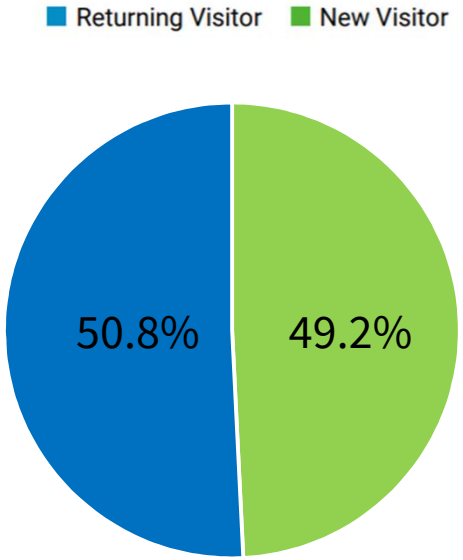


	繁體中文	English
同義詞	彌散	Diffuse
抗原相關性	雙鏈DNA，核小體，組蛋白	dsDNA, nucleosomes, histones
疾病相關性	全身性紅斑狼瘡、藥物性狼瘡、少年型特發性關節炎	SLE, drug-induced lupus, juvenile idiopathic arthritis
描述	細胞核漿呈現均勻螢光染色，根據不同的細胞基質，核仁染色可有可無。分裂期細胞 (中期、後期和末期) 的濃縮染色體呈現強烈及均勻玻璃質染色。	Homogeneous and regular fluorescence across all nucleoplasm. The nucleoli maybe stained or not stained depending on cell substrate. Mitotic cells (metaphase, anaphase, and telophase) have the chromatin mass intensely stained in a homogeneous hyaline fashion.

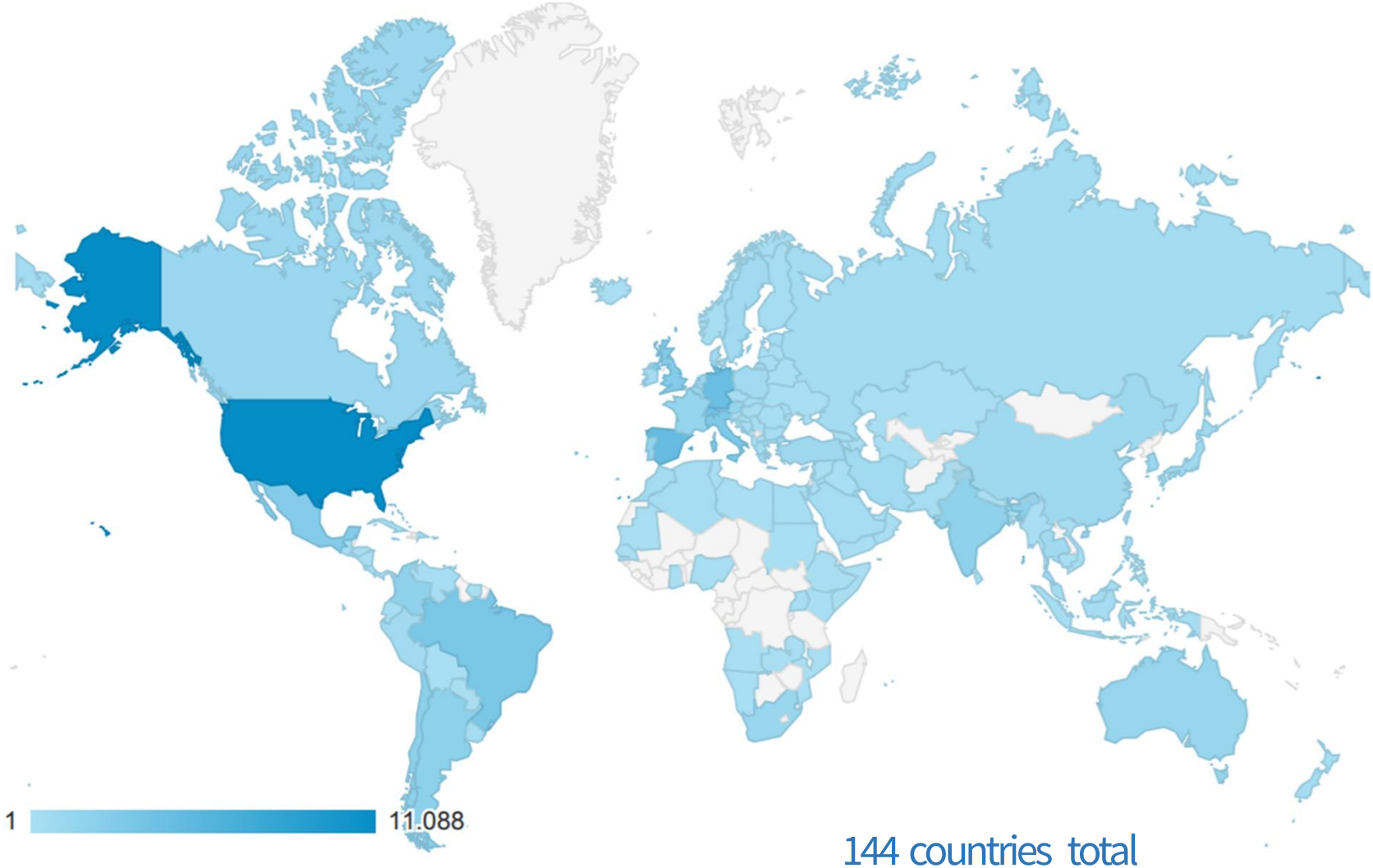
Website visits - overview



Total visits	Total visitors	Total views
83,838	41,176	575,177



Source: Google Analytics - July 19, 2015 - August 19, 2017



Source: Google Analytics - July 19, 2015 - August 19, 2017

	Countries	Views
1	USA	13,211
2	Spain	5,431
3	Germany	5,025
4	Switzerland	4,340
5	Brazil	3,639
6	Italy	3,290
7	Mexico	3,115
8	United Kingdom	2,813
9	Chile	2,324
10	Colombia	2,230
11	Argentina	2,229
12	India	2,203
13	Portugal	1,755
14	France	1,562
15	Belgium	1,549
16	Australia	1,517
17	Austria	1,442
18	South Africa	1,292
19	Canada	1,280
20	South Korea	1,235
21	Hong Kong	1,171
22	Netherlands	1,162
23	Taiwan	1,109
24	China	939
25	Japan	840

Quest

Mini-ICAP

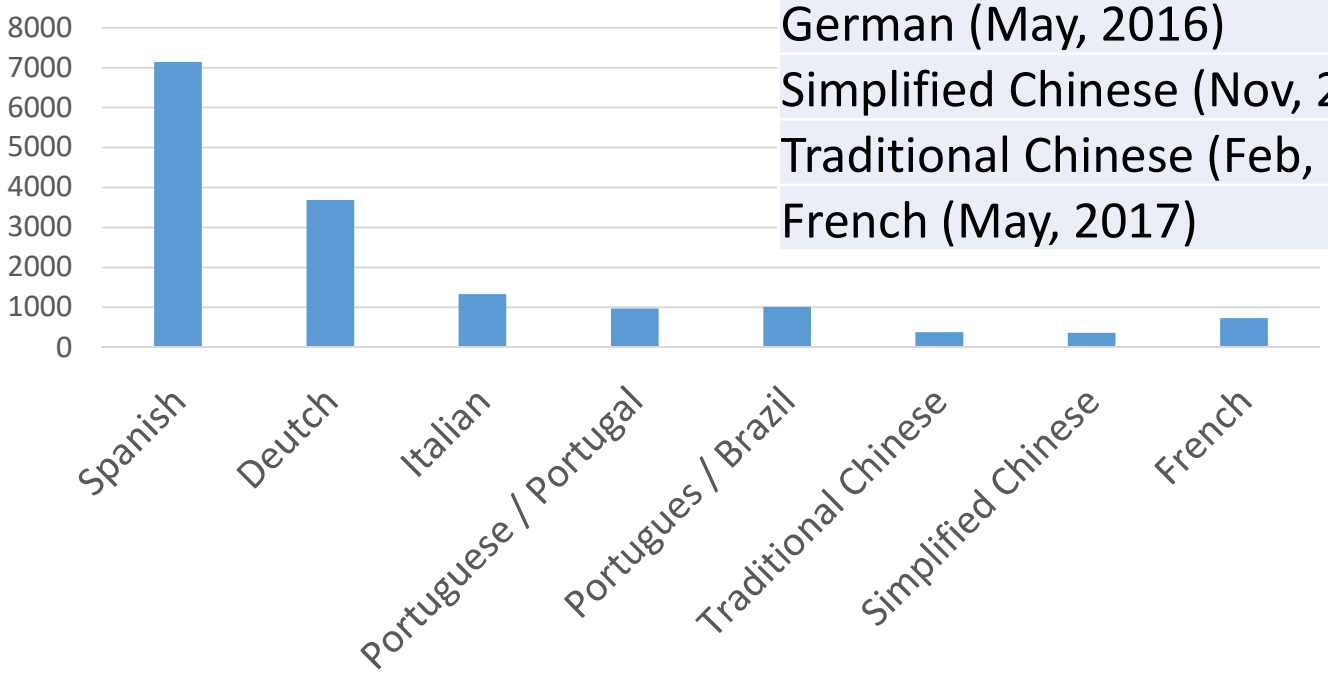
144 countries total

Source: Google Analytics - July 19, 2015 - August 19, 2017

Considering a total of 15,609 visits (excluding english access)

Access by Language

Language	Visits	%
Portugues/Brazil (Dec, 2015)	1,009	6.5
Spanish (Feb, 2016)	7,14	45.7
Portuguese/Portugal (Feb, 2016)	973	6.2
Italian (Mar, 2016)	1,335	8.6
German (May, 2016)	3,687	23.6
Simplified Chinese (Nov, 2016)	360	2.3
Traditional Chinese (Feb, 2017)	378	2.4
French (May, 2017)	727	4.7



ICAP image submission – why?

- All images are welcome for the ICAP collection. Including from:
  - ICAP committee members
  - Industry (HEp-2 slide manufacturers)
  - Any individual
- Main purpose is to have representations from many.
- Note that images submitted to ICAP represents transfer of all image copyright to ICAP.
- All images will be evaluated by members of the ICAP committee.
- Feedback will be provided if certain images are not accepted.

Checklist before submission:

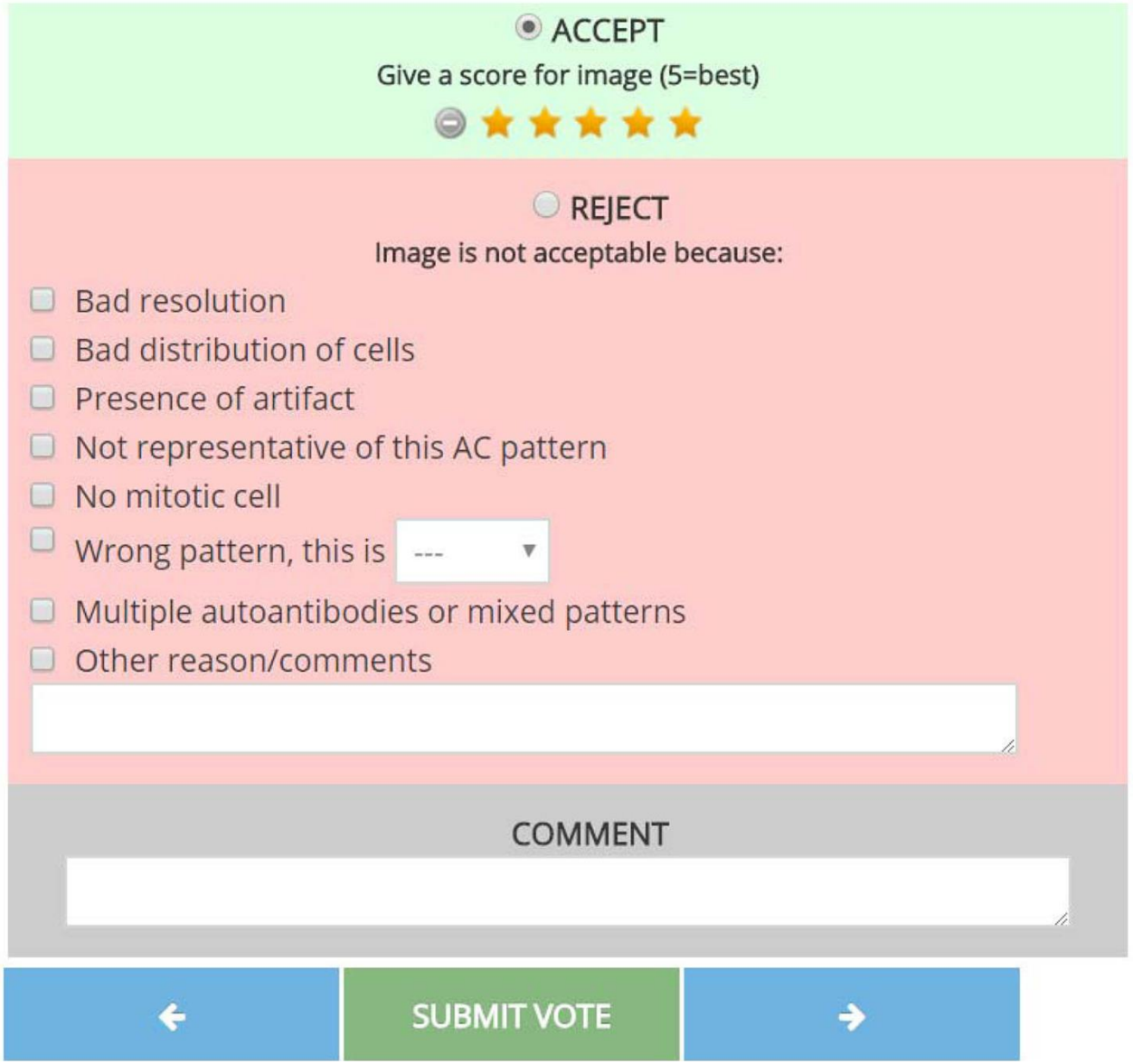
- Image in *perfect focus*?
- Image should have *good distribution* of at least 15 interphase cells and at least one mitotic cell.
- Images can be either in green/monochrome color.
- Specify magnification – most images should be 400x
- Image resolution and size acceptable?
- Absence of artifacts?
- Avoid any features that do not represent a given pattern (except to illustrate mixed patterns).

Checklist before submission (cont'):

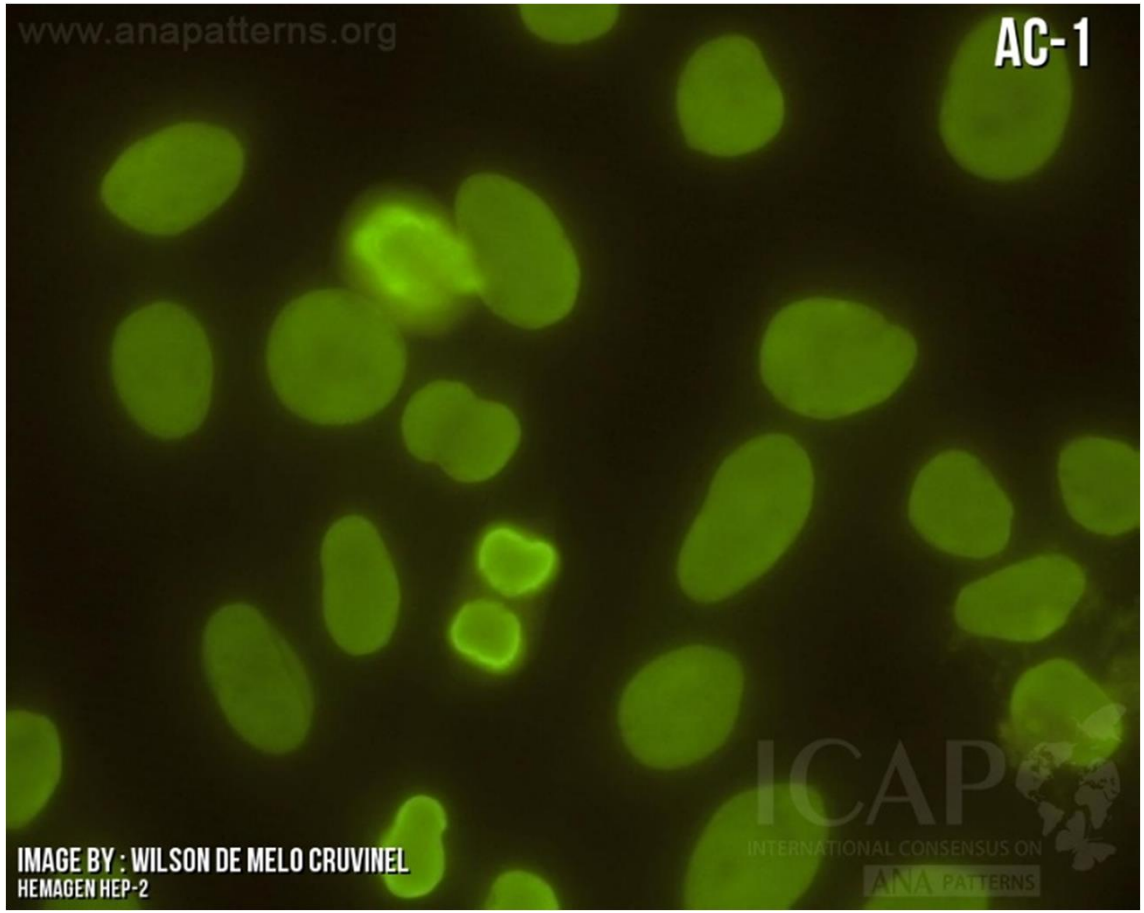
- Specify manufacturer of HEp-2 cells.
- Specify the person responsible for the submitted image – to be listed for credit.
- Commonly used counterstains such as DAPI are acceptable but it should not interfere with nuclear patterns.
- Prefer file formats: jpg, TIFF.
- Submit images to: echan@ufl.edu
- Before submitting a large number of images, send a typical image for us to check first.

Image voting process:

images voted by ICAP committee members



How images are displayed



Upper left corner: semi-hidden website address www.ANApatterns.org

Upper right corner: AC-# designation

Lower left corner: contributor and source of HEp-2 substrate

Lower right corner: semi-hidden ICAP logo

Current initiatives

- Collected more images per pattern
- Include more ANA HEp-2 substrates
- More translations (Turkish, Japanese, Dutch)
- Develop online training courses (Andrade, de Melo Cruvinel)
- Develop consensus on ANA reporting; communicate with disease criteria committees

ICAP future

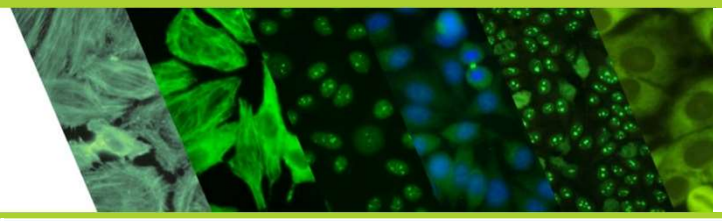
- More discussion/presentations
- Training needs to be addressed
- Using standard sera, for example the ASC/CDC ANA standards (www.AutoAb.org)
- Use the www.ANApatterns.org ICAP images
- Use of additional subcellular markers (i.e. monoclonal antibodies) for co-localization validations

Online Educational Program Planning

- Training modules are being planned for the next two years.
- They will include videos – PowerPoint-based and mostly text based. The latter will allow us to translate readily to other languages.
- The following is an outline for 4 modules each about 1 hour in length.

- **Module #1. Introduction**
  - Introduction to ICAP; How to navigate ICAP website; Basics in ANA training.
- **Module #2. Basic ANA patterns**
  - How to distinguish between positives and negatives
  - Overview of the Competent-Level ICAP patterns
  - Guideline on ANA reporting
  - Trainee will be challenged with images to be classified
  - Trainee will be challenged with question on clinical and immunologic meaning of AC patterns
- **Module #3. Advance ANA patterns**
  - Overview of Expert-level ICAP patterns
  - Trainee will be challenged with images to be classified and question on clinical and immunologic meaning of AC patterns
- **Module #4. Mixed patterns and troubleshooting**
  - Overview of mixed patterns
  - Introduction of FAQs (frequently asked questions) database to be developed as a resource for the community

ICAP
INTERNATIONAL CONSENSUS ON ANA PATTERNS



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4th ICAP Dresden, Sept 26 2017

9:30 – 11:00	Clinical relevance of AC (Anti-Cell) patterns (Jan Damoiseaux and Carlos Alberto von Mühlen) • Introduction, established guideline (Jan) • AC-1 to AC-14 nuclear patterns (Jan) • AC-15 to AC-23 cytoplasmic patterns (Carlos)
11:30 – 11:50	• AC-24 to AC-28 mitotic patterns (Manfred Herold)
11:50 – 12:20	Establishment of 2 new AC patterns: AC-0 and AC-29 (Manfred Herold and Werner Klotz) • Rationale for having these examples/patterns • Limitations • AC-0 negative examples (Manfred) • AC-29 Topo I-like description (Werner) • AC-29 – clinical relevance (Manfred)
12:20 – 12:50	Limits in defining AC patterns in the daily laboratory practice (Luis)
12:50 – 13:00	Does double staining co-localization help with assigning AC patterns? (Ed)
13:00 – 13:30	A re-visit/discussion in ANA reporting (moderate by Jan Damoiseaux) • Cytoplasmic positive is reported as ANA+ (Carlos) • Cytoplasmic positive is not reported as ANA+ (Michael Grünwald) • Anti-cellular antibodies = ANA? (Luis)

End