

International Consensus on Antinuclear Antibody Patterns (ICAP) 2025: what's new?

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Current Role of ANA

- From a screening test for connective tissue diseases to a tool for **patient stratification**
- Contribution to **phenotypic and prognostic** characterization

Therapeutic Implications

- Definition of **therapeutic targets** based on autoantibody profiles
- Selection of **responders** to biologic drugs
- Monitoring of treatment efficacy and adherence through **antibody profiling**

Challenges and Perspectives

- Standardization, harmonization of testing methods and interpretation
- Need for integrated clinical-serological databases
- Toward individual immunological profiling

What are the goals of ICAP?

- Promote harmonization of autoantibody nomenclature
- Refine interpretation of HEp-2 IFA patterns
- Emphasize immunological associations of HEp-2 IFA patterns
- Optimize HEp-2 IFA usage in patient care



ICAP Coordinators



Members



Honorary Member (deceased)



SPECIAL ARTICLE

Dr Eng M. Tan: a tribute to an enduring legacy in autoimmunity

MJ Fritzler¹ and EKL Chan²

¹University of Calgary, Cumming School of Medicine, Calgary, Canada; and ²Department of Oral Biology, University of Florida, Gainesville, USA

At the age of ninety years, Dr Eng Meng Tan has had a remarkable impact on the accumulated knowledge of autoimmune diseases, including seminal findings in systemic lupus erythematosus (SLE) and a wide range of other autoimmune diseases. Dating to the first description of the Sm (Smith) autoantibody in SLE, his focus has been the use of autoantibodies as probes to identify and elucidate novel cellular molecules and then translating these discoveries into biomarkers and immunoassays for a wide range of these diseases and, later, cancer. He led efforts to standardize autoantibody nomenclature and testing protocols. Through his mentorship a great number of trainees and collaborators have had remarkably successful careers, and by that virtue he has garnered a remarkable continuing legacy. *Lupus* (2017) 26, 208–217.

Key words: Autoantibodies; autoantigens; systemic lupus erythematosus; systemic autoimmune rheumatic diseases

Family, friends, former fellows, and colleagues recently gathered in La Jolla, California to celebrate the ninetieth birthday and over half a century of biomedical accomplishments of Dr Eng Meng Tan. Dr Eng Tan was born in Malaysia and immigrated to the United States where he received his MD degree from the Johns Hopkins University School of Medicine, Baltimore, in 1956. He continued training in internal medicine at Duke University Hospital in Durham, North Carolina, and Case Western University Hospitals in Cleveland, Ohio, where, under the mentorship of Melvin Kaplan he began studies of experimental renal disease. He was awarded a post-doctoral fellowship from the Arthritis Foundation in 1962 to explore autoantibodies in systemic lupus erythematosus (SLE) in Henry Kunkel's laboratory at The Rockefeller University in New York.¹ In 1965 Dr Tan was appointed Assistant Professor at Washington University School of Medicine in St. Louis, Missouri, and three years later was invited to join an eminent group of immunologists lead by Dr Frank Dixon at The Scripps Clinic and Research Foundation in La Jolla, California. By 1970 he was a Full Member and Head of the Division of Allergy and Immunology at Scripps.

In 1977, Dr Tan and his laboratory moved to the University of Colorado Health Sciences Center in Denver, Colorado, where he held the position of Head of the Division of Rheumatic Diseases. He returned to Scripps in 1982 to become Director of the newly established W. M. Keck Autoimmune Disease Center, which included the Divisions of Clinical Immunology, Rheumatology Research, and Clinical Rheumatology at the later renamed The Scripps Research Institute (TSRI). He is currently Professor Emeritus at TSRI.

Dr Tan's research interests have been in the field of autoimmunity with a special focus on the molecular and physiological nature of cellular antigens that are the targets of human autoantibodies and then translating these discoveries into diagnostic biomarkers in clinical medicine. This interest spanned the study of autoantibodies in systemic autoimmune rheumatic diseases (SARDs) such as SLE, rheumatoid arthritis, systemic sclerosis, Sjögren's syndrome, and other autoinflammatory conditions, to a more recent interest in autoantibodies in cancer (Table 1).

His approach to clinical and research medicine has been an exemplar of how information from clinical medicine and cell and molecular biology can be interconnected and thus further the understanding of pathogenic pathways in disease.¹⁵⁰

During his fellowship years in the laboratory of Henry Kunkel, Dr Tan made several seminal discoveries that were the inspiration for much of the

www.anapatterns.org



Eng Meng Tan 1927–2024

“He Taught Us to Always Go Deeper”

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ANA Patterns

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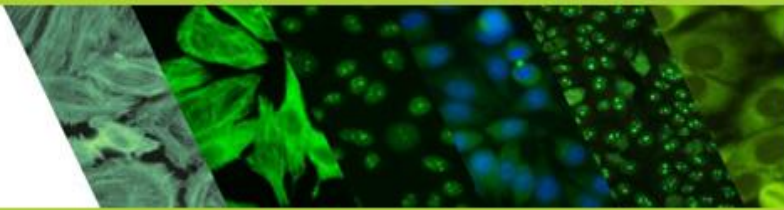
English Português Español Italiano Dutch Deutsch 简体中文 繁體中文 Français Türkçe Русский Bosanski Magyar Ελληνικά 한국어 日本語 ไทย Українська

Welcome to ANApatterns.org, the official website for the International Consensus on Antinuclear Antibody (ANA) Patterns (ICAP). ICAP was initiated as a workshop aiming to thoroughly discuss and to promote consensus regarding the richness and nuances of morphological patterns observed in the indirect immunofluorescence assay on HEp-2 cells (HEp-2 IFA). The ICAP initiative was implemented at the 12th International Workshop on Autoantibodies and Autoimmunity (IWAA, São Paulo, Brazil) by members of the Autoantibody Standardization Committee (ASC), a subcommittee of the International Union of Immunological Societies (IUIS) Quality Assessment and Standardization Committee and affiliated with the Centers for Diseases Control and Prevention (CDC). The ICAP committee is operating as an ASC sub-committee.

Illustrative images were submitted for each pattern and ICAP members voted and selected the most representative ones paying attention to pixel dimension, resolution, and size. The highest ranked images for each pattern are displayed on this web site. (For an introduction of the website with some graphic images, [click here](#).)

The ICAP committee acknowledges that the term ANA is outdated as discussed in several publications [1, 2] and yet ANA is still most commonly used in the current literature. We have proposed to use the term HEp-2 IFA to precisely describe the test in practice and used in most ICAP publications [3, 4]. Anti-Cell (AC) is used in ICAP coding of HEp-2 IFA patterns [3, 4]. Although the term anti-cellular antibody has been used in place of ANA by ICAP [2] and others [1], there is support for and reservations about its accuracy because the term "anti-cellular" also encompasses a wide spectrum of autoantibodies detected by other assays – e.g. ANCA, ASMA, APCA.

1. Agmon-Levin, N., et al., International recommendations for the assessment of autoantibodies to cellular antigens referred to as anti-nuclear antibodies. Ann Rheum Dis, 2014. 73(1): p. 17-23.
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3. Damoiseaux, J., et al., Clinical relevance of HEp-2 indirect immunofluorescent patterns: the International Consensus on ANA patterns (ICAP) perspective. Ann Rheum Dis, 2019. 78(7): p. 879-889.



English

Chinese

Greek

Thai

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Spanish

Bosnian

Japanese

German

Italian

Korean

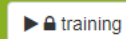
Russian

Portuguese

Website translations - team efforts

We thank the many colleagues from different countries to help with ICAP and these translations





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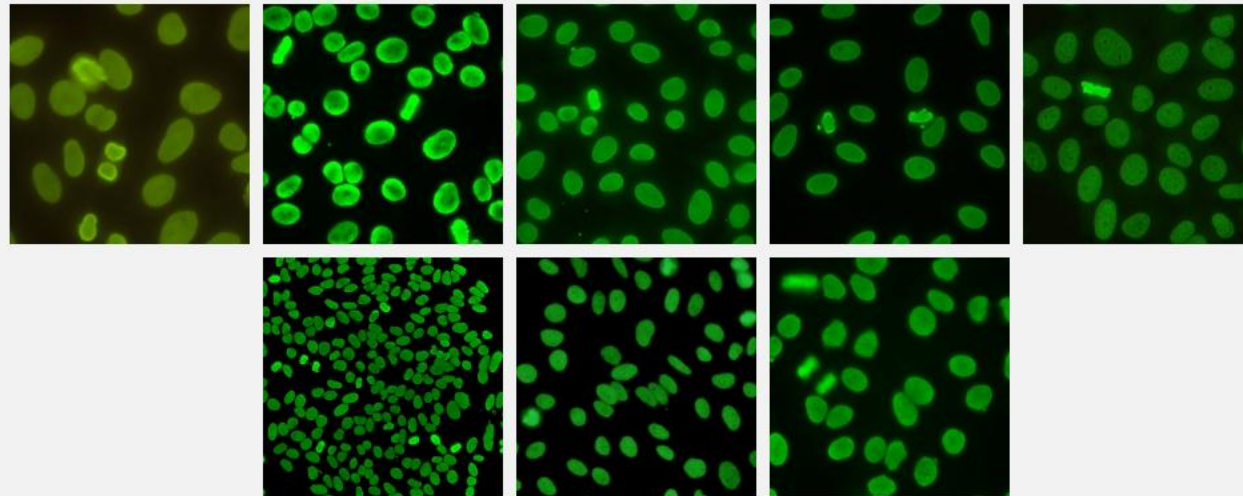
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AC-1 - Nucleare Omogeneo



Italiano

English

Sinonimo	Diffuso	Diffuse
Descrizione	Fluorescenza omogenea e regolare nel nucleoplasma. I nucleoli potrebbero dare segnale fluorescente o meno, a seconda del substrato cellulare. Le cellule mitotiche (metafase, anafase e telofase) hanno un'intensa fluorescenza a livello della cromatina, con colorazione ialina omogenea.	Homogeneous and regular fluorescence across all nucleoplasm. The nucleoli may be 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.
Associazione Antigenica	dsDNA, nucleosomi, istoni	dsDNA, nucleosomes, histones

Associazione Clinica

Informazioni di primo livello

**Rilevanza clinica
& Lista delle abbreviazioni**

Clinical Relevance

First level information

About Clinical Relevance & List of Abbreviations

- Presente in pazienti con LES, epatite cronica autoimmune o artrite idiopatica giovanile
- In caso sospetto clinico di il LES, si raccomanda l'esecuzione del test per anticorpi anti-dsDNA, da soli o in combinazione con il complesso dsDNA/istoni (nucleosomi/cromatina); gli anticorpi anti-dsDNA sono inclusi tra i criteri classificativi per il LES (15, 16)

- Found in patients with SLE, chronic autoimmune hepatitis or juvenile idiopathic arthritis
- If SLE is clinically suspected, it is recommended to perform a follow-up test for anti-dsDNA antibodies, alone or in combination with dsDNA/histone complexes (nucleosomes/chromatin); anti-dsDNA antibodies are included in the classification criteria for SLE (15, 16)

From association to clinical relevance

Ann Rheum Dis 2019;**78**:879–889.

Recommendation

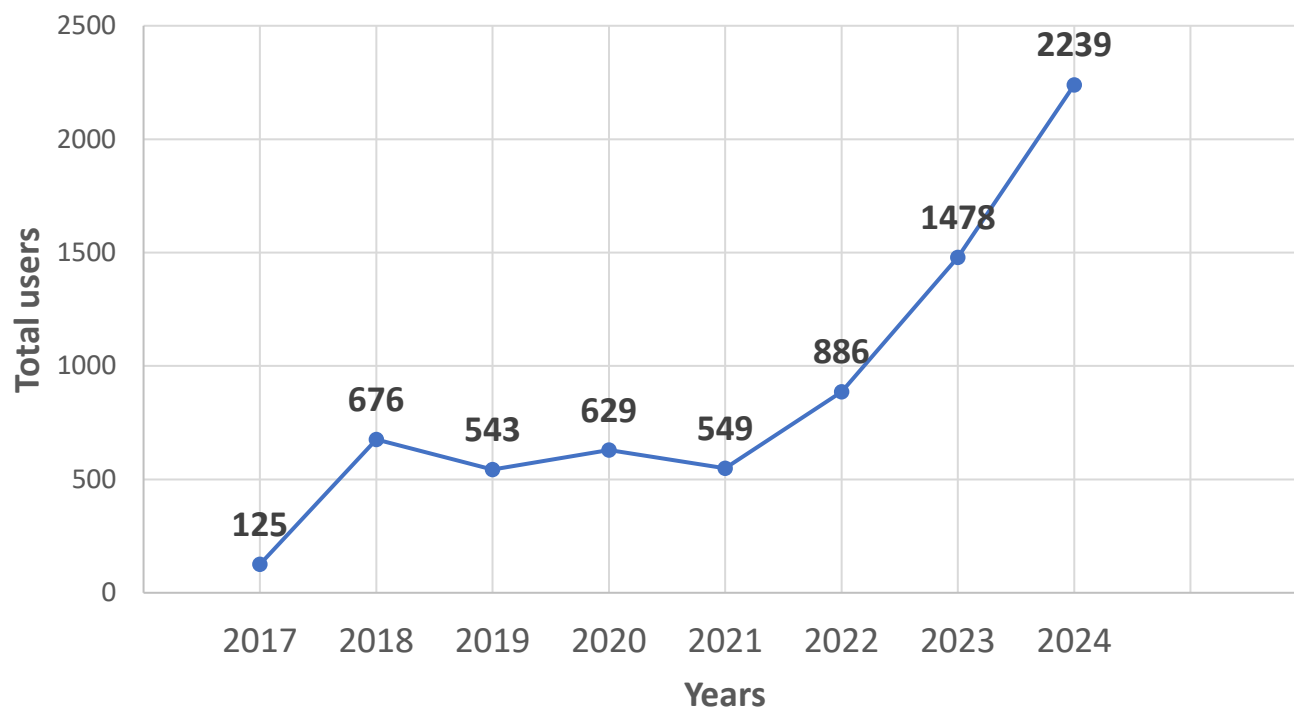


Clinical relevance of HEp-2 indirect immunofluorescent patterns: the International Consensus on ANA patterns (ICAP) perspective

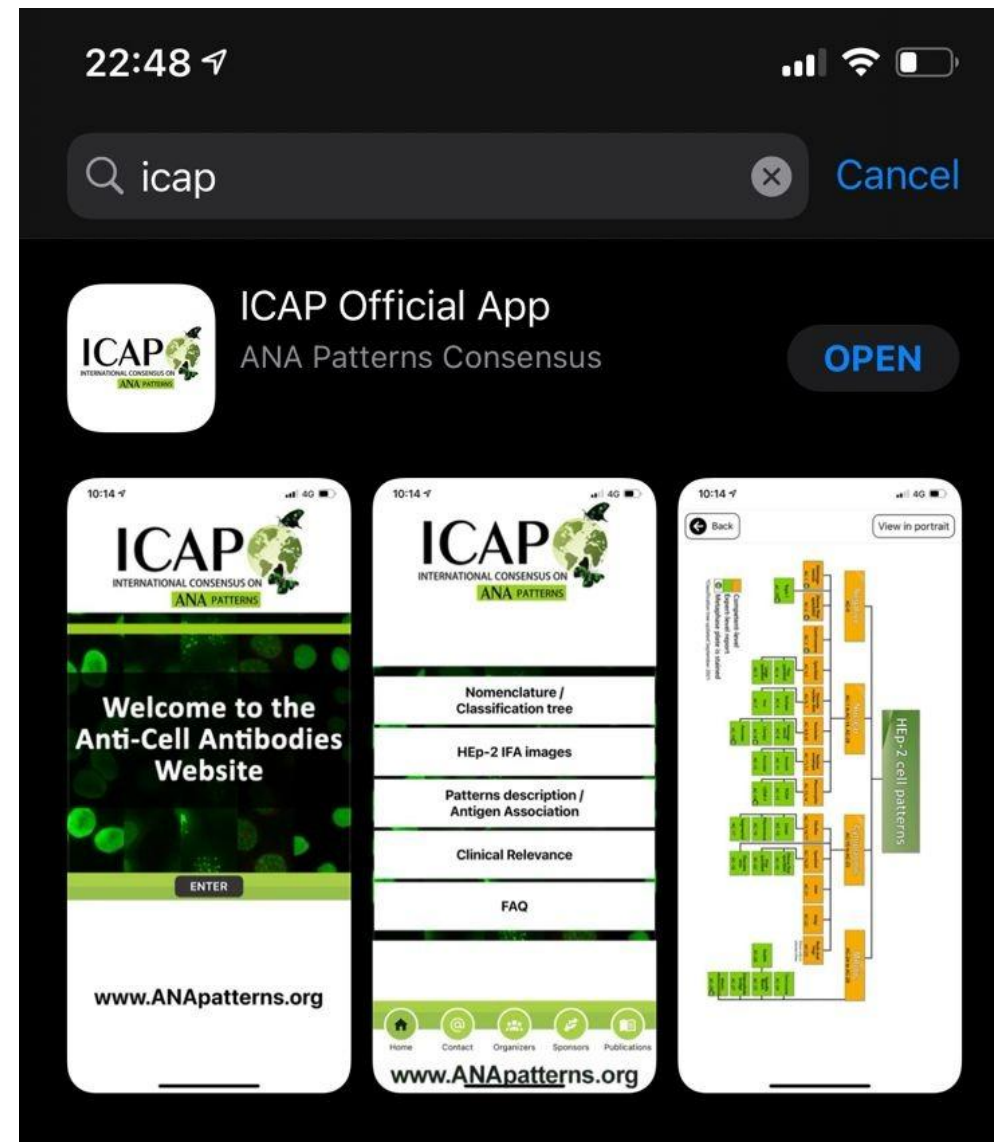
Jan Damoiseaux,¹ Luis Eduardo Coelho Andrade,² Orlando Gabriel Carballo,^{3,4} Karsten Conrad,⁵ Paulo Luiz Carvalho Francescantonio,⁶ Marvin J Fritzler,⁷ Ignacio Garcia de la Torre,⁸ Manfred Herold,⁹ Werner Klotz,¹⁰ Wilson de Melo Cruvinel,¹¹ Tsuneyo Mimori,¹² Carlos von Muhlen,¹³ Minoru Satoh,¹⁴ Edward K Chan¹⁵

Number of registered users by year

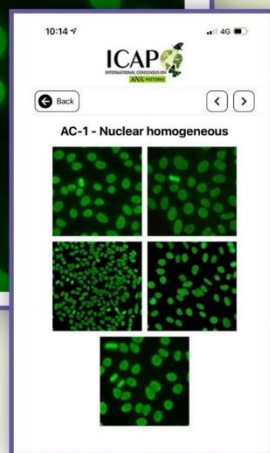
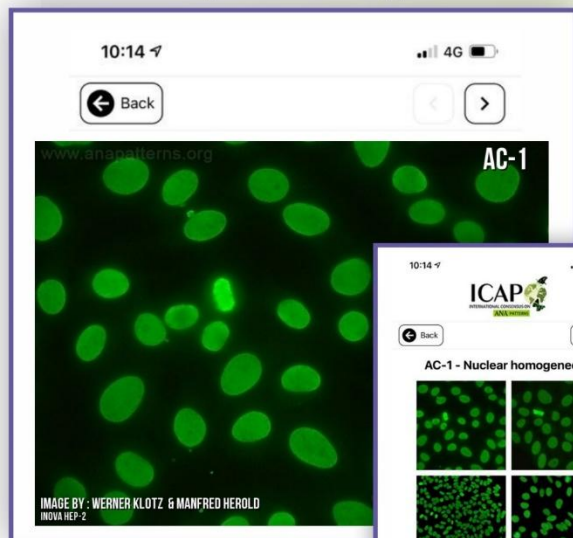
ANApatterns Users by Year



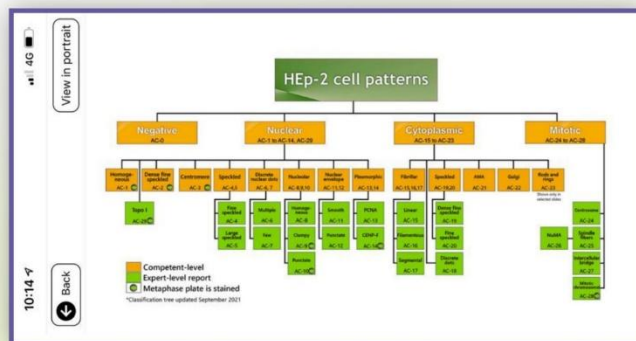
Source: Anapatterns website (Survey in August 9,2025)



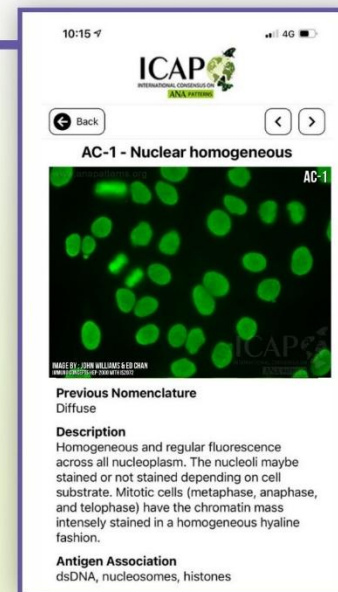
HEp-2 IFA images



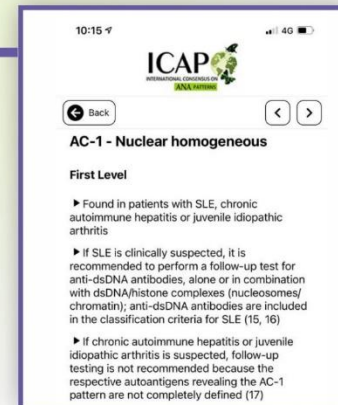
Nomenclature / Classification tree



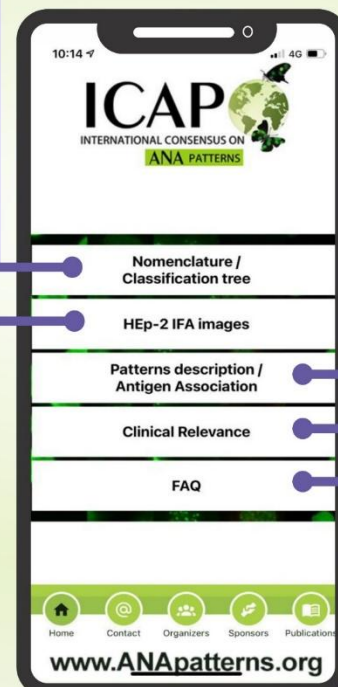
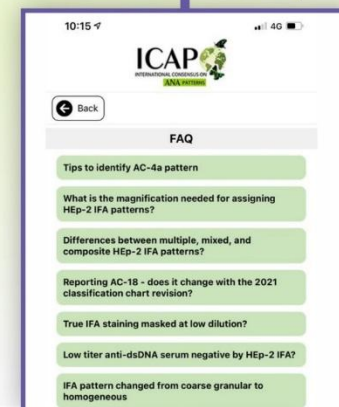
Patterns description Antigen Association



Clinical Relevance



FAQ

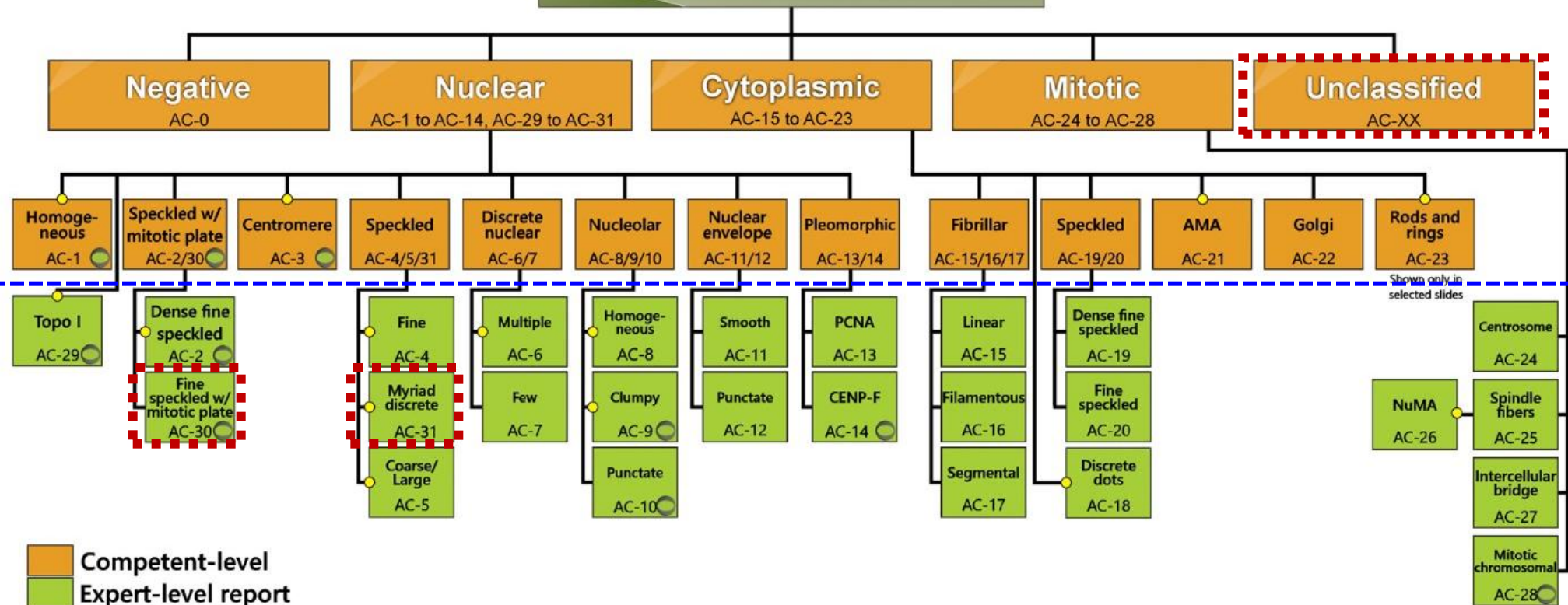


Available in both iOS and Android operating systems

Feb 2025 Chart

HEp-2 cell patterns

31 patterns catalogued by ICAP
in addition to AC-0 & AC-XX



Competent-level patterns

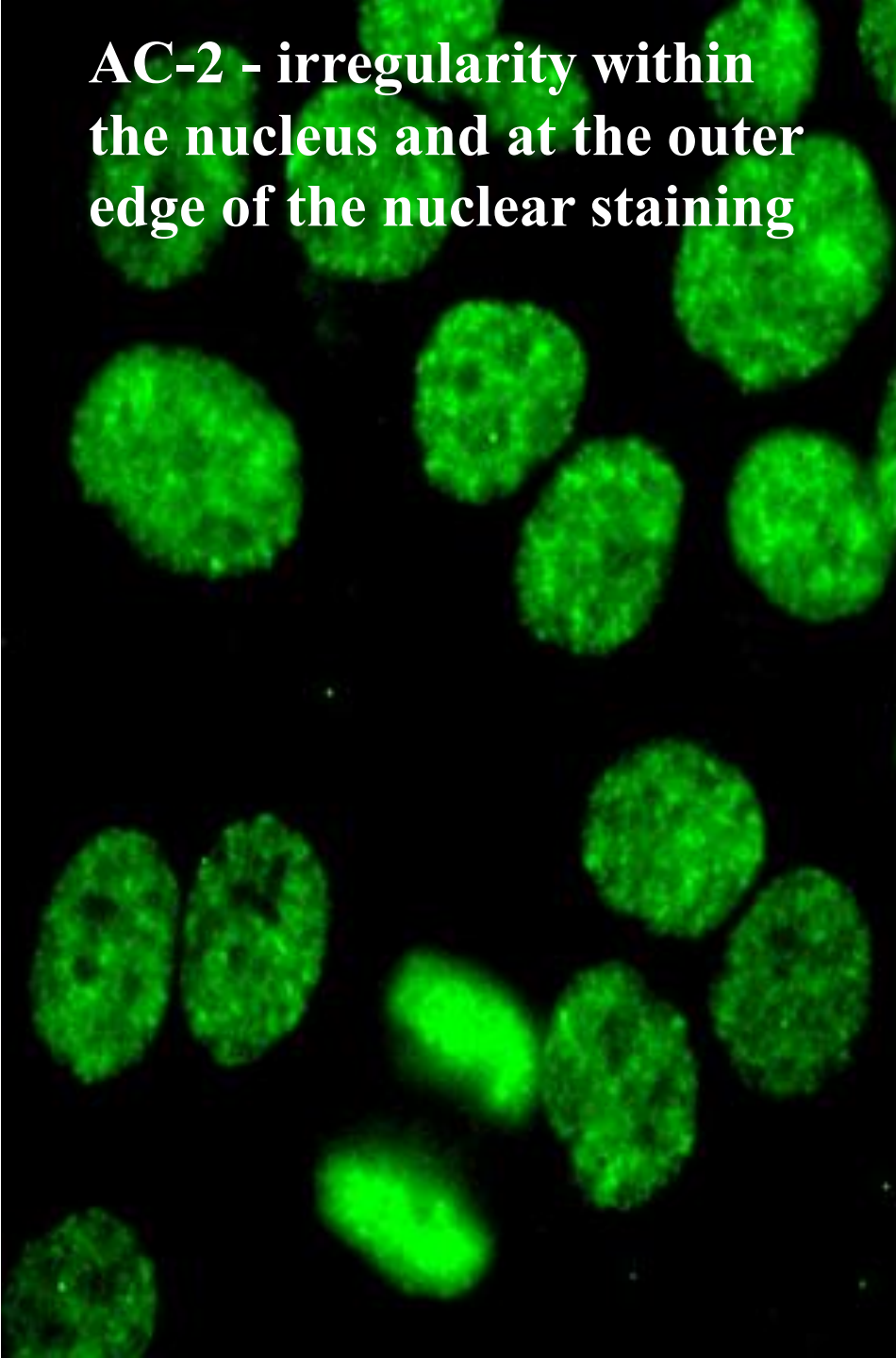
Expert-level patterns

- Competent-level
 - Expert-level report
 - Metaphase plate is stained
 - Reference materials available at www.AutoAb.org
- *Classification tree updated February 2024

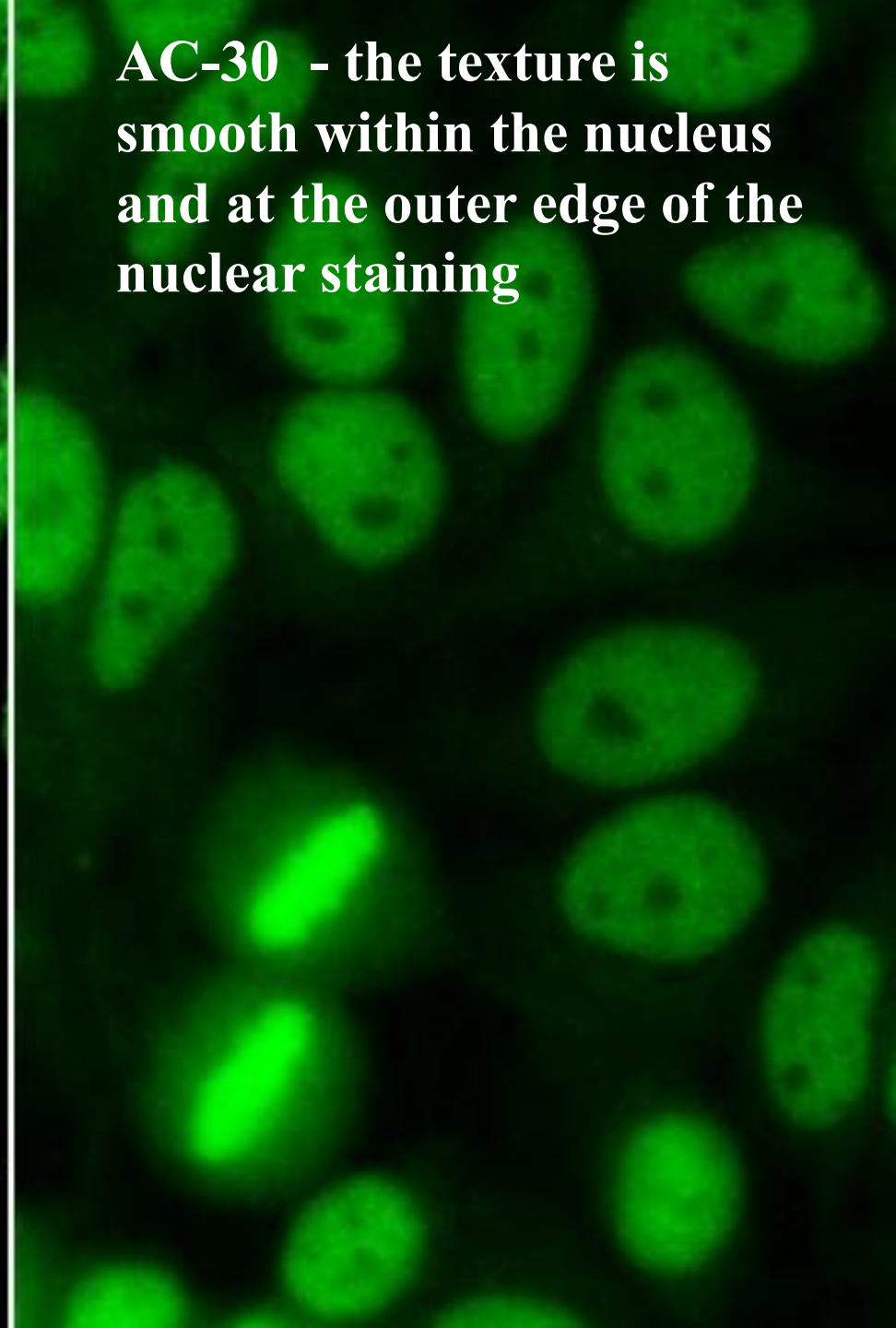


AC-30 - Fine
Nuclear Speckled
with Mitotic Plate
– formerly pseudo-DFS

**AC-2 - irregularity within
the nucleus and at the outer
edge of the nuclear staining**



**AC-30 - the texture is
smooth within the nucleus
and at the outer edge of the
nuclear staining**



Autoantibody associations of AC-2 and AC-30

AC-30

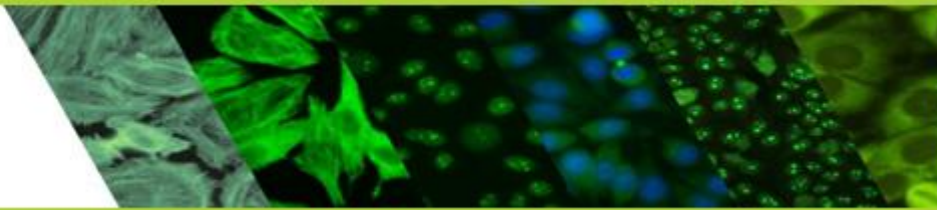
- dsDNA
 - Nucleosome
 - Histones
 - Sm/U1
 - TSS/SSA/Ro60
- Some of these autoantibodies

Most frequently, NONE

AC-2

- DFS70 (LEDGF-p75)

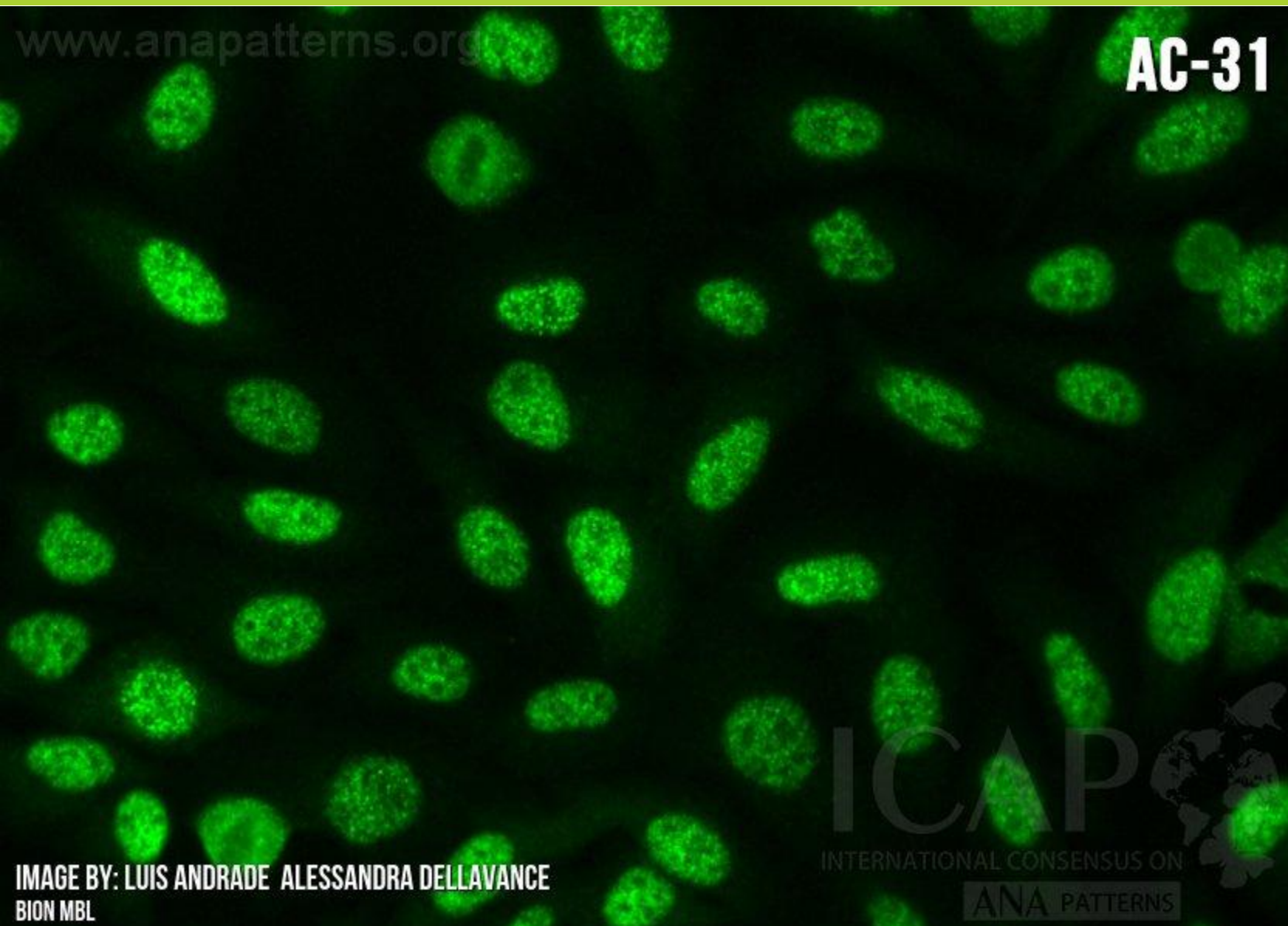
Seldom anti-DFS70-negative



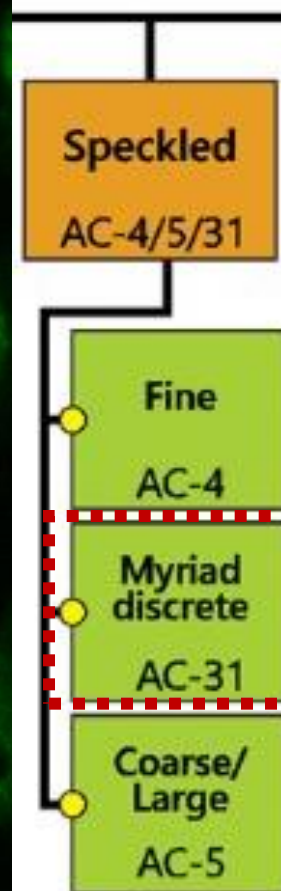
AC-30 - Clinical Relevance

First level information

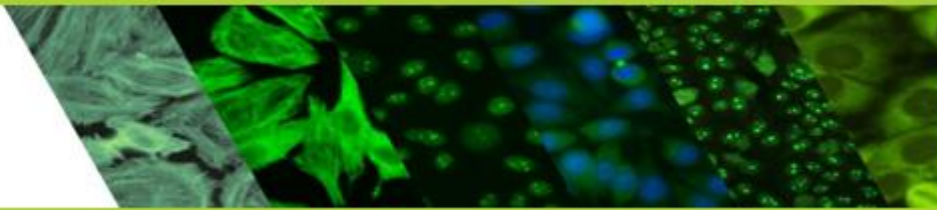
- The AC-30 pattern is commonly observed in individuals without any apparent autoimmune disease. However, since it may reflect the combined reactivity of several antinuclear antibodies, the AC-30 pattern can occasionally be seen in patients with systemic autoimmune rheumatic diseases, especially in cases with multiple antinuclear antibodies [2, 5].



AC-31



AC-31
Myriad discrete
nuclear
speckled
– formerly AC4a

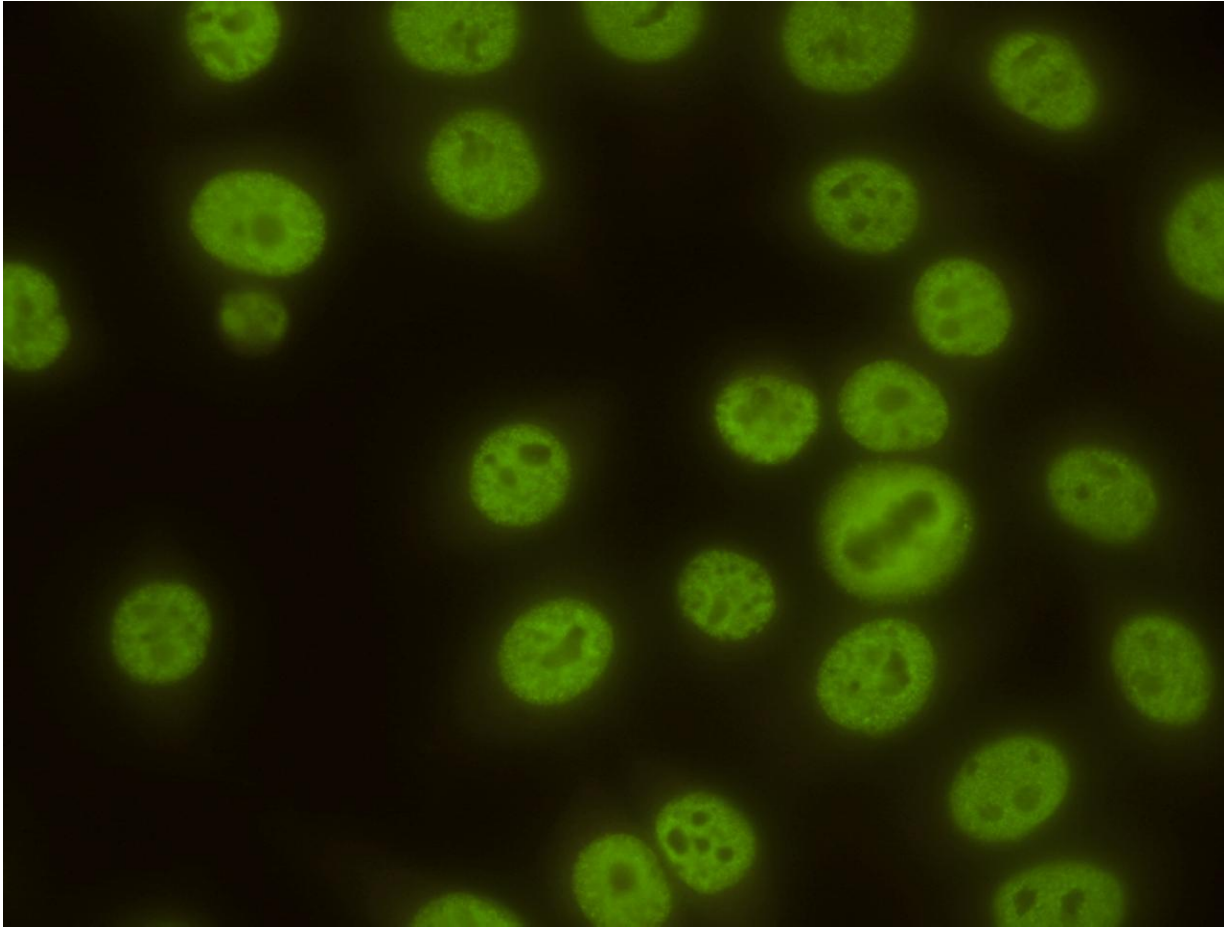


AC-31 - Clinical Relevance

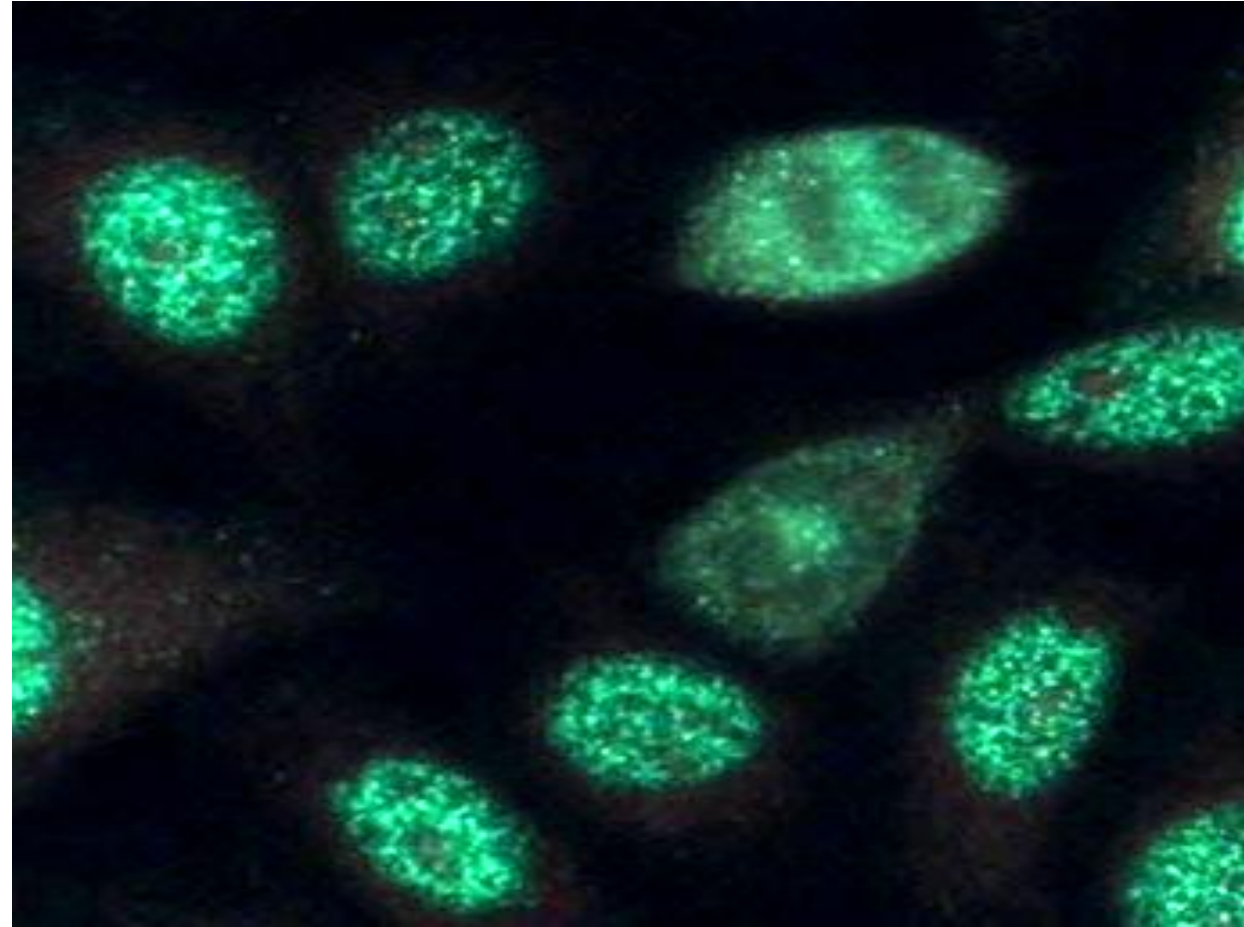
First level information

- Because of the strong association with anti-TROVE2/Ro60 antibodies, the AC-31 pattern is frequently seen in patients with systemic lupus erythematosus (SLE) and Sjögren's disease (SjD). It is not commonly observed in healthy individuals, as opposed to the AC-4 plain fine speckled nuclear pattern that is one of the most frequent HEp-2 IFA patterns in asymptomatic individuals and patients with no systemic autoimmune disease.

AC-4



AC-31



Autoantibody associations of AC-4 and AC-31

AC-4

- TROVE2/Ro60 (SS-A/Ro60)
- SS-B/La
- Mi-2
- TIF
- α 1 β
- Ku

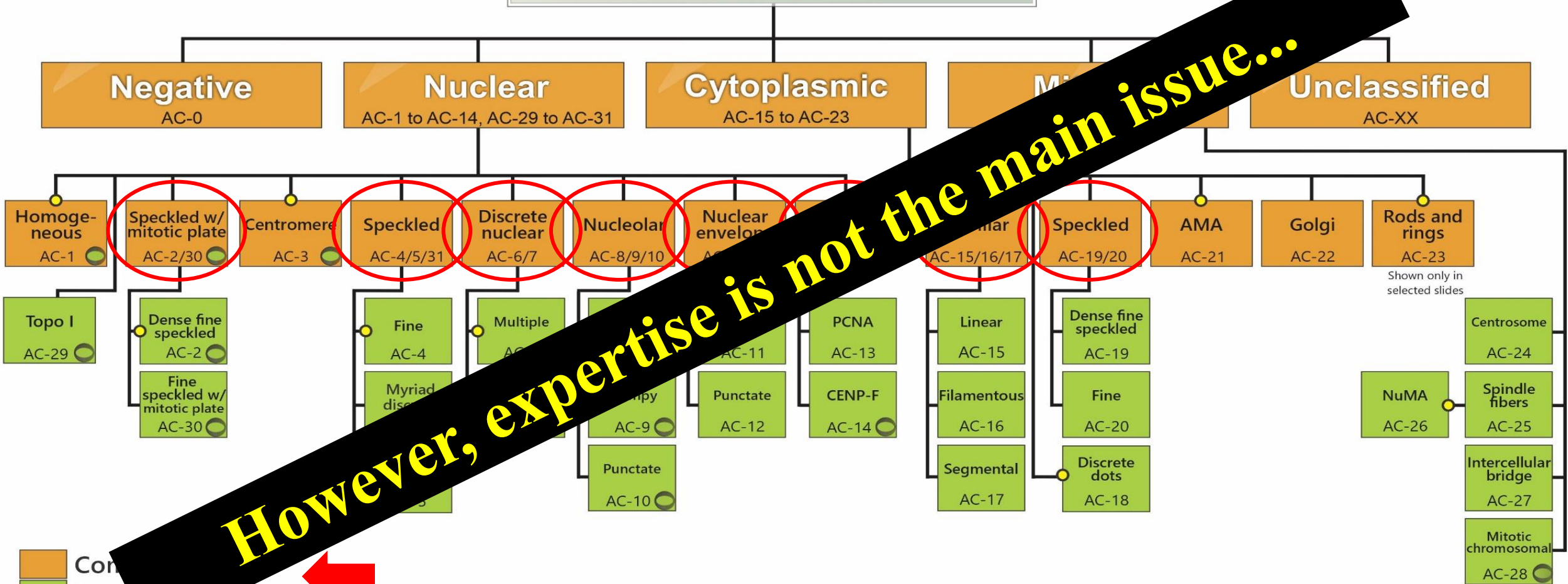
Most frequently, NONE

AC-31

- TROVE2/Ro60 (SS-A/Ro60)
- With or without SS-B/La

Seldom anti-TROVE2-negative

Hep-2 cell patterns



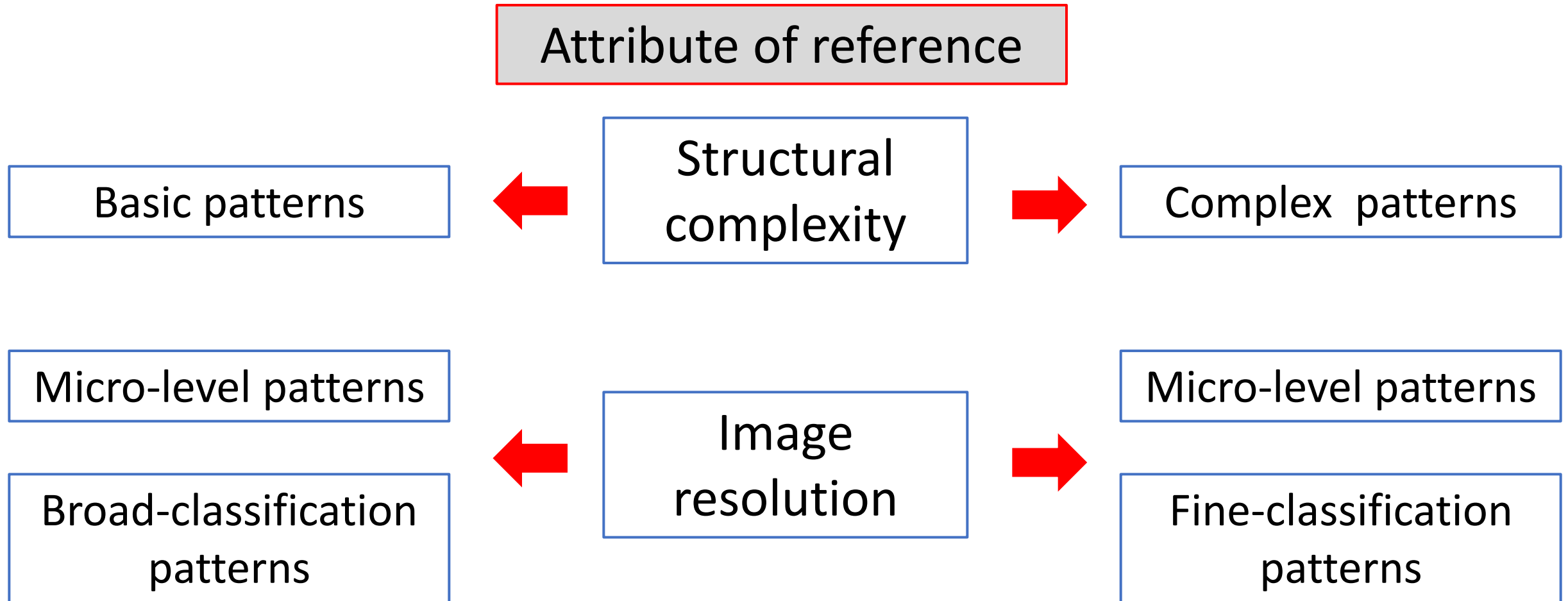
However, expertise is not the main issue...

- Confidence
- Expert report
- Metaphase plate is stained

Reference materials available at www.AutoAb.org

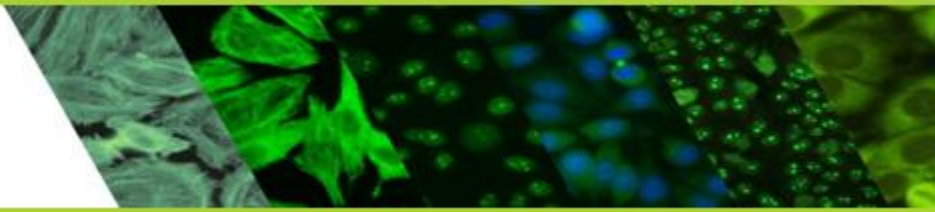
*Classification tree updated February 2024

Possible alternative designations for competent/expert-level patterns



General comments on AC- pages updates

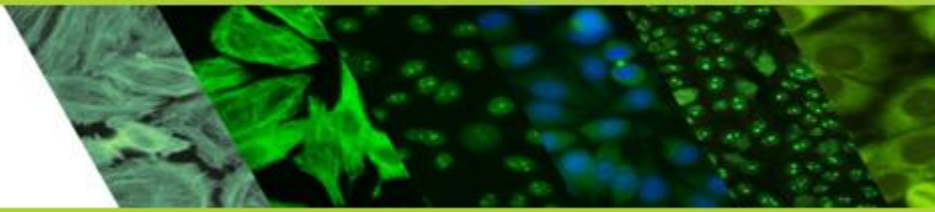
- **Descriptions of patterns:** more precise on what are stained and sometimes including what are not stained.
- **More information:** Some full names of antigens and full name of diseases are provided.
- **References:** Renumbering, additions, deletions, and updates.



AC-7 (Few nuclear dots)

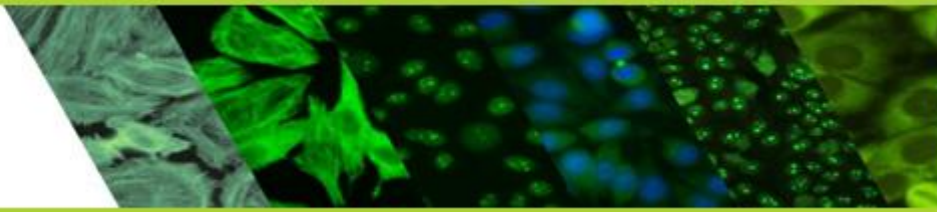
Clinical Relevance Second level information:

The detection of both anti-p80-coilin (AC-7) and anti-DFS70 (AC-2) was reported in Japan and it is also the experience in some reference laboratories in Europe. The implication is that AC-7 thus can be found in people without SARD as reported (*Goto et al 2006*).



AC-8 (Homogeneous nucleolar)

Description: Diffuse fluorescence of the entire nucleolus, while the metaphase plate shows no staining. **Frequently seen in combination with a fine speckled nuclear staining (AC-4).**



AC-13 (PCNA) AC-14 (CENP-F)

Clinical Relevance (Second level information):

Other nuclear pleomorphic patterns that are distinct from AC-13 or AC-14 should be reported as unclassified patterns (AC-XX) with an appropriate description.

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NEW TRAINING MODULE RELEASED!



Module 2: AC-XX PATTERNS
(Unusual HEp-2 IFA staining
patterns not catalogued in the
ICAP classification tree)

This training presents general information
about coding unusual HEp-2 IFA staining
patterns under the generic code AC-XX.

This module focuses on
the AC-XX patterns, which
include unusual HEp-2 IFA
patterns not yet catalogued
in the official ICAP
classification tree.

To access the module,
simply register, log in, and
click on the training icon in
the top menu of the
platform.

Access:
www.ANAPatterns.org

ICAP current initiatives

- Online ICAP training module #2 on AC-XX is online and others are in the making.

RECOMMENDATIONS ON REPORTING AC-XX PATTERNS



Module 2:
RECOMMENDATIONS ON
REPORTING AC-XX
PATTERNS

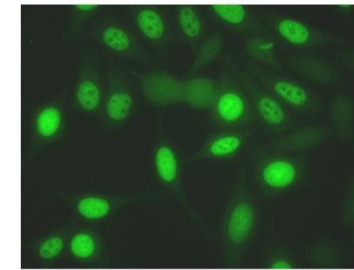
[VIEW DETAILS](#)

[VER DETALLES](#)

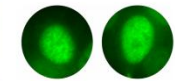
RECOMMENDATIONS ON REPORTING AC-XX PATTERNS

www.ANAPatterns.org

AC-XX SG2NA Nuclear Pattern



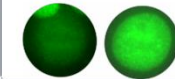
Fine speckled nuclear staining of S/G2 interphase cells



G1 interphase cells not stained



Metaphase plate not stained (or with a very weak peripheral fine speckled staining)



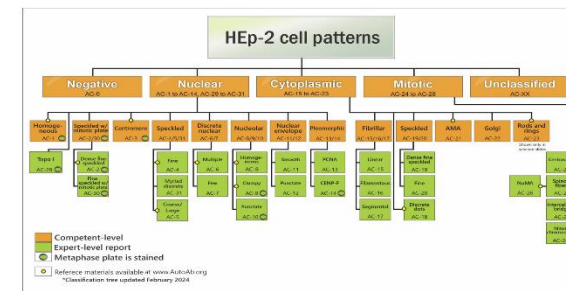
No staining of nucleoli

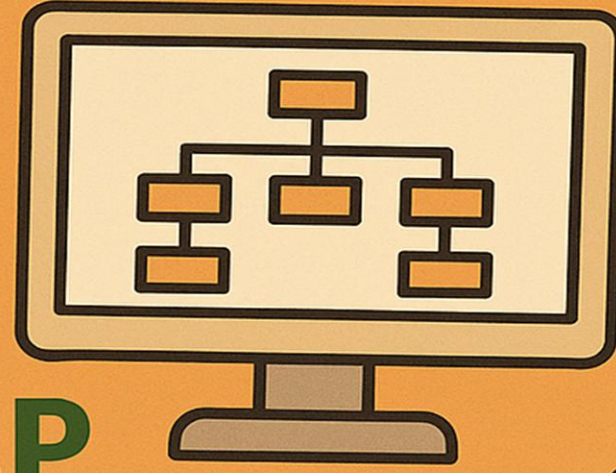


Landberg G, Tan EM. *Exp Cell Res*. 1994;212(2):265-61.
Muro Y, Chan EK, Landberg G, Tan EM. *Biochem Biophys Res Commun*. 1995; 27:207(3):1029-37.
Guffroy A, Dima A, Nespola B et al. *Joint Bone Spine*. 2016;83(3):330-4.

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WHY AC-XX?



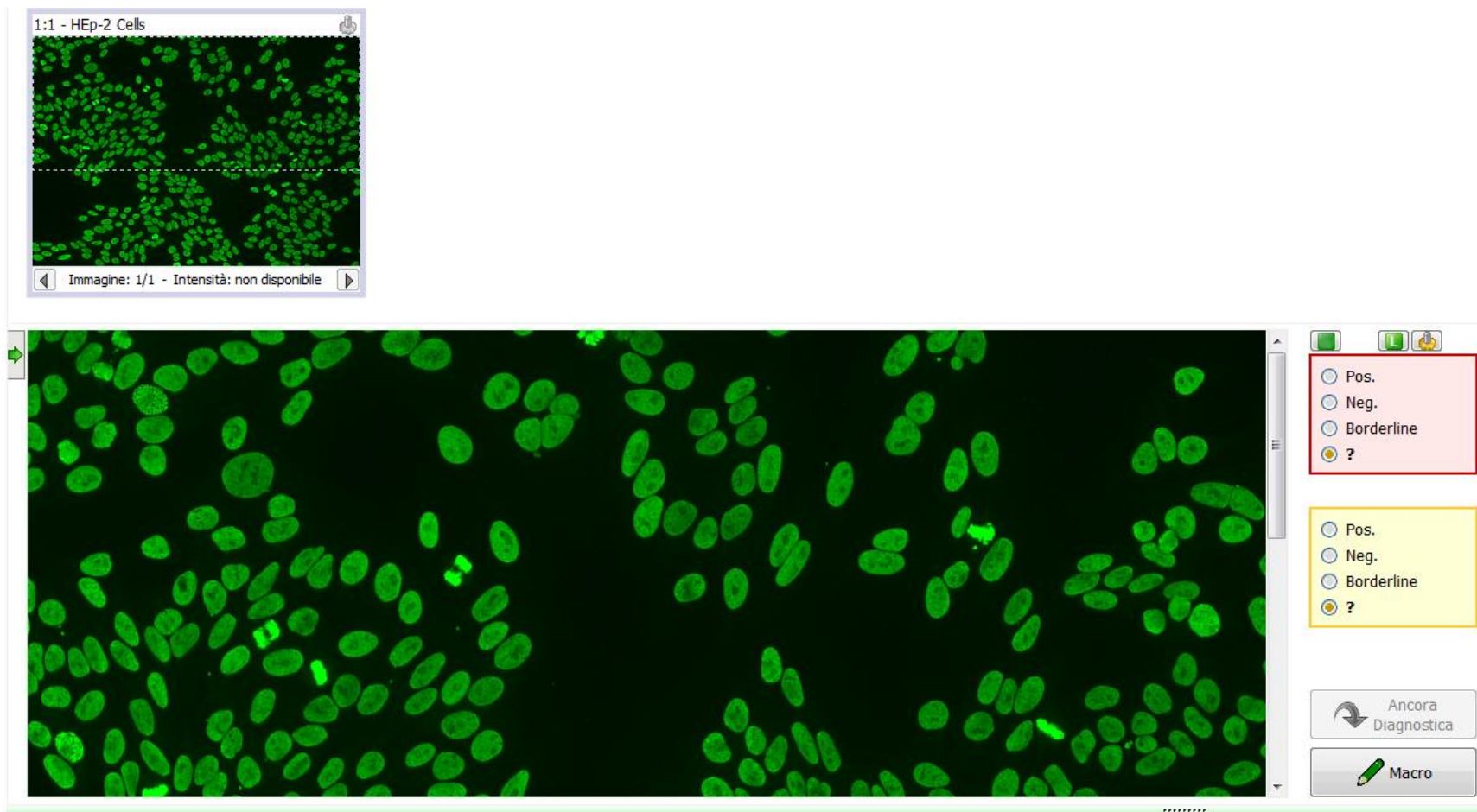


ICAP NOMENCLATURE

should be implemented
in all our daily work
tools



ICAP and middleware



Controllo: 9

PK

Positive/Negative

- ☒ POSITIVO
- ☒ NEGATIVO
- ☒ BORDERLINE
- ☐ NON VALUTABILE

Pattern

Classificatore ...

- ☒ OMOGENEO (AC-1)
- ☒ CENTROMERICO (AC-3)
- ☒ SPECKLED (AC-4,5)
- ☒ MULTI NUCLEAR DOTS (AC-6)
- ☒ NUCLEOLARE (AC-8)
- ☒ MEMBRANA NUCLEARE (AC-11-12)
- ☒ CITOPLASMATICO GRANULARE (...)
- ☒ MITOTICI (AC-24,25,26,27,28)

Ancora ...

- ☐ DENSE FINE SPECKLED (AC-2)
- ☐ FEW NUCLEAR DOTS (AC-7)
- ☐ PCNA-LIKE (AC-13)

☐ Reclamare il risultato del computer

Valida il risultato finale



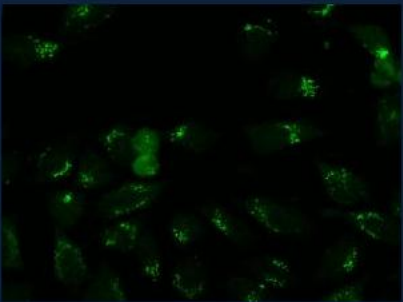
Atlante /

ANA ICAP

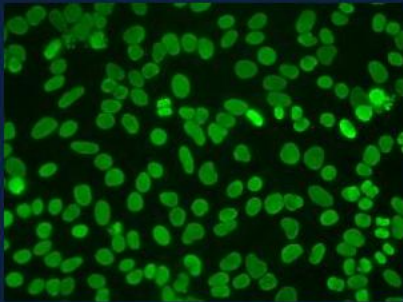


FITC

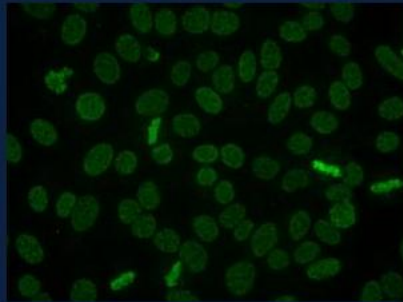
DAPI



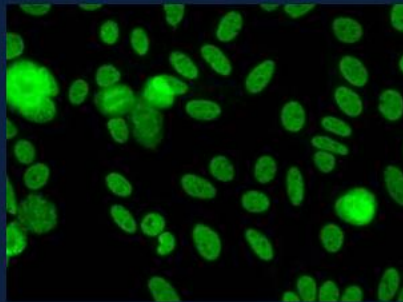
AC-22, Golgi-like



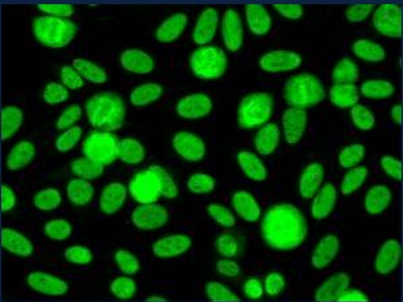
AC-1, Homogeneous



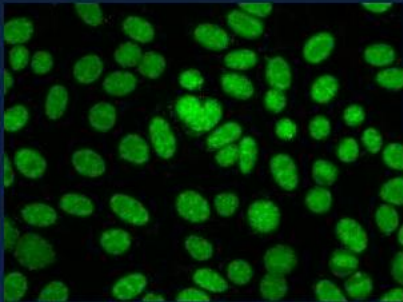
AC-2, DFS70



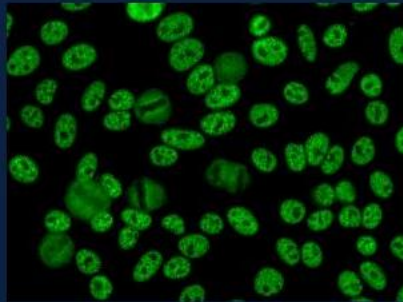
AC-4, Mi2, Speckled



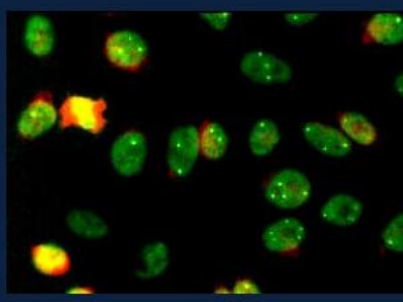
AC-4, Ku, Speckled



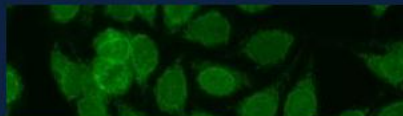
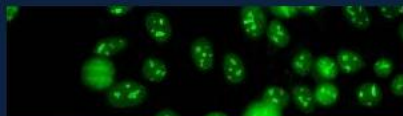
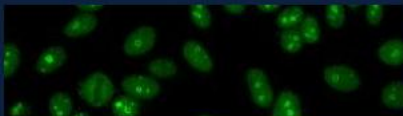
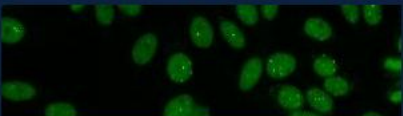
AC-4, SSB/La, Speckled



AC-5, Speckled



AC-7, p80 coilin



HOME

FULL RUN

SCANNING

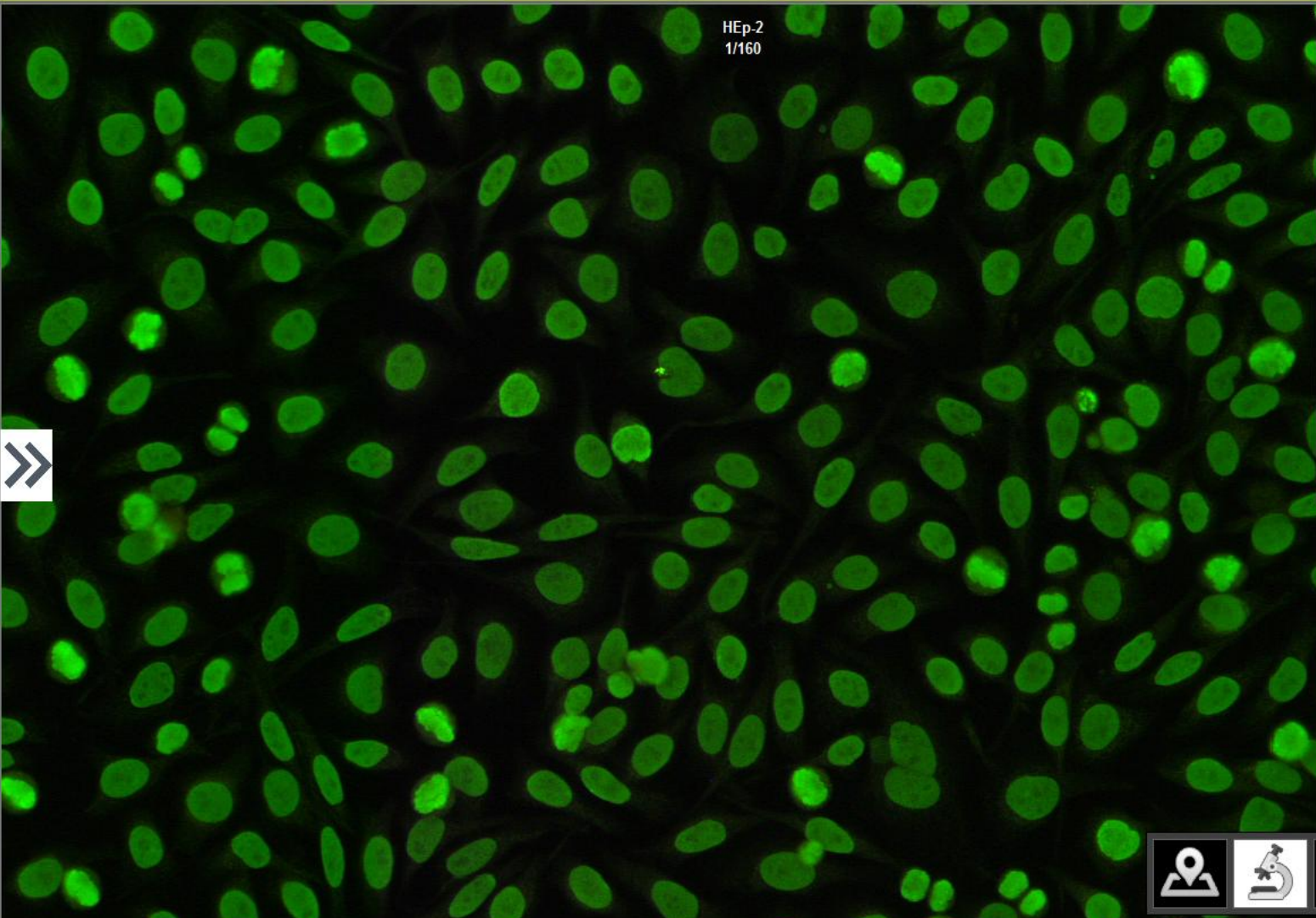
VALIDATION

ARCHIVE



VALIDATION
Session: Maria prove lotto 094 e IM...





HEp-2
1/160

Fit

4x

10x

20x

40x

20.0x



Patient info

Sample Id: 4340126638 Patient Id: 

Name: xxxxxxxx Last name: xxxxxxxx

Gender: xxxxxxxx Age: xxxxxxxx

Test Result: POSITIVE (1/160)

R-S-W	Titration	Raw result	Result	Invalid	
1-1-6	1/80	POS. 91%			
1-1-7	1/160	POS. 59%			

Patterns: AC-1

Details

Atlas

AC-1 (91%)	AC-8	AC-3
AC-5	AC-4	AC-6
AC-7	AC-21	AC-11

Extra titrations

1	2	4	8	16	20	32	40
---	---	---	---	----	----	----	----

Additional

Extra tests

History

Patient

Mitoses





VALIDATE



< Campioni ^ ▾ Helios 2 - Campione 10/10

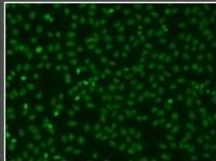
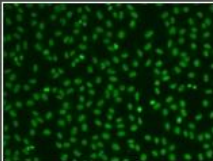
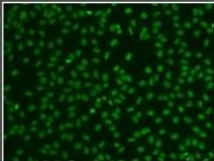
 Id: 0611760505
07/06/2021
Serum

Id: f4t4g
♀ Omogeneo ANA
Data di nascita: 03/02/1966
58 Anni

▾ Dettaglio

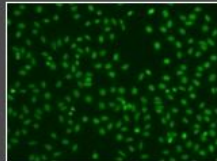
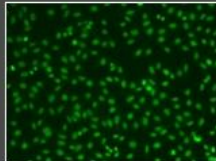
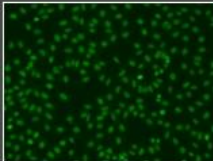
   

Test		Ris. Qn.	Ris. Ql.	Commento
	ANA	X		fdfdsfdsfdsfdsdf test
		Diluizione	Pattern	Add Pattern
	^	80	AC1_Omogeneo	
	  			
	EEPT 1:640			
ANA Titolo		1:640		

Id: 111370223IB
07/06/2021
Serum

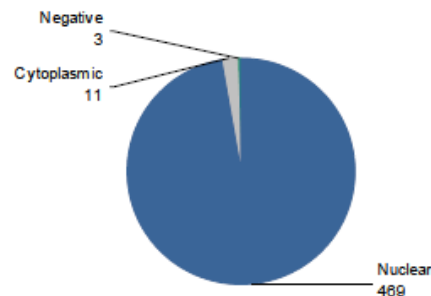
Id: 111370223IB
07/06/2021
Immunologia
Routine

07/06/2021
ANA Titolo, ANA

Test	Ris. Qn.		Ris. Ql.	Commento	
ANA				internal comment	
	Diluizione	Risultato	Pattern	Add Pattern	
	80	1	AC1_Omogeneo		
					
	 EEPT 1:5120				
ANA Titolo	1:5120				

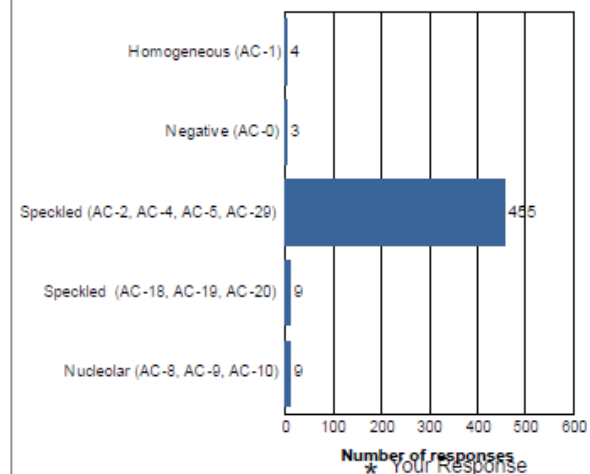
ICAP and UK NEQAS

ANA- IIF - Location of staining in HEp-2/2000 cells

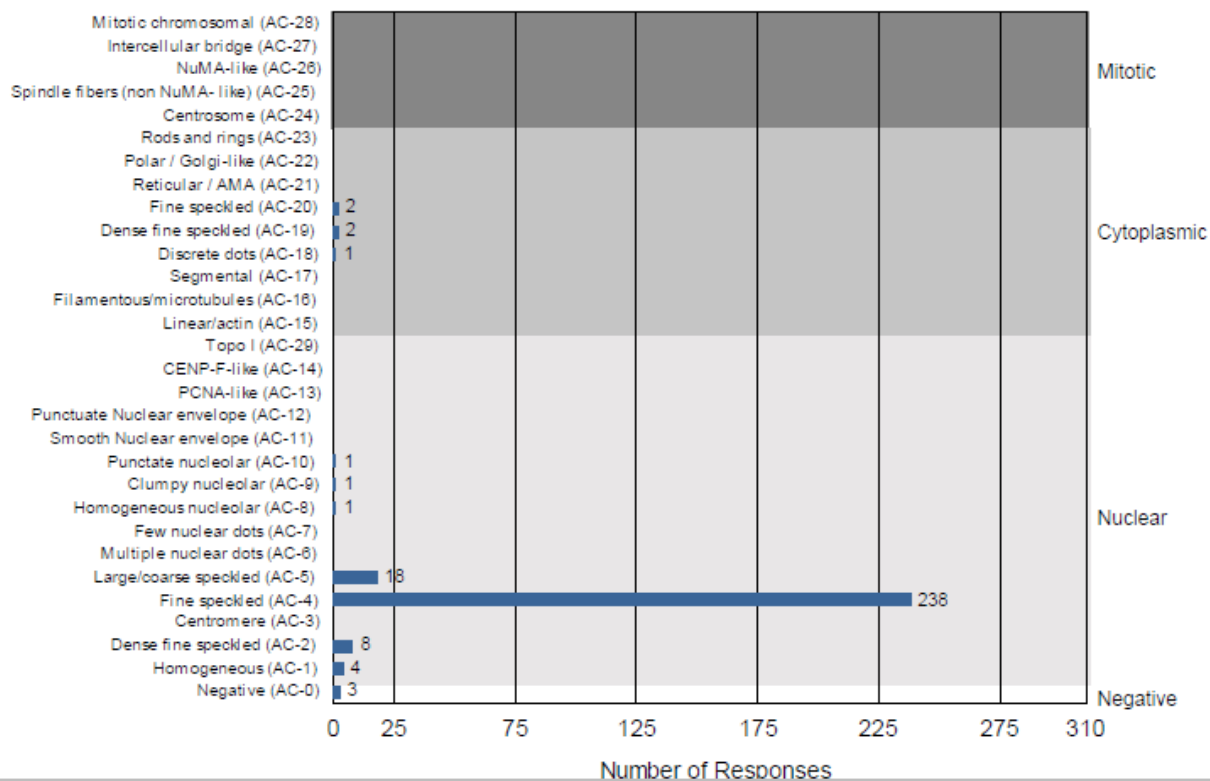


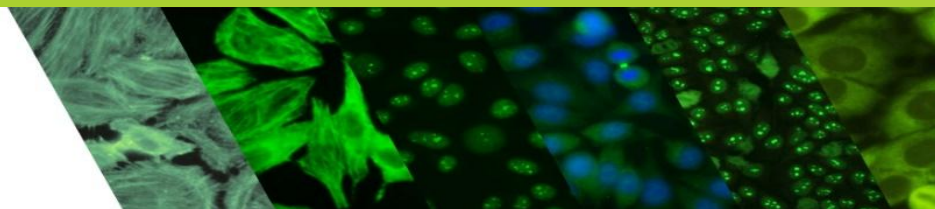
Your Response:

ANA- IIF Staining patterns



AC pattern breakdown





Italian model for the anti-nuclear antibody (ANA) test report

SURNAME, NAME				
Test	Matrix	Results	Units	Range
HEp-2 indirect immunofluorescence assay test (Antinuclear Antibody - ANA) <i>Method: IFA on HEp-2 cells</i> <i>Screening Dilution: 1:80</i> Pattern Titer Possible antigen association: U1RNP, Sm, SS-A/Ro60, SS-B/La, Mi-2, TIF1y, Ku, RNA Polymerase III	<i>Serum</i>	Positive	<i>* Titer</i>	<1:80
			Nuclear Speckled (AC-4,5) 1:160	

ANA nomenclature and associated specificities are in accordance with the International Consensus on ANA Pattern ICAP (www.ANApatterns.org).
Titers <=1:160 in the absence of anti-ENA, anti ds-DNA antibodies positivity and/or clinical signs are to be considered negative.

Standardization of the nomenclature of patterns and further harmonisation of the ANA test, including estimation of antibody levels and combinations with specific assays, may contribute to a better interpretation of ANA testing

