

# Atualização sobre os consensos de FAN: VI Consenso brasileiro e Consenso Internacional (ICAP)

**Wilson de Melo Cruvinel**



**PUC  
GOIÁS**

**ICAP**  
INTERNATIONAL CONSENSUS ON  
ANA PATTERNS

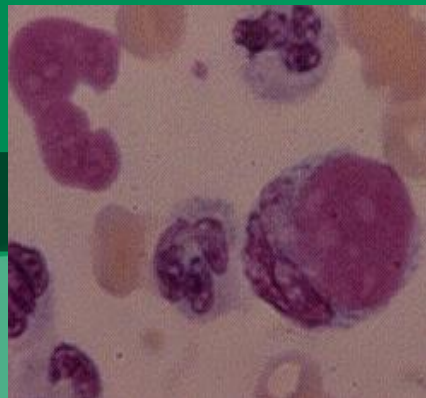


**CBA**  
Consenso Brasileiro de  
Autoanticorpos

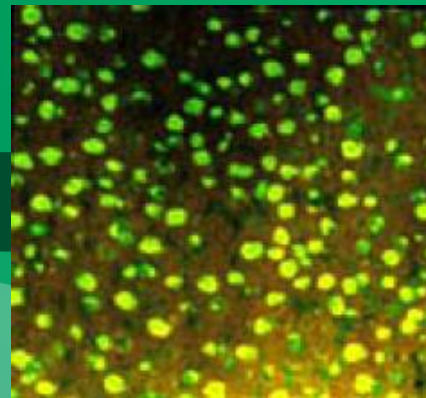
# TÓPICOS

- ▶ Perspectiva histórica e necessidade de padronização
- ▶ O Consenso Brasileiro
- ▶ O Consenso Internacional
- ▶ Últimas recomendações dos Consensos
- ▶ Acesso às informações dos Consensos
- ▶ Palavra aberta

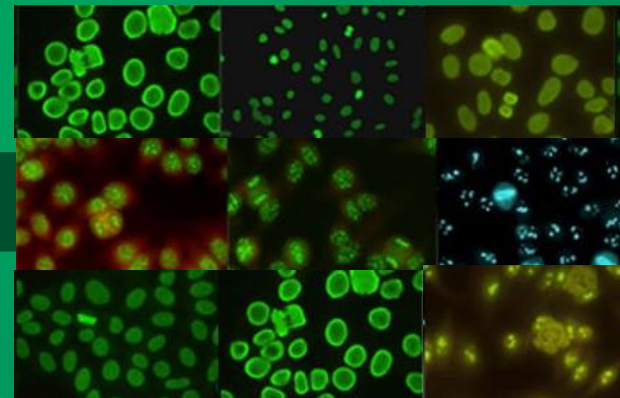
# Perspectiva histórica e necessidade de padronização



LE



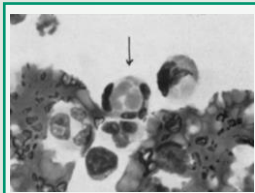
Fígado de Rato



HEp-2

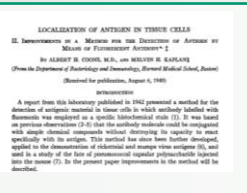


# Perspectiva histórica e necessidade de padronização



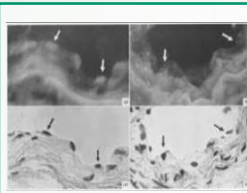
**Hargraves et al.**  
Célula LE

(1948)



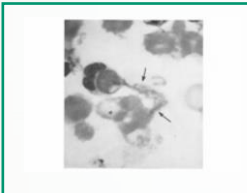
**Coons and Kaplan**  
Immunofluorescence method

(1950)



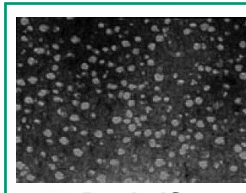
**Friou et al.**  
IFA for ANA detection

(1958)



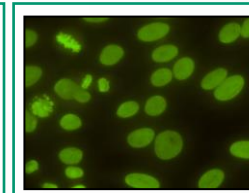
**Holman, Deicher & Kunkel**  
LE cell and LE serum factors

(1959)



**Beck JS**  
Nuclear staining on Rat liver

(1961)



**Eng Tan**  
Auto antibodies in HEp-2 cells.

(1970)



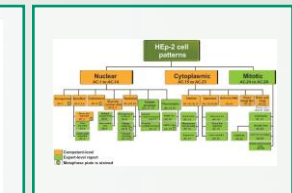
**AutoAB.org**  
Autoantibody Standardization Committee

(1980)



**Francescantonio, et al.**  
Brazilian Consensus

(2000)



**Chan, et al.**  
International Consensus

(2015)

# Dificuldades no Brasil (década de 90)

- ❖ Soros de referência
- ❖ Nomenclatura heterogênea
- ❖ Ausência de critérios de leitura
- ❖ Ausência de classificação dos padrões
- ❖ Poucas associações
- ❖ Poucas publicações
- ❖ Parâmetros de qualidade?

# O Consenso Brasileiro

[www.HEp-2.com.br](http://www.HEp-2.com.br)

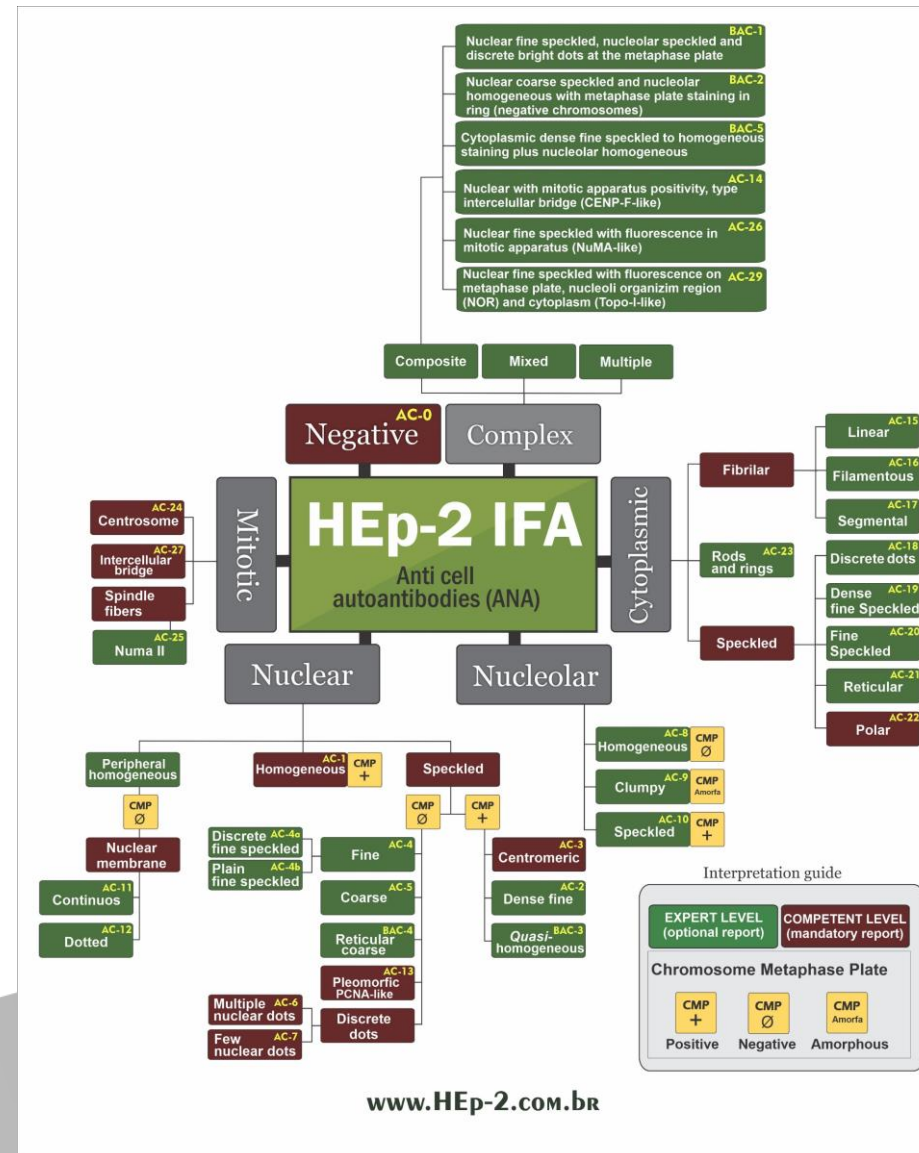


**CBA**  
Consenso Brasileiro de  
**Autoanticorpos**

# CONSENSO BRASILEIRO

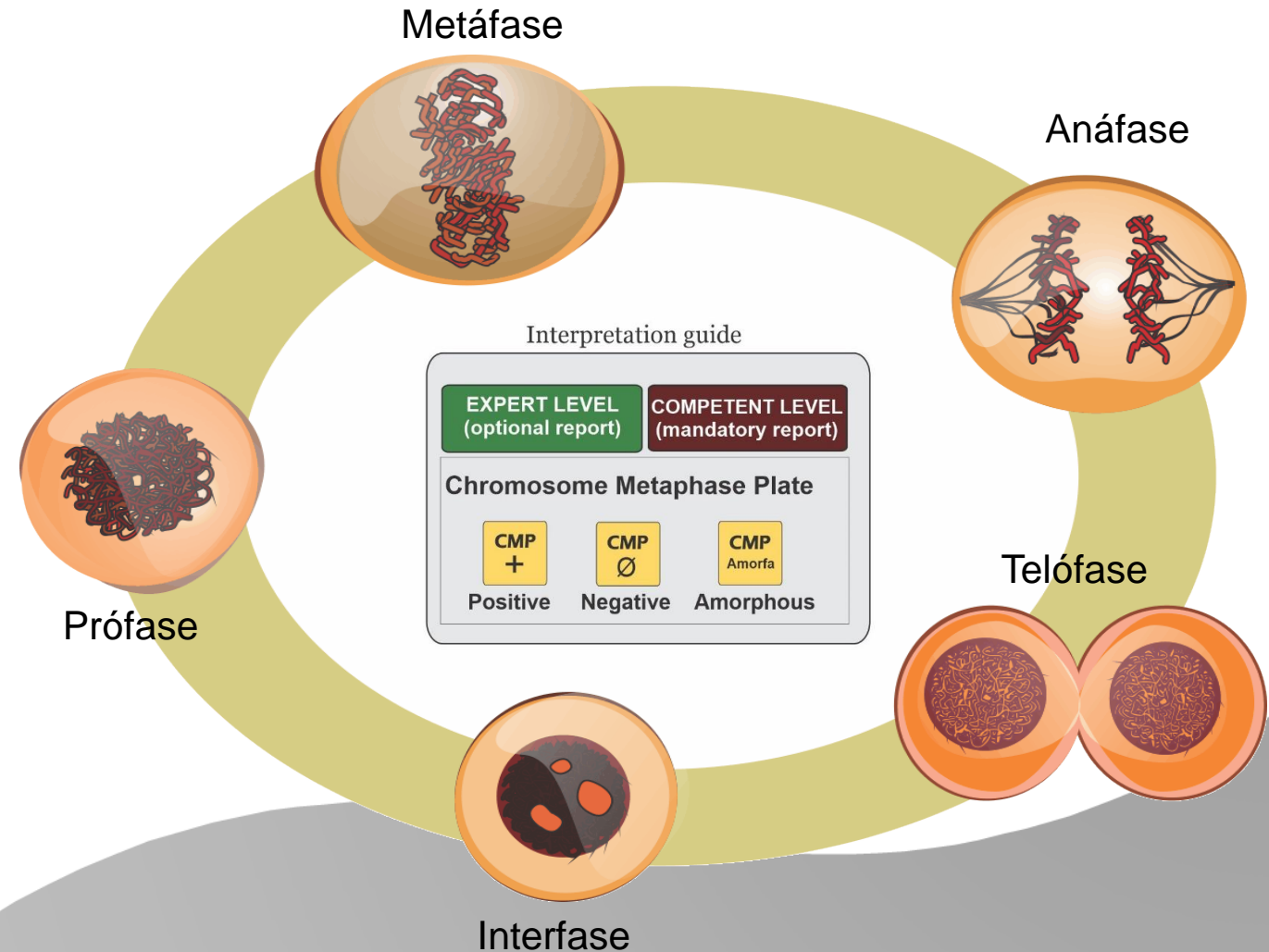
## Francescantônio e colaboradores.

- Nomenclatura e caracterização dos padrões
- Critérios de leitura da lâmina com foco na avaliação morfológica do padrão.
- Grupos de classificação
- Recomendações técnicas (diluição de triagem, diluição, titulação de conjugado, CQ).
- Terminologia do teste e laudo
- Harmonização



# CONSENSO BRASILEIRO

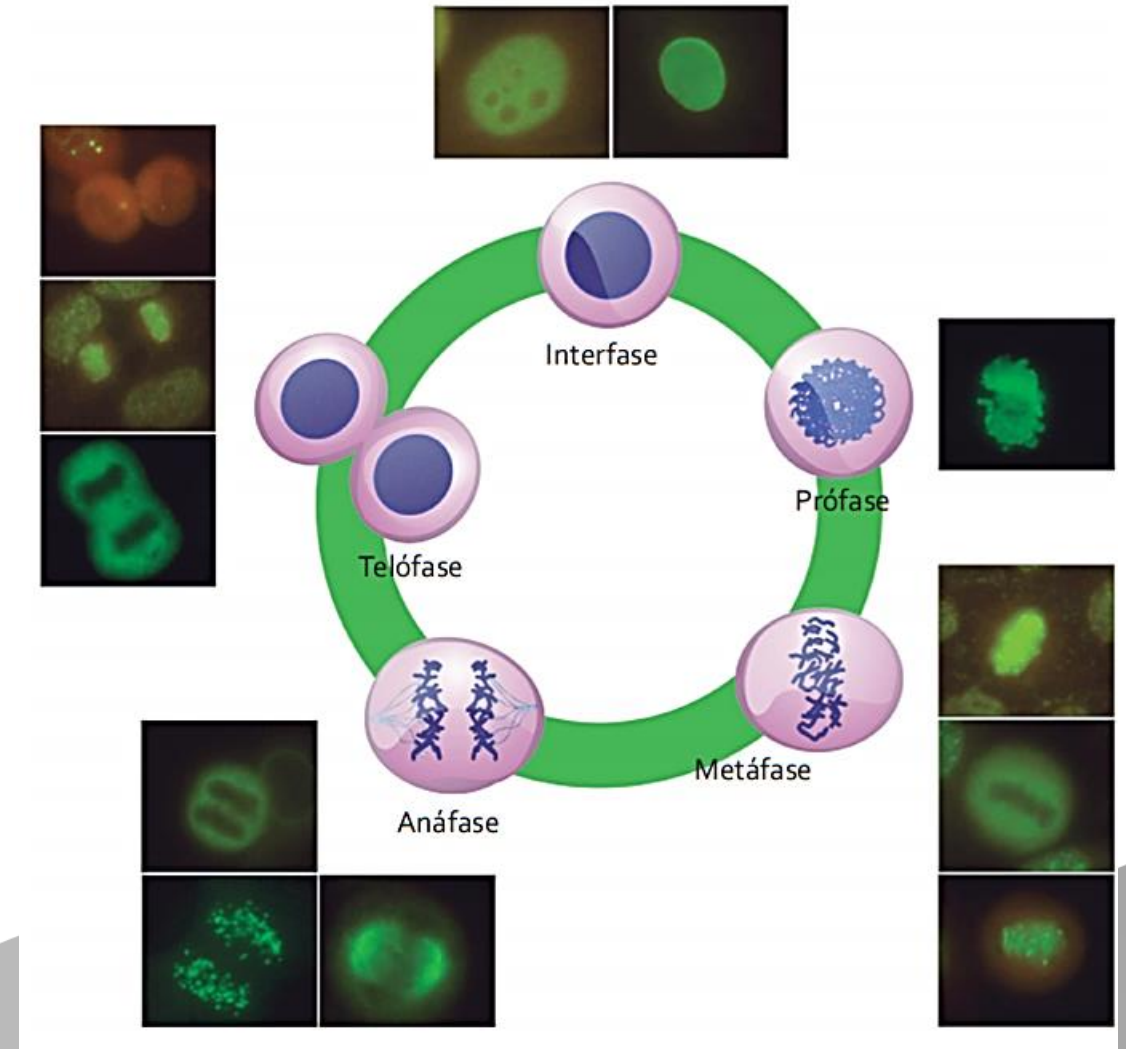
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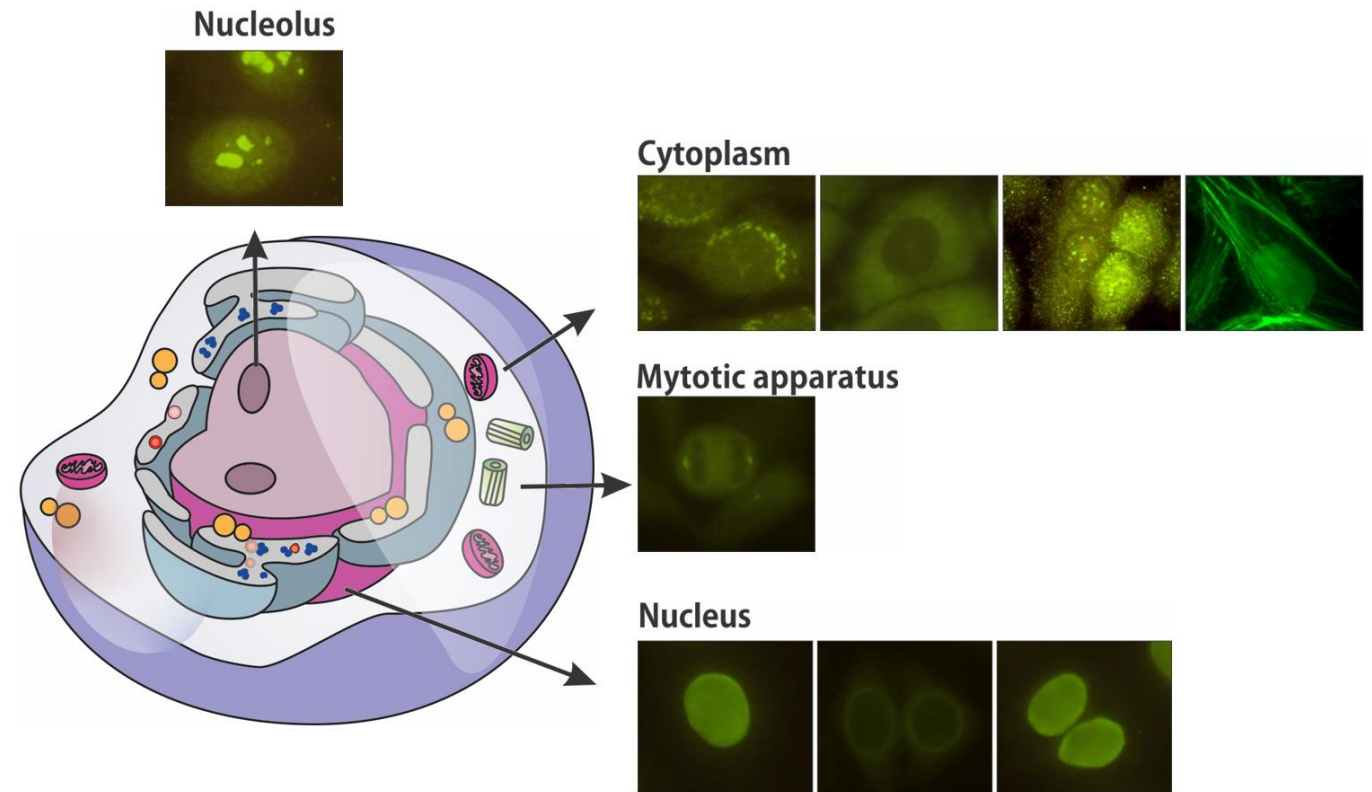
# CONSENSO BRASILEIRO

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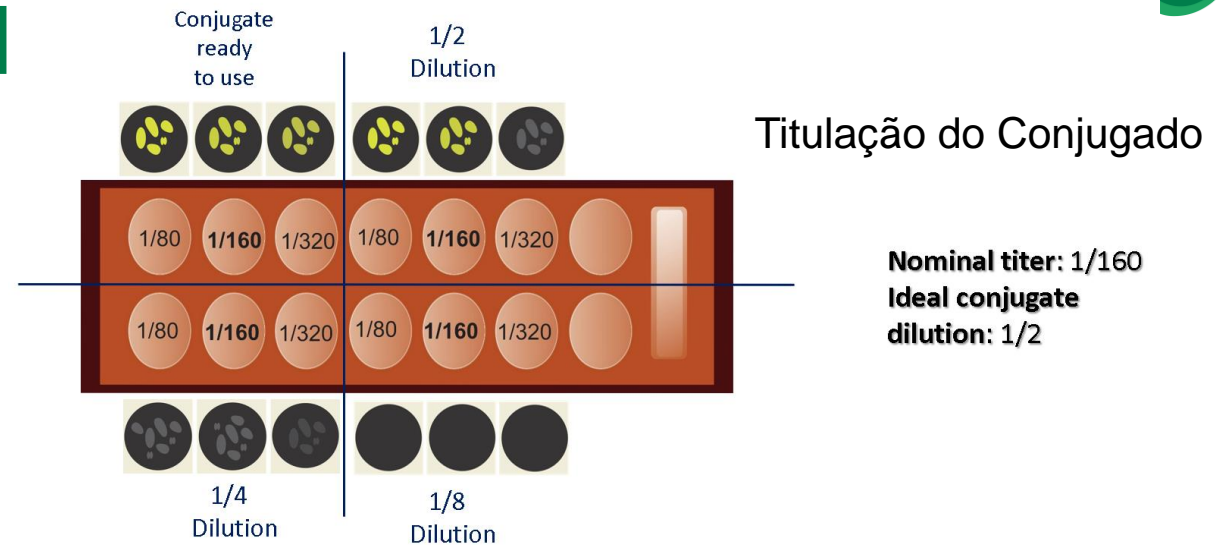
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# CONSENSO BRASILEI

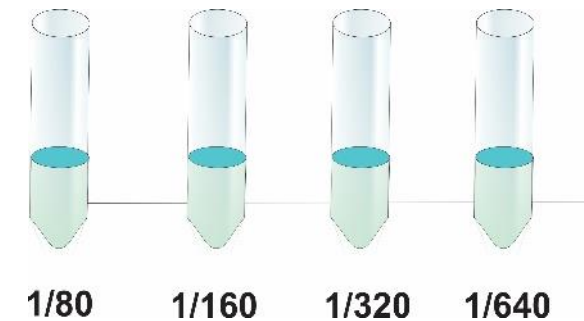
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- Terminologia do teste e laudo
- Harmonização



Triagem

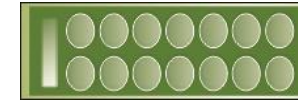


Diluição



# CONSENSO BRASILEIRO

- Nomenclatura e caracterização dos padrões
- Critérios de leitura da lâmina com foco na avaliação morfológica do padrão.
- Grupos de classificação
- Recomendações técnicas (diluição de triagem, diluição, titulação de conjugado, CQ).
- Terminologia do teste e laudo
- Harmonização



Nome do teste

**FAN - Pesquisa de Anticorpos Anticélula**

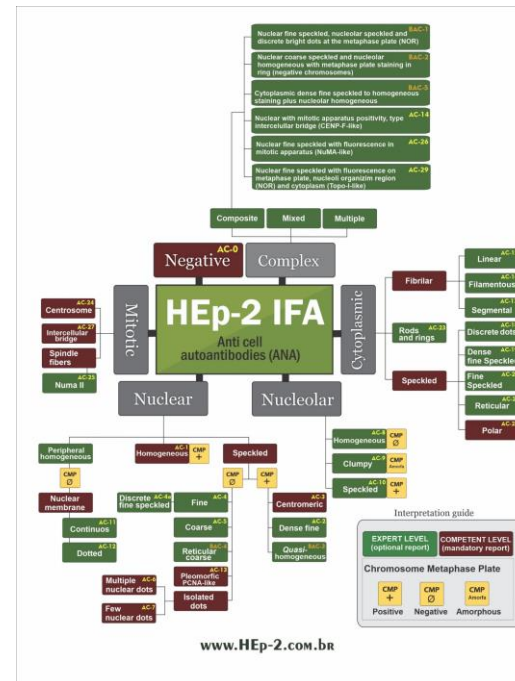
Metodologia

**IFI HEp-2**

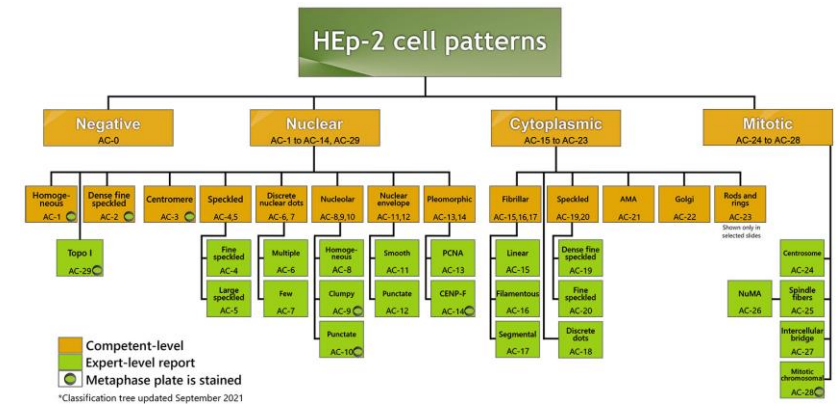
# CONSENSO BRASILEIRO

## CBA

- Nomenclatura e caracterização dos padrões
- Critérios de leitura da lâmina com foco na avaliação morfológica do padrão.
- Grupos de classificação
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- Harmonização



## ICAP



# Consensos no Brasil



# O Consenso Internacional

[WWW.ANAPATTENRS.ORG](http://WWW.ANAPATTENRS.ORG)



# Estrutura do ICAP



**Dr. Edward K. L. Chan**



**Dr. Luiz Eduardo Coelho Andrade**



Українська

ἰὸ ὕ

日本語

한국어

Ελληνικά

Magyar

Bosanski

Русский

Türkçe

Français

繁體中文

简体中文

Deutsch

Dutch

Italiano

Español

Português Brazil

Portugues Portugal

English



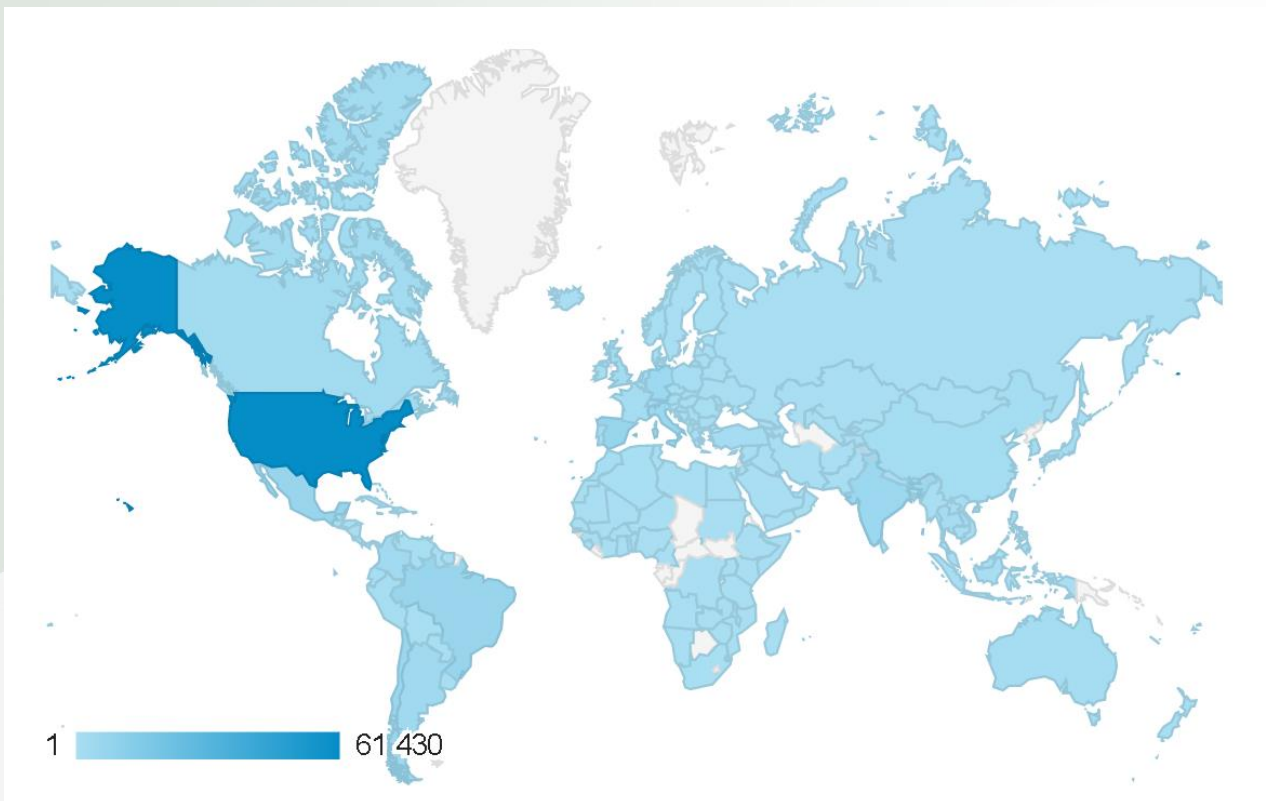


# Necessidades e Objetivos do ICAP

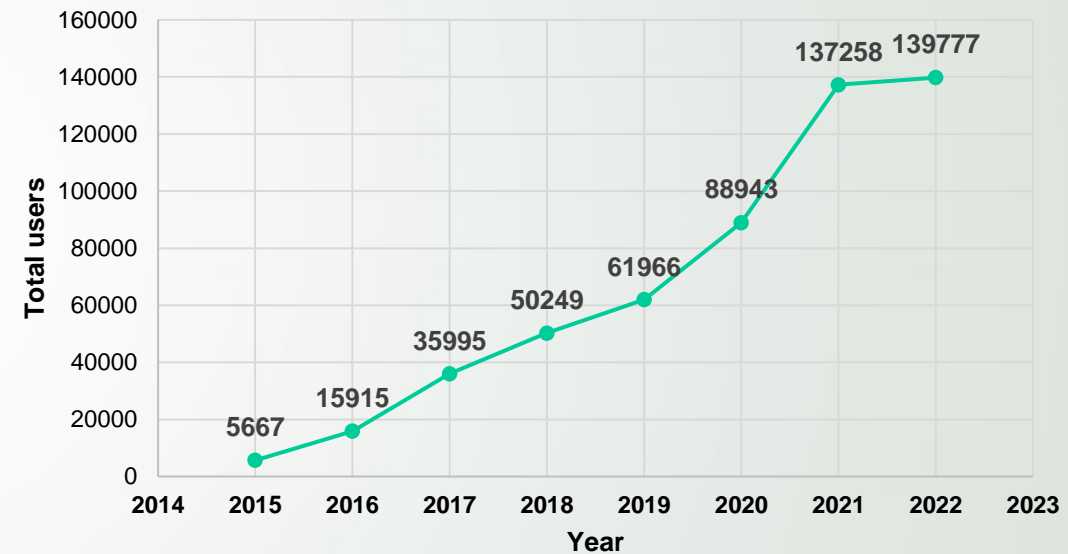
- ❖ Autoanticorpos são relevantes biomarcadores
  - ❖ ACR reconhece IFI HEp-2 como “padrão-ouro”
  - ❖ Ainda existem divergências e dúvidas a certa da interpretação desses achados.
- 
- ❖ Harmonizar a nomenclatura no âmbito mundial
  - ❖ Estabelecer diretrizes para a realização e interpretação do teste

# Usuários do ICAP

154.233 usuários no último ano 184 países

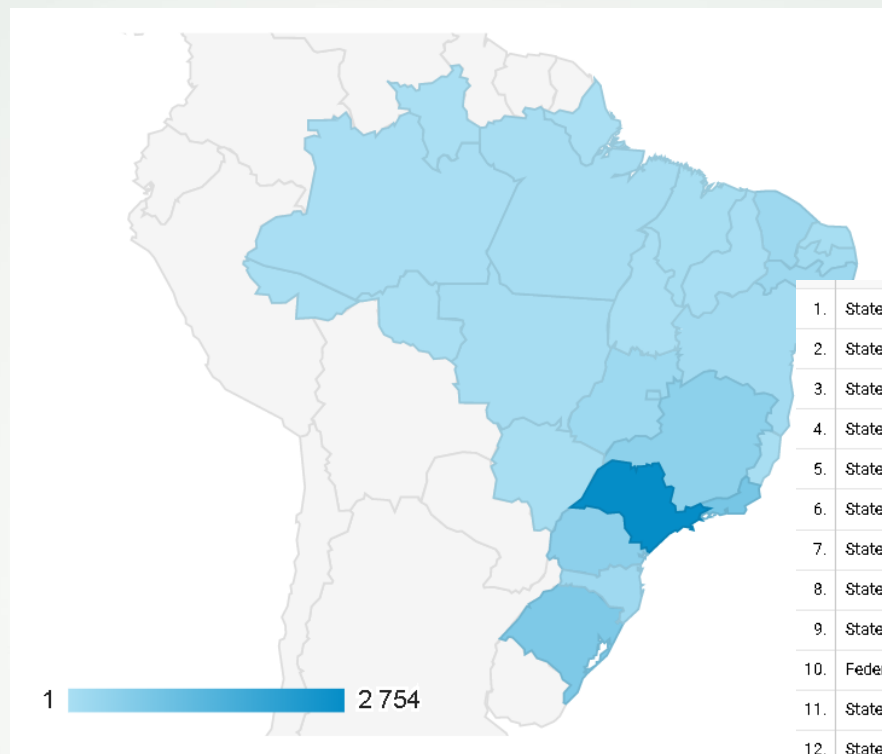


























Anapatterns Users - Google Analytics



ICAP Registered users: **6582**

1.	 United States	<b>61 430</b> (39,60%)
2.	 Spain	<b>6 562</b> (4,23%)
3.	 Mexico	<b>6 504</b> (4,19%)
4.	 Brazil	<b>6 406</b> (4,13%)
5.	 Chile	<b>5 576</b> (3,59%)
6.	 India	<b>5 250</b> (3,38%)
7.	 Italy	<b>5 223</b> (3,37%)
8.	 Germany	<b>4 798</b> (3,09%)
9.	 Taiwan	<b>3 615</b> (2,33%)
10.	 Argentina	<b>3 521</b> (2,27%)

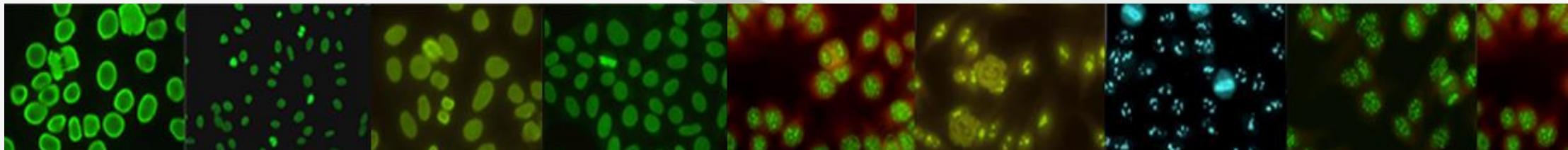


1.	State of Sao Paulo	2 754	 39,39%
2.	State of Rio de Janeiro	854	 12,22%
3.	State of Rio Grande do Sul	743	 10,63%
4.	State of Parana	493	 7,05%
5.	State of Minas Gerais	485	 6,94%
6.	State of Pernambuco	226	 3,23%
7.	State of Ceara	220	 3,15%
8.	State of Goias	211	 3,02%
9.	State of Santa Catarina	189	 2,70%
10.	Federal District	179	 2,56%
11.	State of Bahia	124	 1,77%
12.	State of Paraiba	118	 1,69%
13.	State of Para	56	 0,80%
14.	State of Mato Grosso	53	 0,76%
15.	State of Rio Grande do Norte	51	 0,73%
16.	State of Maranhao	46	 0,66%
17.	State of Espirito Santo	40	 0,57%
18.	State of Mato Grosso do Sul	37	 0,53%
19.	State of Piaui	28	 0,40%
20.	State of Amazonas	20	 0,29%
21.	State of Sergipe	15	 0,21%
22.	(not set)	12	 0,17%
23.	State of Alagoas	11	 0,16%
24.	State of Rondonia	9	 0,13%
25.	State of Tocantins	9	0,13%

# Organização do ICAP



- 3 grupos de padrões (e Negativos)  
(Nucleares, Citoplasmático e Mitóticos)
- 2 divisões de classificação  
(Nível competente e nível especialista)
- 29 padrões reconhecidos (e AC-0)  
(AC-XX)



# Anti-Cell pattern codes: guia de interpretação



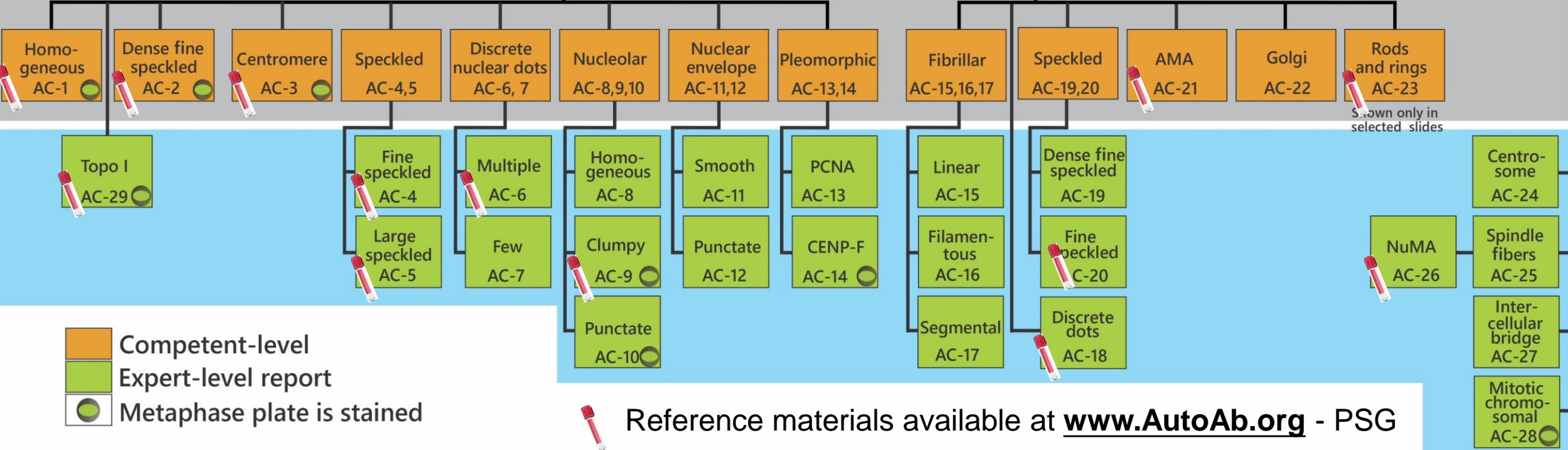
# HEp-2 cell patterns

## Negative AC-0

## Nuclear AC-1 to AC-14, AC-29

## Cytoplasmic AC-15 to AC-23

## Mitotic AC-24 to AC-28



**Previous Nomenclature** Diffuse

**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.

**Antigen Association** dsDNA, nucleosomes, histones

#### Clinical Relevance

*First level information*

[About Clinical Relevance & List of Abbreviations](#)

- ▶ 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)
- ▶ If chronic autoimmune hepatitis or juvenile idiopathic arthritis is suspected, follow-up testing is not recommended because the respective autoantigens revealing the AC-1 pattern are not completely defined (17)

*Notes: Although autoantibodies to Topoisomerase I (formerly Scl-70) may be reported as nuclear homogeneous, they typically reveal a composite AC-29 HEp-2 IIFA pattern; as such, clinical suspicion of SSc may warrant follow-up testing for reactivity to this antigen (14, 18)*

*Although AC-1 is the most prevalent pattern in chronic autoimmune hepatitis, other HEp-2 IIFA patterns may occur, but also for these patterns the autoantigens are not completely defined (19)*

#### *First level information references*

14. Andrade LEC, Klotz W, Herold M, et al. International consensus on antinuclear antibody patterns: definition of the ac-29 pattern associated with antibodies to DNA topoisomerase I. Clin Chem Lab Med 2018;56:1783-8.
15. Conrad K, Schössler W, Hiepe F. Autoantibodies in systemic autoimmune diseases: a diagnostic reference. 2. 3th edn. Autoantigens autoantibodies autoimmunity, 2015.
16. Petri M, Orbai AM, Alarcón GS, et al. Derivation and validation of the systemic lupus international collaborating clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum 2012;64:2677-86.
17. Conrad K, Schössler W, Hiepe F. Autoantibodies in organ specific autoimmune diseases. a diagnostic reference. 8. 2th edn. Autoantigens autoantibodies autoimmunity, 2017.
18. Dellavance A, Gallindo C, Soares MG, et al. Redefining the Scl-70 indirect immunofluorescence pattern: autoantibodies to DNA topoisomerase I yield a specific compound immunofluorescence pattern. Rheumatology 2009;48:632-7.
19. European Association for the Study of the Liver. EASL clinical practice guidelines: autoimmune hepatitis. J Hepatol 2015;63:971-1004.

#### *Second level information*

None

#### *Second level information references*

None

#### FAQ

##### Low titer anti-dsDNA serum negative by HEp-2 IFA?

- + Question: Can I have a negative HEp-2 IFA result in a sample with positive Crithidia assay at 1/20? The negative HEp-2 IFA was confirmed with slides from different commercial brands

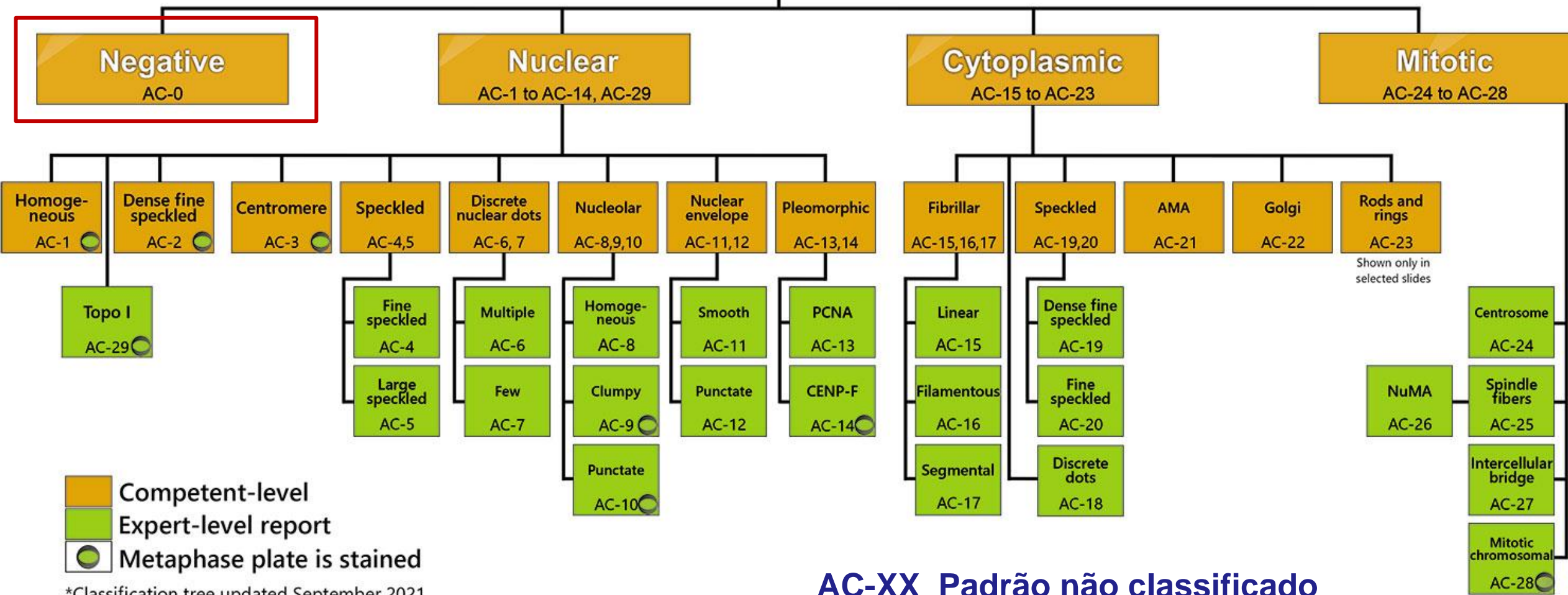
# Recomendações dos Consensos Brasileiro e Internacional



**CBA**  
Consenso Brasileiro de  
**Autoanticorpos**



# Hep-2 cell patterns



**AC-XX Padrão não classificado**

# Caracterização de padrões negativos

DE GRUYTER

Herold et al.: ICAP defines AC-0 and AC-XX — 1801

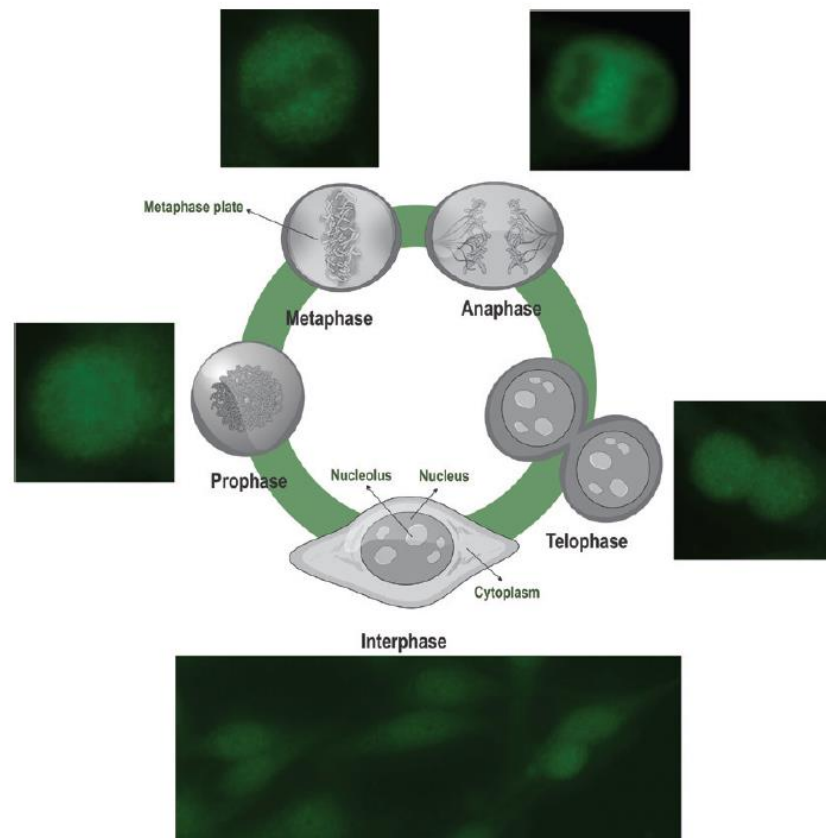


Figure 2: Examples of AC-0 seen in different phases of the cell cycle are planned to be included in the ICAP picture gallery.

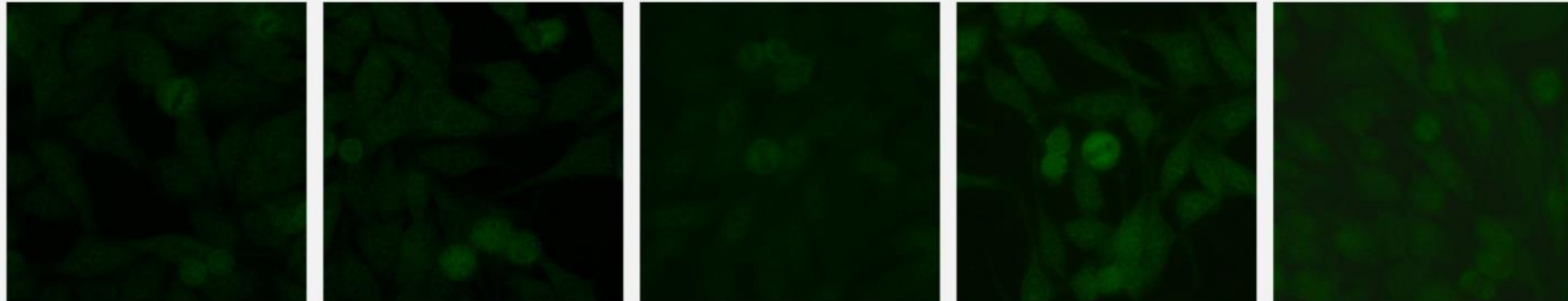
- ❖ Definição de referências locais.
- ❖ Utilização de soros de referência.
- ❖ Considerar aspectos metodológicos que interferem (Marca do kit, lote, conjugado, diluição, controles, potencia da lâmpada,...)

Herold, Manfred, Klotz, Werner, Andrade, Luis E.C., Conrad, Karsten, de Melo Cruvinel, Wilson, Damoiseaux, Jan, Fritzler, Marvin J., von Muhlen, Carlos A., Satoh, Minoru and Chan, Edward K.L.. "International Consensus on Antinuclear Antibody Patterns: defining negative results and reporting unidentified patterns" *Clinical Chemistry and Laboratory Medicine (CCLM)*, vol. 56, no. 10, 2018, pp. 1799-1802.



- 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
- English

←
AC-0 - Negative
→



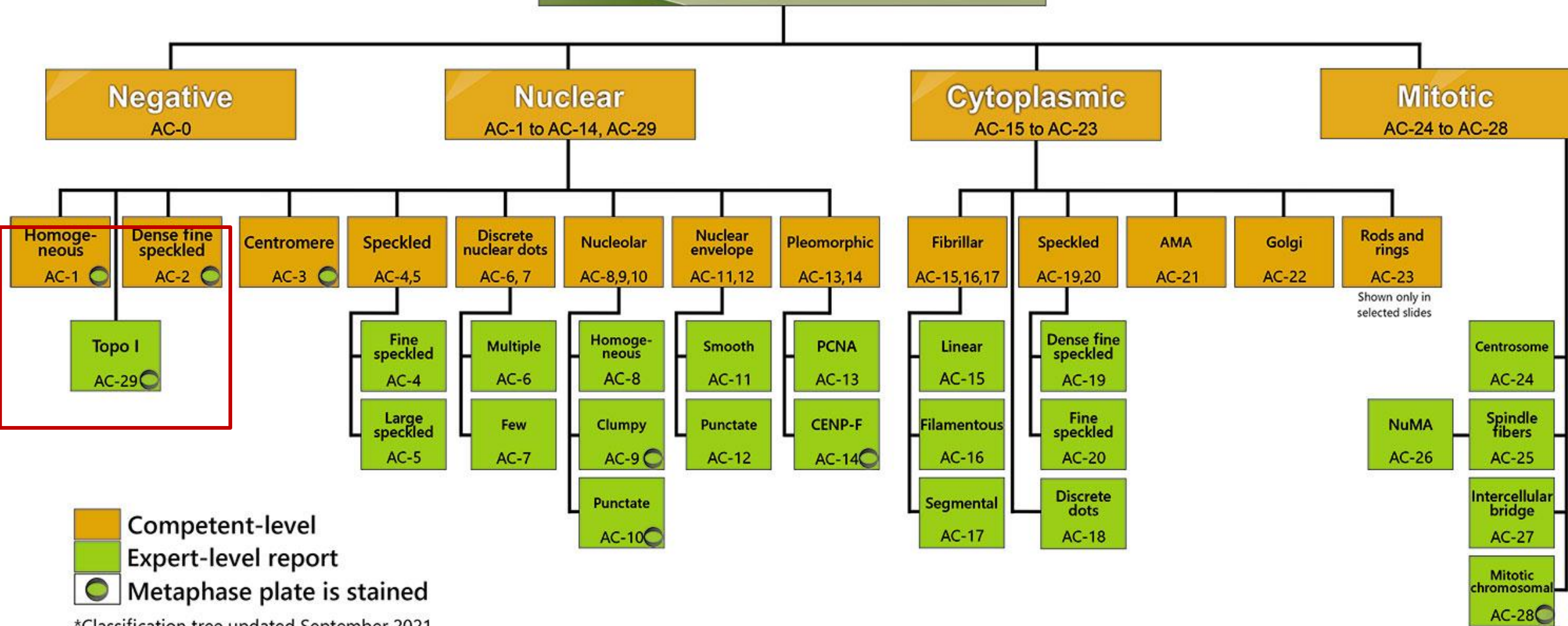
**Previous Nomenclature**    None

**Description**

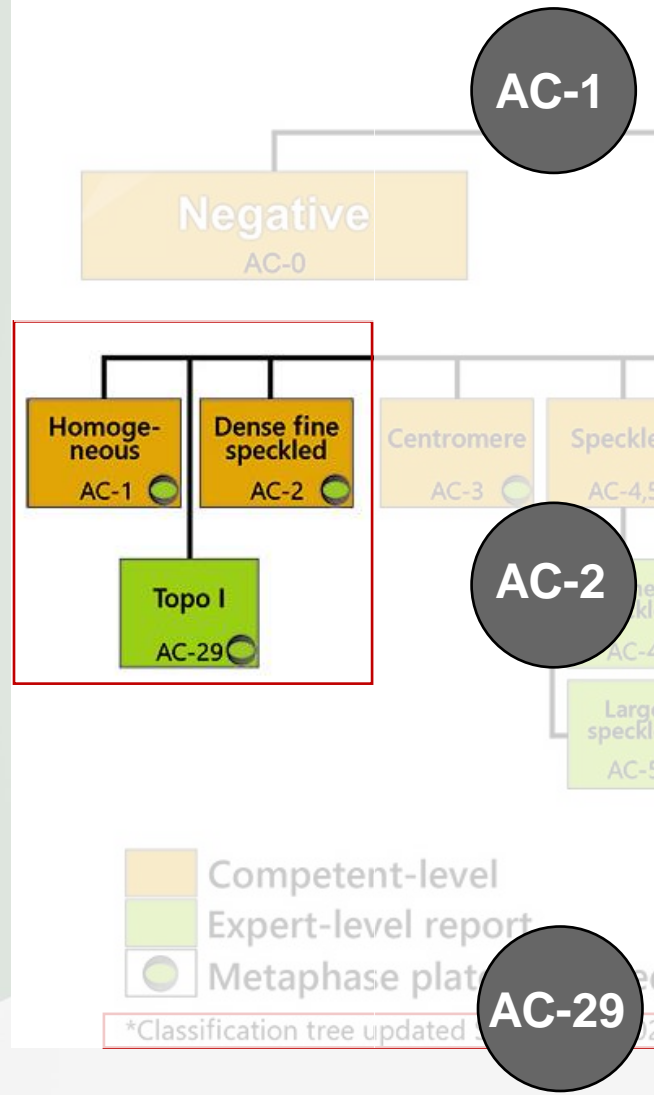
These images are provided as examples of what are considered as ANA-negative as viewed under a microscope. Since a negative ANA can be represented by a number of different images, it should be clear that AC-0 should not be regarded as the definite example but used for comparison purposes only. The guiding feature that links these variable possibilities is the absence of a clear-cut staining in any given subcellular structure. This definition is both subjective and semi-quantitative at best.

There should be a discussion regarding how ANA-positive vs ANA-negative cut-off is determined. There are general consensus that such cut-offs

# HEp-2 cell patterns



\*Classification tree updated September 2021



AC-1

AC-2

AC-29

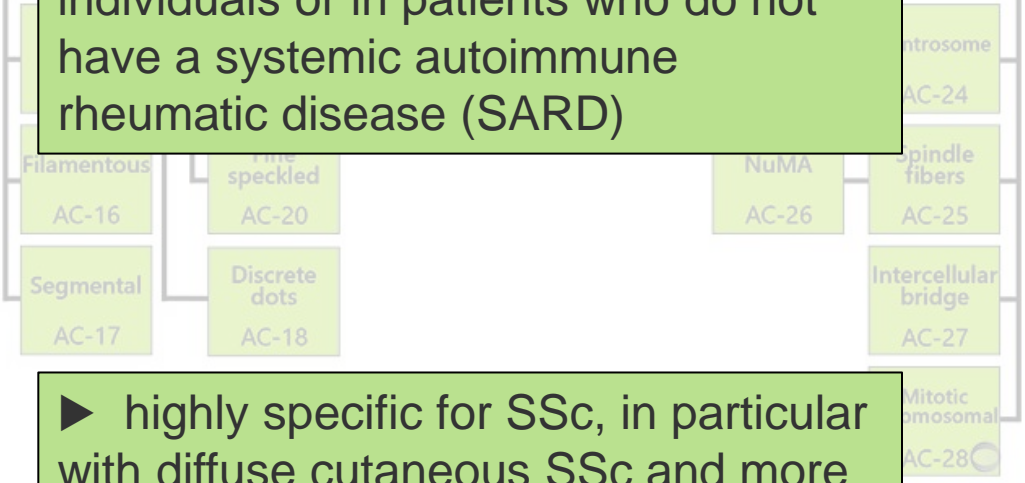


## Relevâncias Clínicas Anapatterns.org

► SLE, chronic autoimmune hepatitis or juvenile idiopathic arthritis

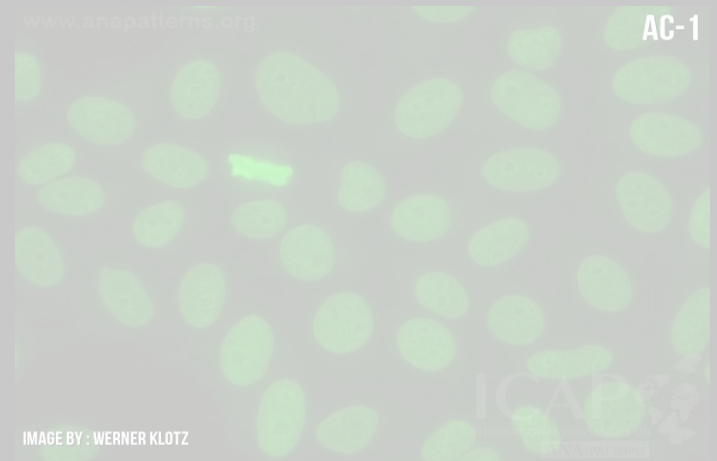


► Commonly found as high titer HEp-2 IIFA-positive in apparently healthy individuals or in patients who do not have a systemic autoimmune rheumatic disease (SARD)



► highly specific for SSc, in particular with diffuse cutaneous SSc and more aggressive forms of SSc

AC-1



► SLE, chronic autoimmune hepatitis or juvenile idiopathic arthritis

AC-2

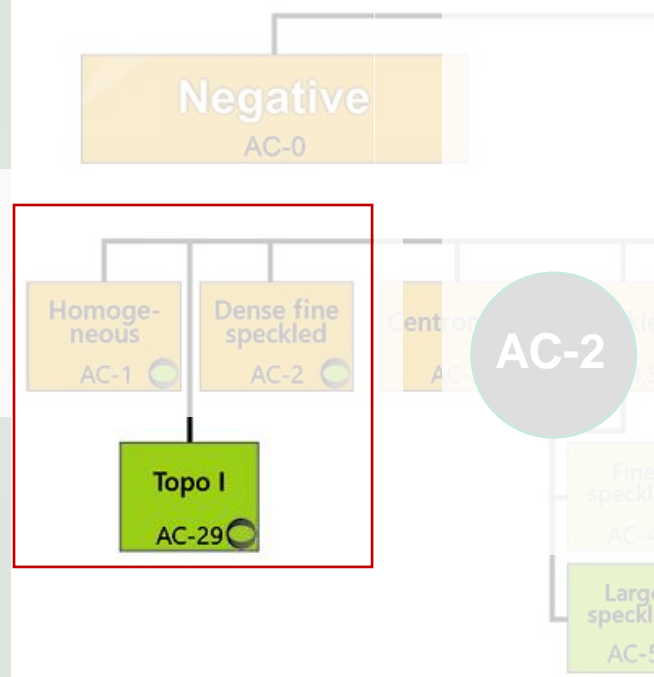


► Commonly found as high titer HEp-2 IIFA-positive in apparently healthy individuals or in patients who do not have a systemic autoimmune rheumatic disease (SARD)

AC-29



► highly specific for SSc, in particular with diffuse cutaneous SSc and more aggressive forms of SSc

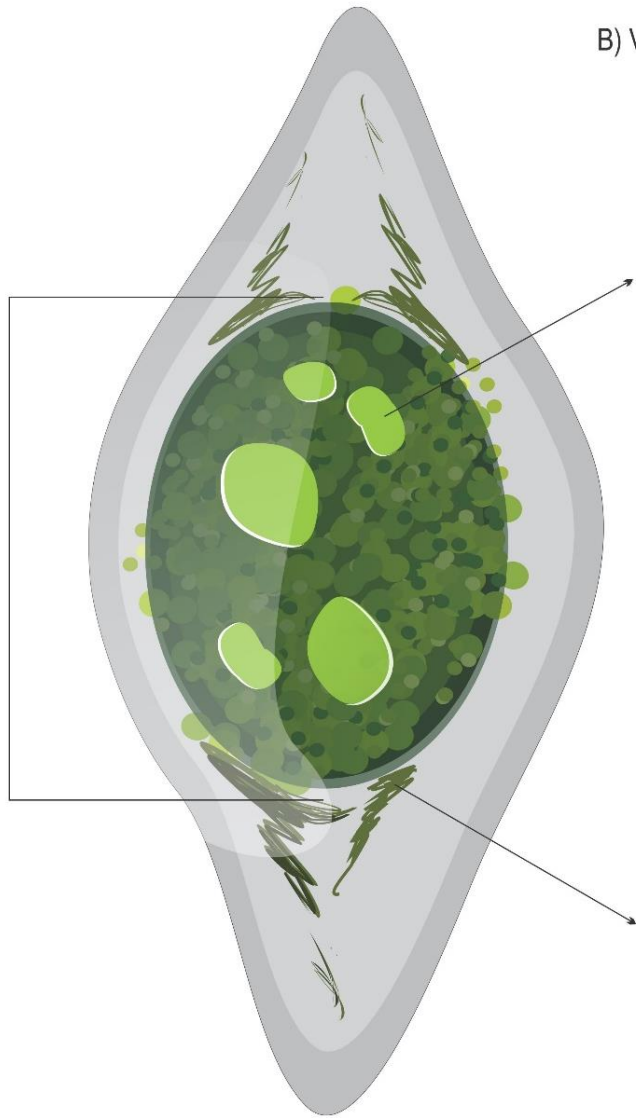
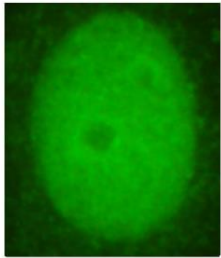


Competent-level  
Expert-level rep  
Metaphase plate is stained

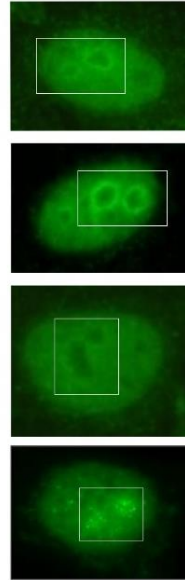
\*Classification tree updated September 202

### Interphase cell

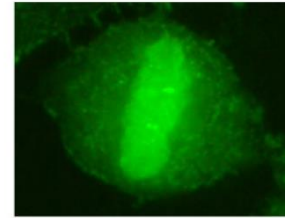
A) Fine speckled Nucleous



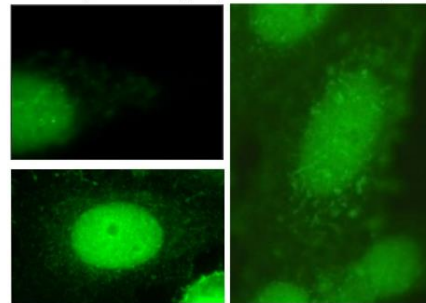
B) Variable nucleolar staining



E) Strong fine speckled staining of condensed chromosomes

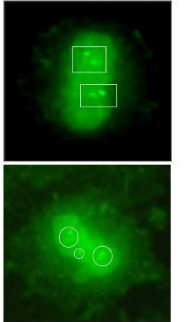
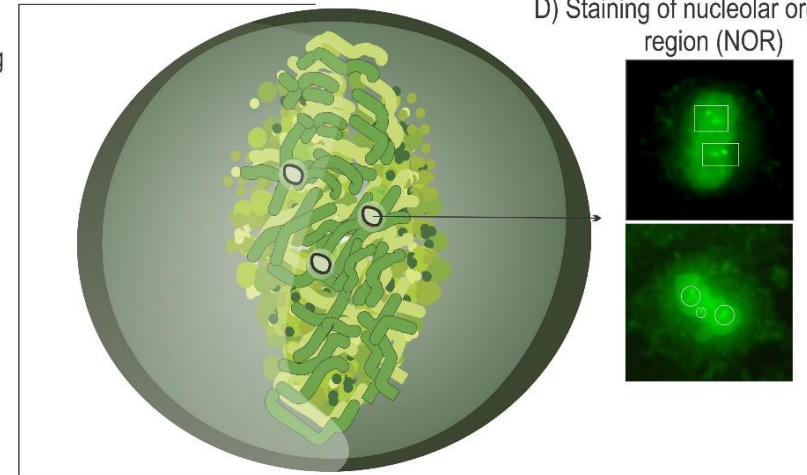


C) Weak cytoplasmic staining

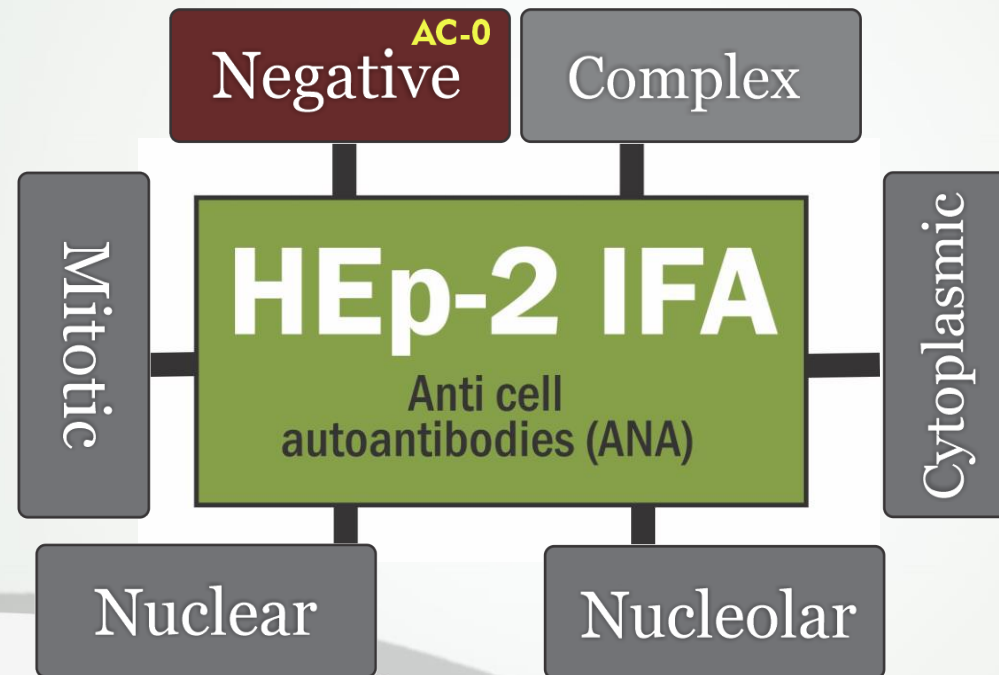


### Metaphase plate in mitotic cell

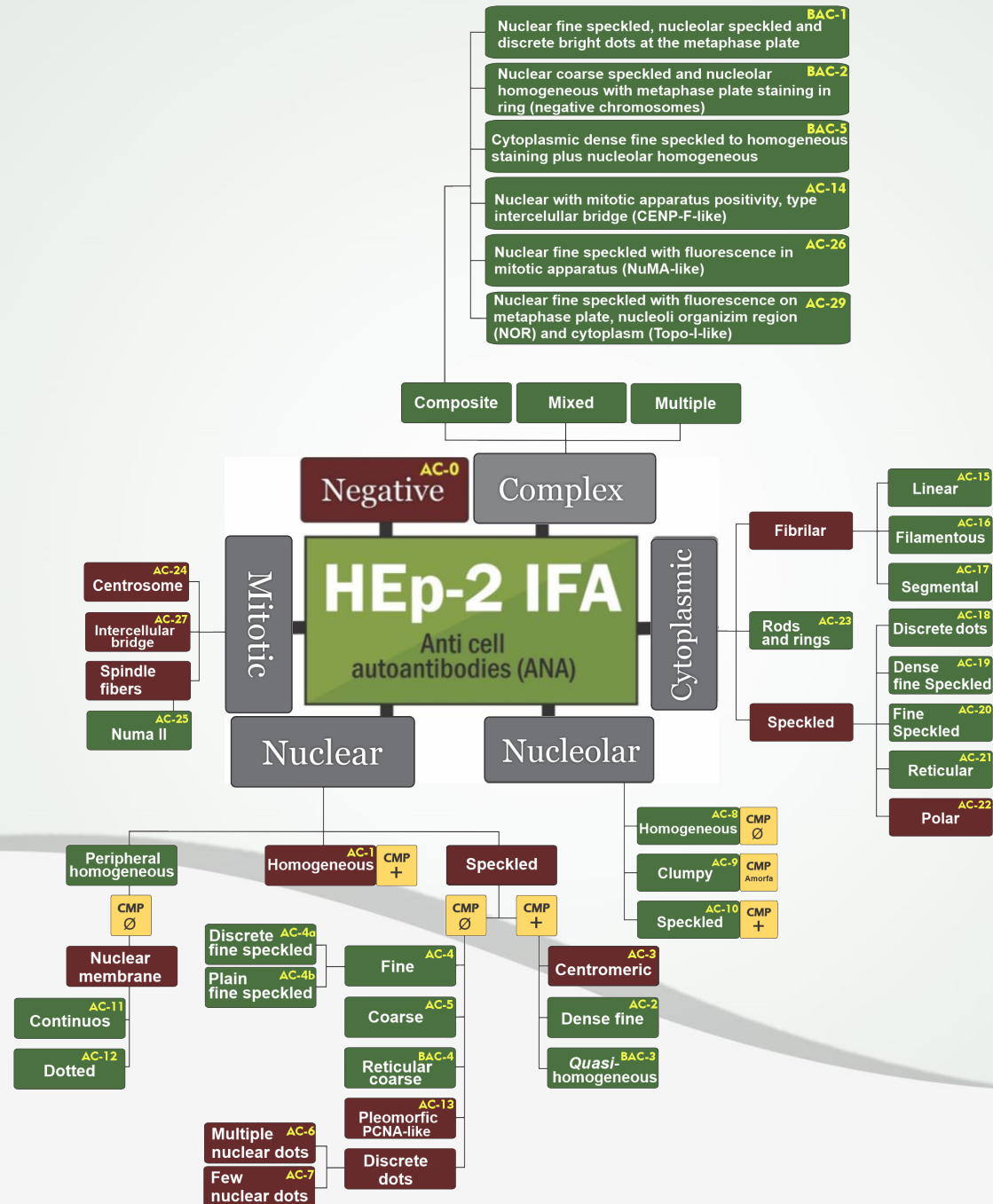
D) Staining of nucleolar organizing region (NOR)



# Classificação por grupo principal



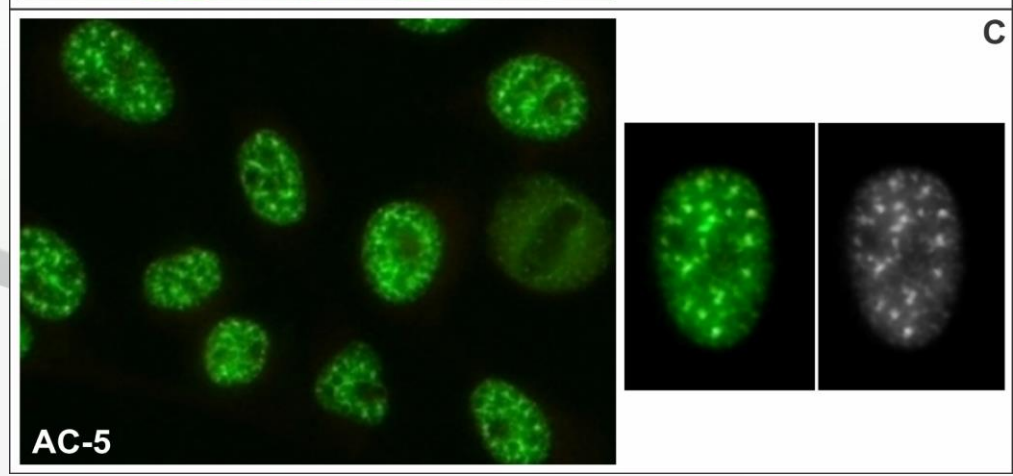
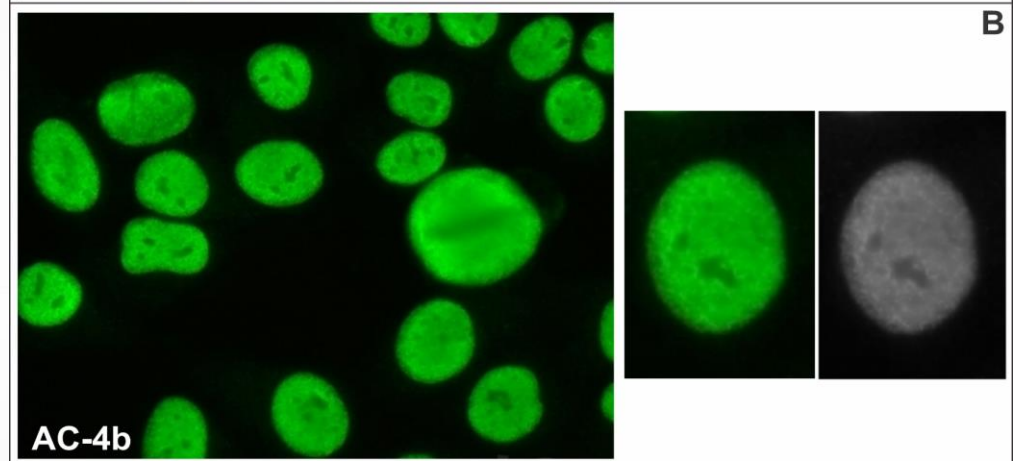
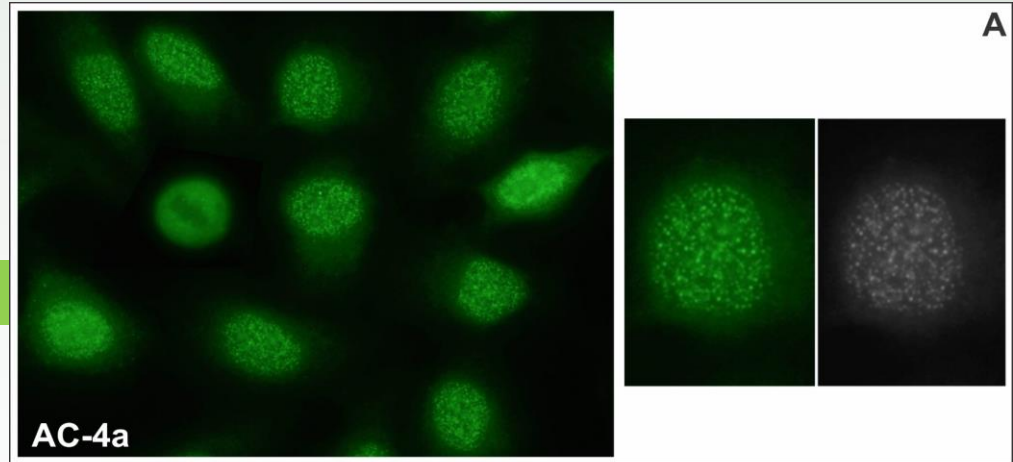
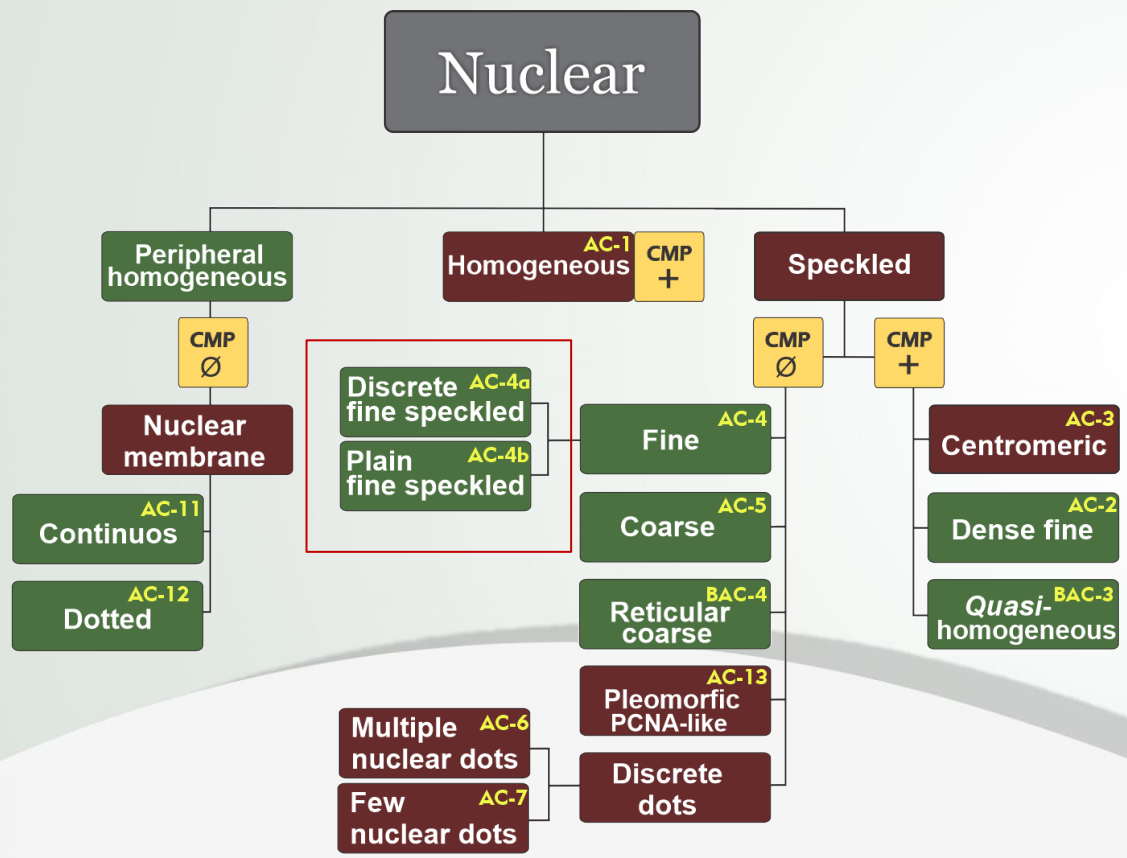




Interpretation guide

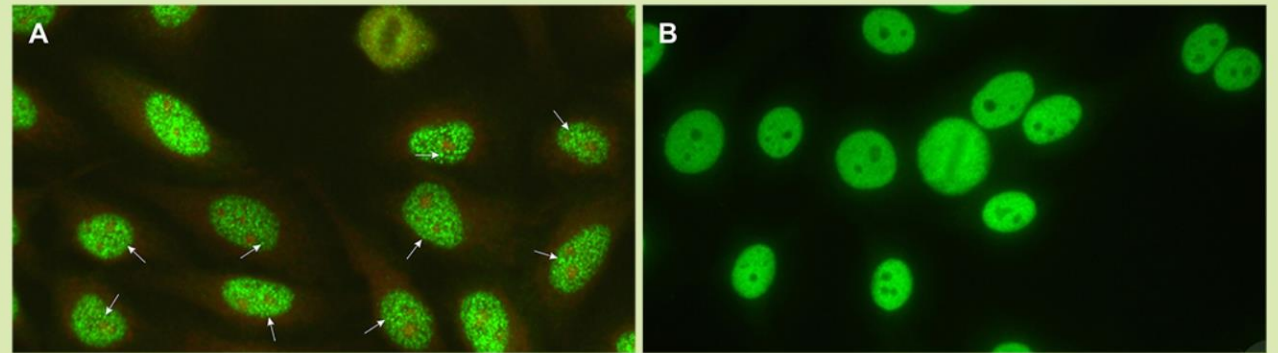
<b>EXPERT LEVEL</b> (optional report)	<b>COMPETENT LEVEL</b> (mandatory report)	
<b>Chromosome Metaphase Plate</b>		
 <b>CMP +</b> Positive	 <b>CMP Ø</b> Negative	 <b>CMP Amorfa</b> Amorphous

# Nova classificação do AC-4 (AC-4a e AC-4b)



+ **Note #2.** A variation of AC-4 (herein designated AC-4a, myriad discrete nuclear speckles) is associated with anti-SS-A/Ro60.

The variant AC-4a pattern (Panel A, myriad discrete speckled) is strongly associated with anti-SS-A/Ro60 antibodies (in human serum and as monoclonal antibodies). In contrast, the plain fine speckled pattern (Panel B, herein designated AC-4b,) is much less frequently associated with anti-SS-A/Ro60. The AC-4 pattern designation should be maintained as an umbrella for cases in which one cannot discriminate AC-4a and AC-4b patterns. The clinical relevance of discriminating AC-4a and AC-4b patterns is based on the different autoantibody associations of these two patterns. The AC-4a pattern strongly suggests the presence of anti-SS-A/Ro60 antibodies that should be confirmed always by antigen-specific immunoassays. The AC-4a pattern is not observed regularly in healthy individuals. In contrast, the AC-4b pattern may be associated with a variety of autoantibodies, including those against Mi-2, TIF-1 $\gamma$ , and Ku. Very often, no defined autoantibody specificity is demonstrated in samples yielding the AC-4b pattern. The AC-4b pattern is one of the most frequent patterns observed in healthy individuals with a positive HEp-2 IFA result.



**FIGURE 1.** Indirect immunofluorescence on HEp-2 cells showing the AC-4a and AC-4b patterns. (A) IUIS/ASC reference serum for anti-SS-A/Ro IS2105 diluted 1:160 exhibiting the characteristic myriad discrete speckled nuclear AC-4a pattern (arrows, discrete tiny nuclear speckles); (B) Humana serum with no reactivity to SS-A/Ro, diluted 1/160, exhibiting the characteristic plain nuclear fine speckled pattern (AC-4b) mostly lacking discrete speckles. Inova HEp-2 slide used. Magnification  $\times 400$ .

**Ref:**

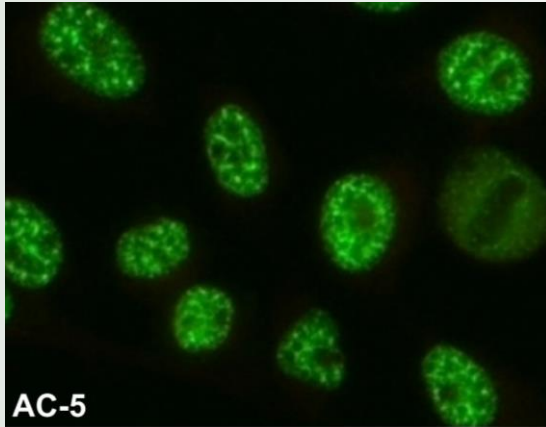
Dellavance A, Alvarenga RR, Rodrigues SH, Barbosa SH, Camilo AC, Shiguedomi HS, Rodrigues SS, Silva CG, Andrade LE (2013) Autoantibodies to 60kDa SS-A/Ro yield a specific nuclear myriad discrete fine speckled immunofluorescence pattern. *J Immunol Methods* 390:35-40. DOI: 10.1016/j.jim.2013.01.006

Rober N, Dellavance A, Ingenito F, Reimer ML, Carballo OG, Conrad K, Chan EKL, Andrade LEC (2021) Strong association of the myriad discrete speckled nuclear pattern with anti-SS-A/Ro60 antibodies: consensus experience of four international expert centers. *Front Immunol* 12:730102. DOI: 10.3389/fimmu.2021.730102

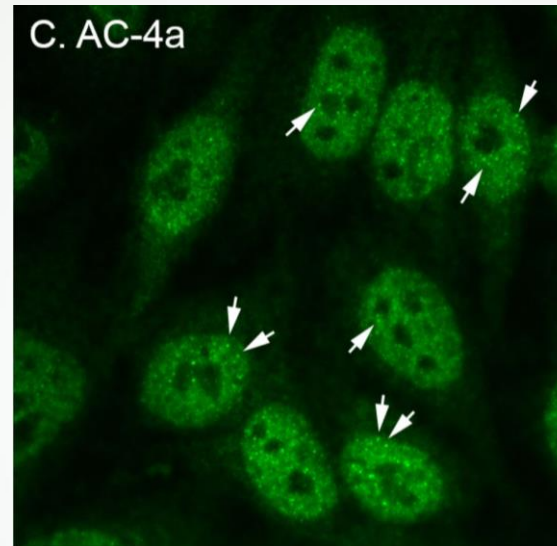
WWW.ANAPATTERNS.ORG

Imagem:  
Dra. Alessandra Delavance, 2021.

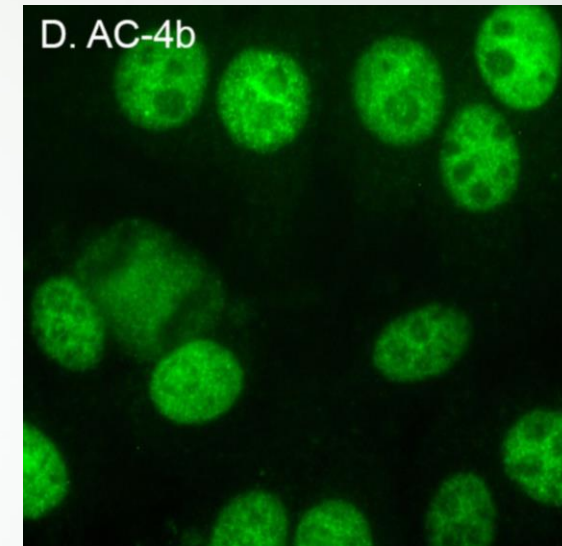
## AC-5



## AC-4a



## AC-4b



**Associação**

Anti-SS-A/Ro60

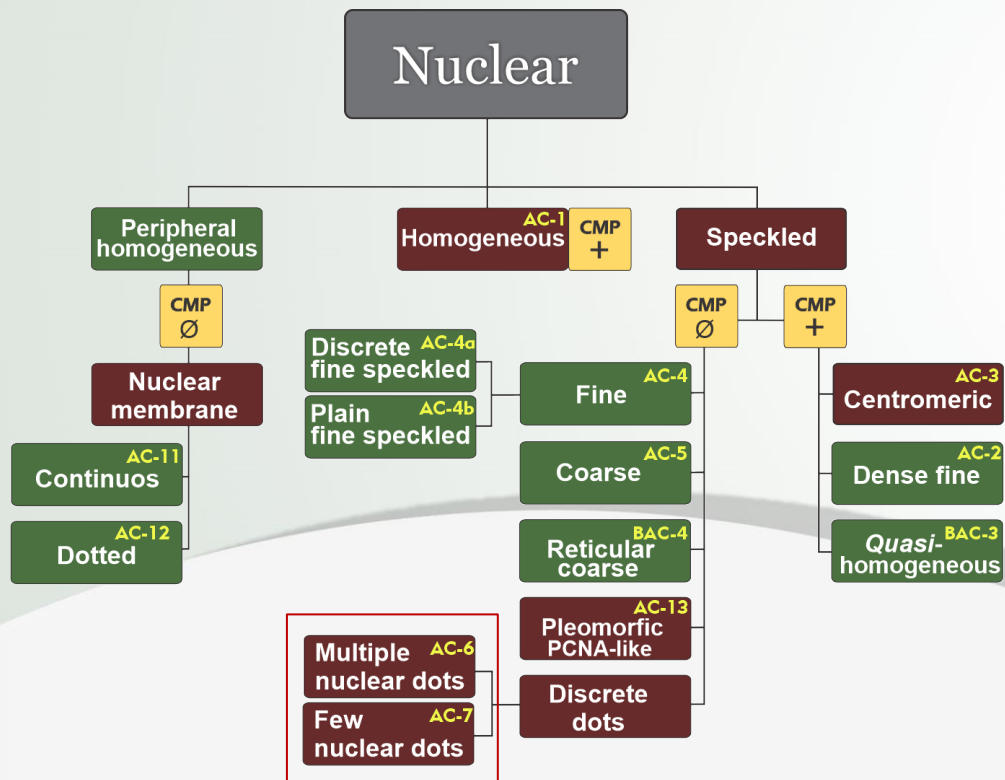
Anti-Mi-2, TIF-1 $\gamma$ , and Ku ou  
Autoanticorpos não definidos.

**Relato em hígidos**

Não

Sim

# Classificação AC-6 e AC-7



AC-6

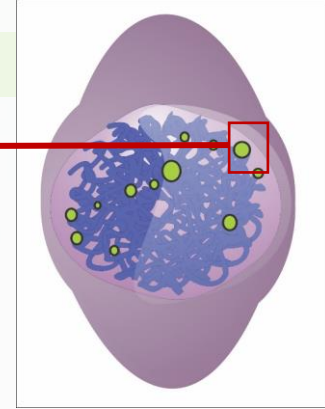
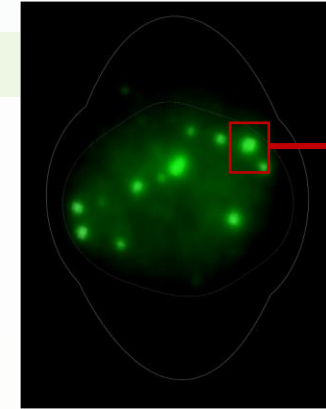
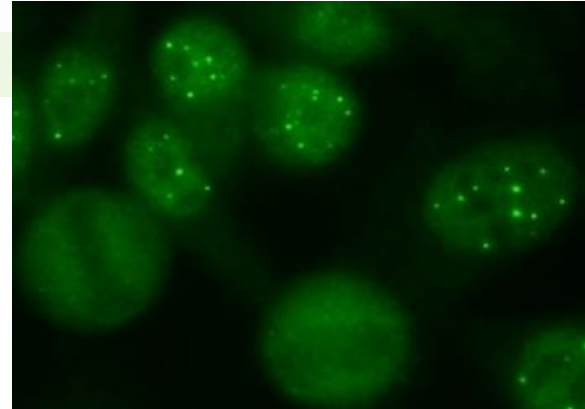


PML NUCLEAR BODIES

6 a 20 corpos nucleares



Sp-100  
PML proteins  
MJ/NXP-2



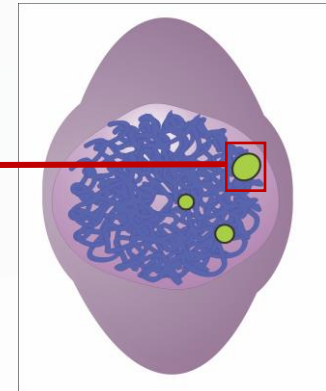
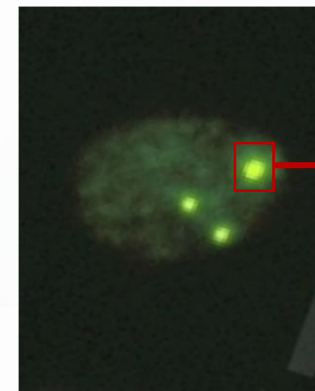
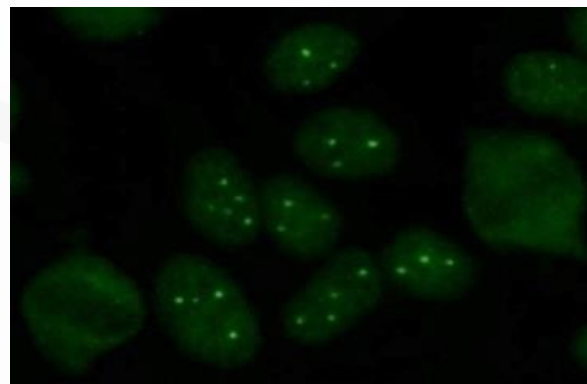
AC-7



CAJAL BODIES (CB)

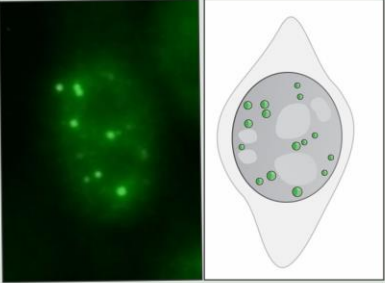
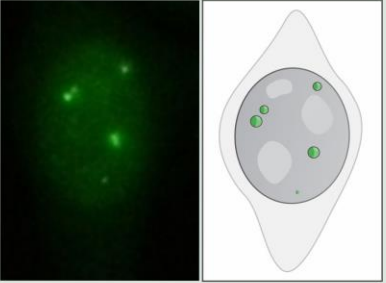
1 a 6 corpos nucleares

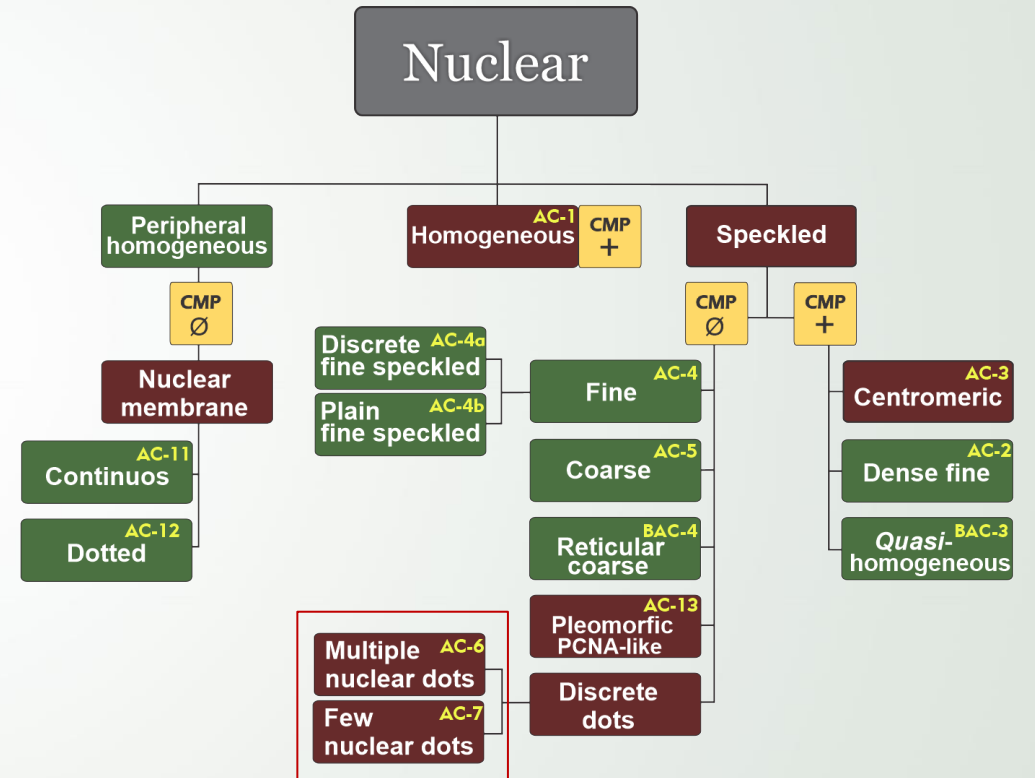
p80-coilin  
SMN



## AC-6

## AC-7

Associated Antigens	Sp-100 PML proteins MJ/NXP-2	p80-coilin SMN
IIFA Pattern description	Countable discrete nuclear speckles (6 to 20 nuclear dots per cell) distributed over the cell nucleus, sparing the nucleoli, and the chromosomes in mitotic cells. The other cell compartments are not fluorescent and metaphase chromatin in mitotic cells usually negative.	Countable discrete speckles (1 to 6 nuclear dots/cell in most cells). These are known as Cajal bodies or coiled bodies. The other cell compartments are not fluorescent and metaphase chromatin in mitotic cells usually negative.
Aspect of Interphase cells and schematic view		
Clinical relevance	Broad spectrum of autoimmune diseases, including primary biliary cholangitis, autoimmune myopathy / dermatomyositis, as well as other inflammatory conditions.	Low positive predictive value for any disease.
Follow-up test	If primary biliary cholangitis is clinically suspected, it is recommended follow-up tests for anti-Sp100 (and PML/Sp140) antibodies. If dermatomyositis is clinically suspected, it is recommended follow-up test for anti-MJ/NXP-2 antibodies.	Specific immunoassays for these autoantibodies are currently not commercially available.



# Padrões complexos

**BAC-1**  
Nuclear fine speckled, nucleolar speckled and discrete bright dots at the metaphase plate

**BAC-2**  
Nuclear coarse speckled and nucleolar homogeneous with metaphase plate staining in ring (negative chromosomes)

**BAC-5**  
Cytoplasmic dense fine speckled to homogeneous staining plus nucleolar homogeneous

**AC-14**  
Nuclear with mitotic apparatus positivity, type intercellular bridge (CENP-F-like)

**AC-26**  
Nuclear fine speckled with fluorescence in mitotic apparatus (NuMA-like)

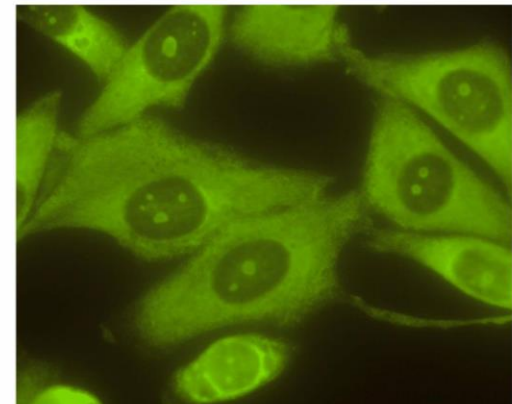
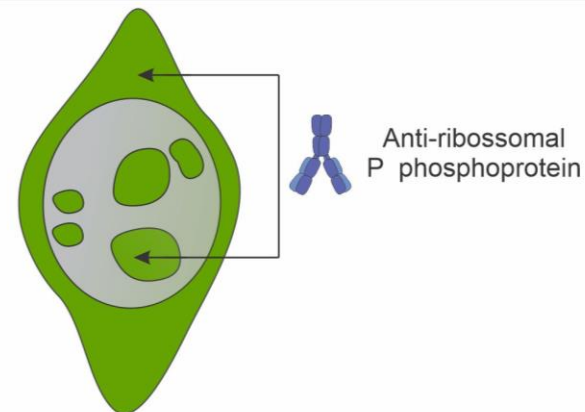
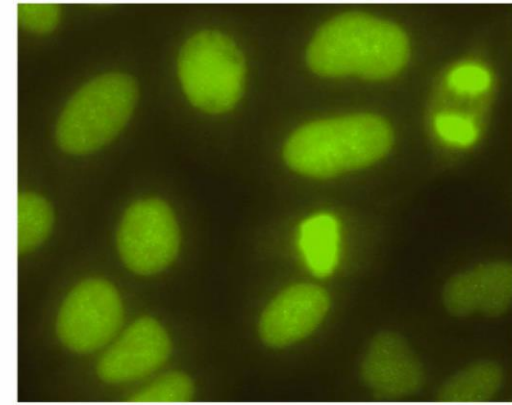
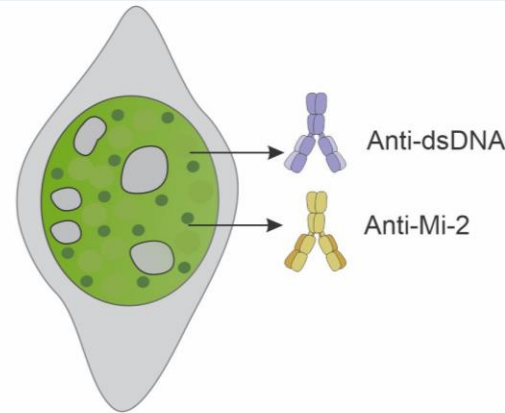
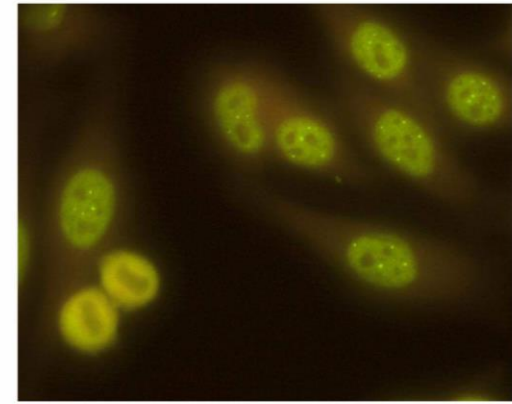
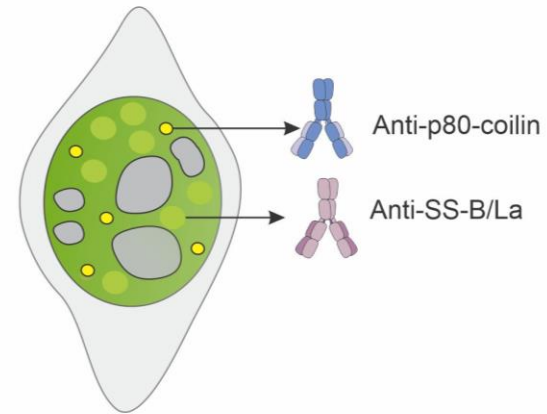
**AC-29**  
Nuclear fine speckled with fluorescence on metaphase plate, nucleoli organization region (NOR) and cytoplasm (Topo-I-like)

Composite

Mixed

Multiple

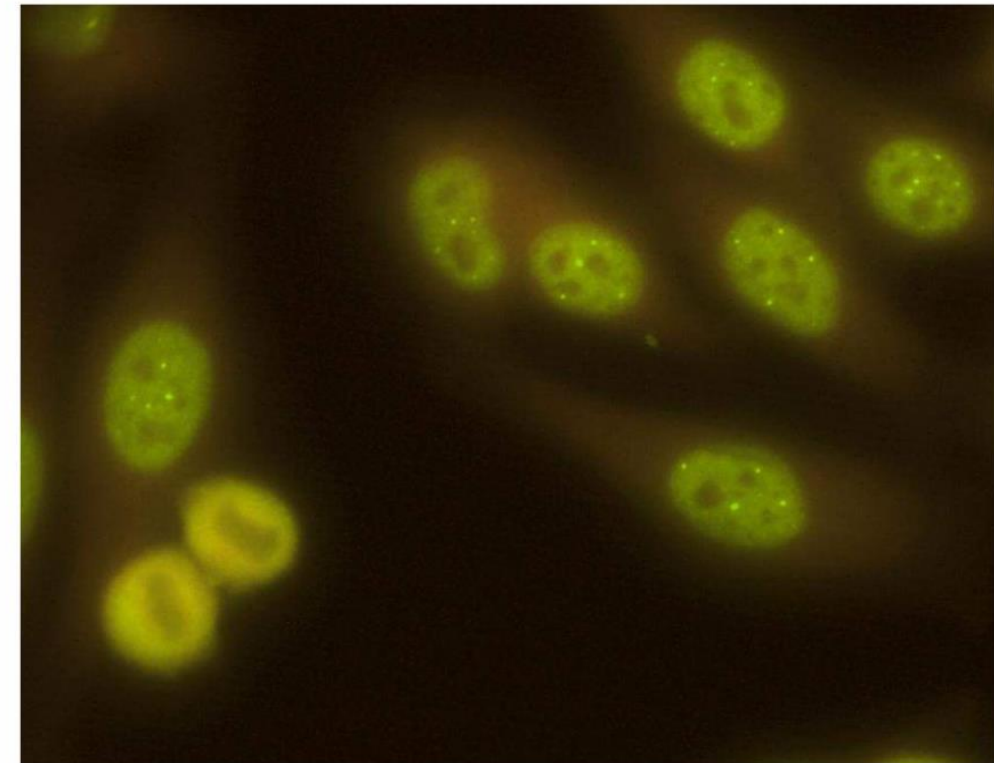
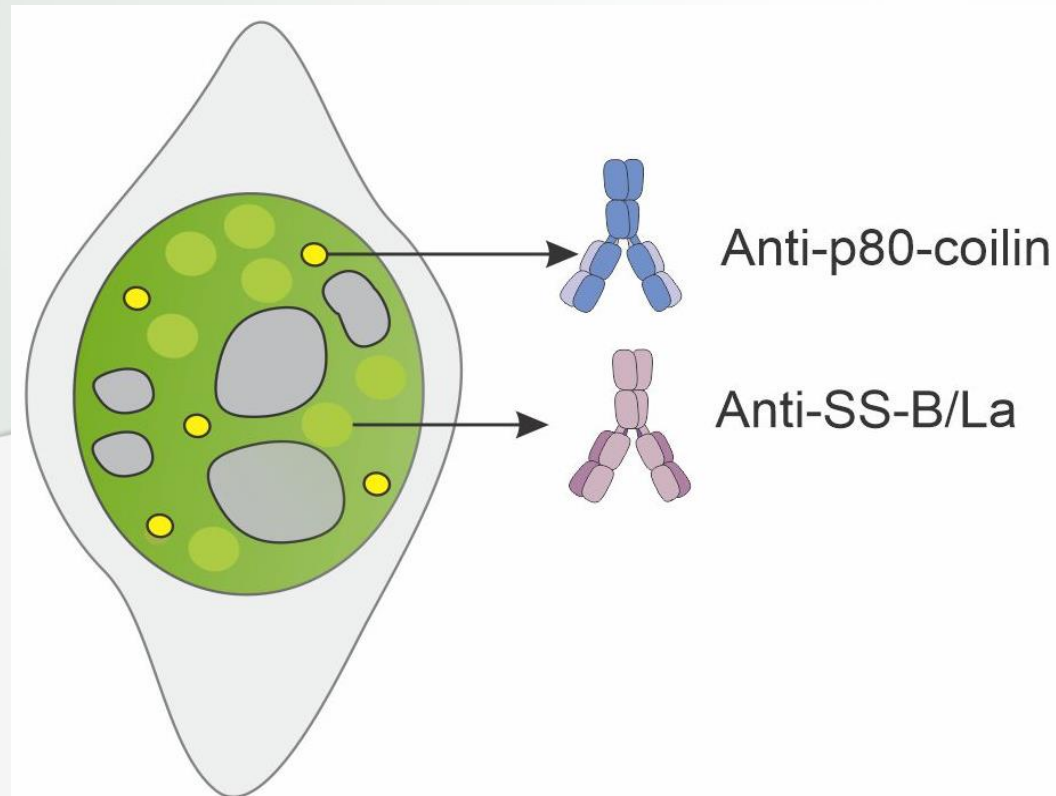
Complex



# Classificação dos padrões complexos

## PADRÃO MÚLTIPLO

Mais de um autoanticorpo está presente e cada padrão pode ser identificado individualmente.  
Exemplo: AC4/AC-7.

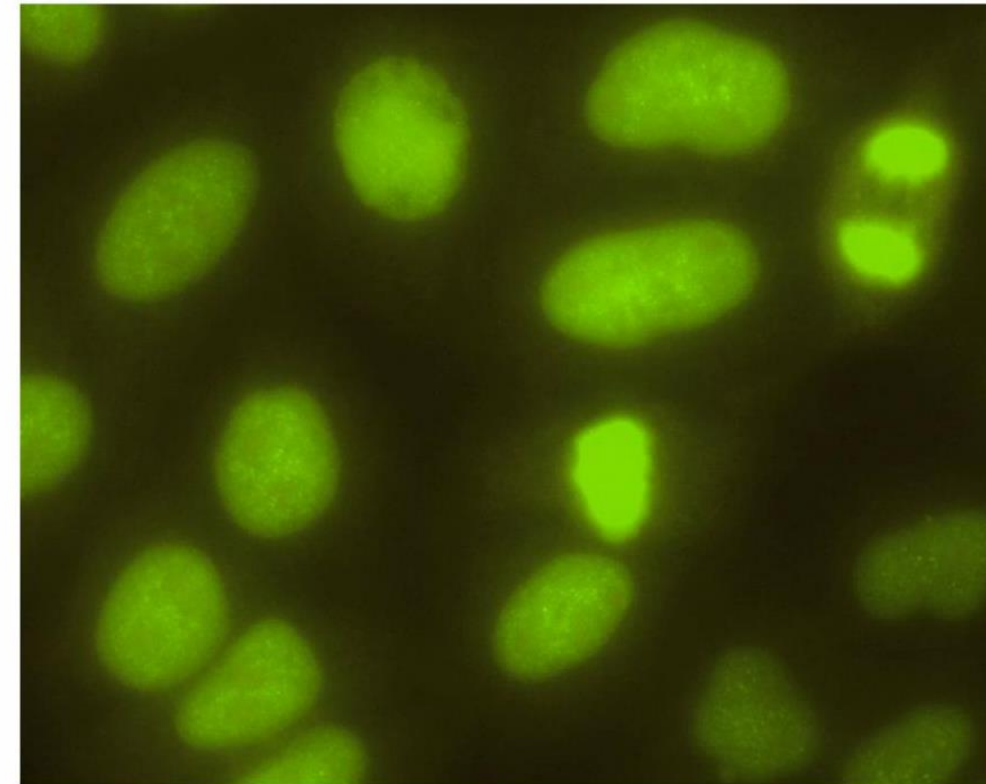
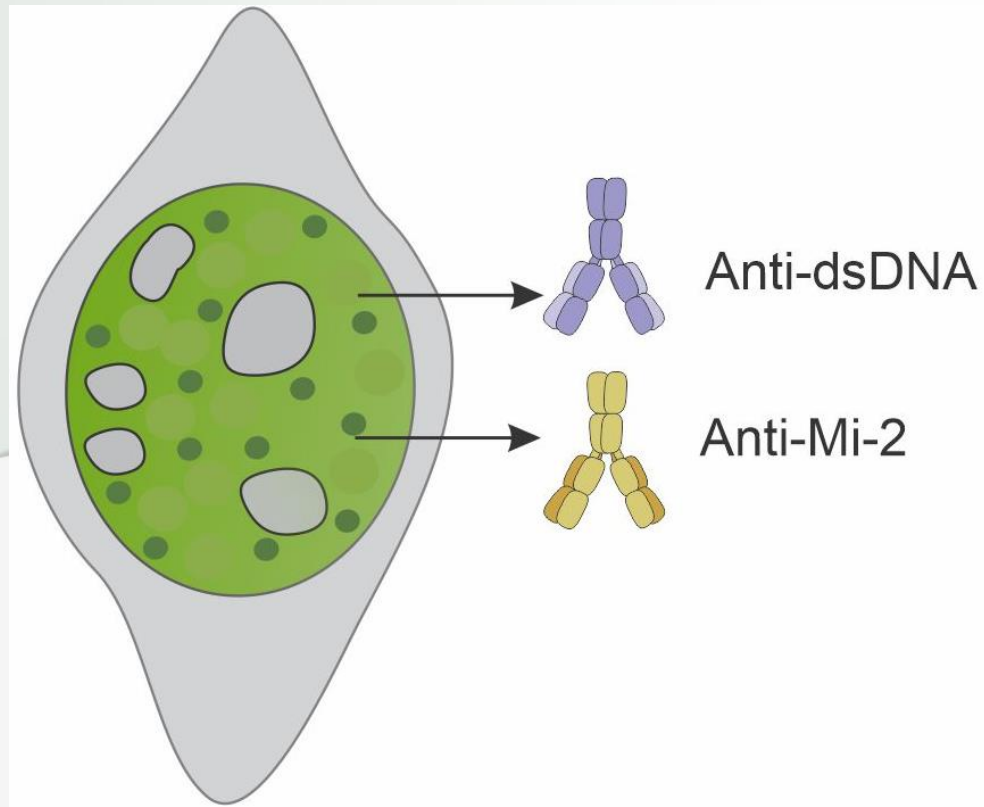




# Classificação dos padrões complexos

## PADRÃO MISTO

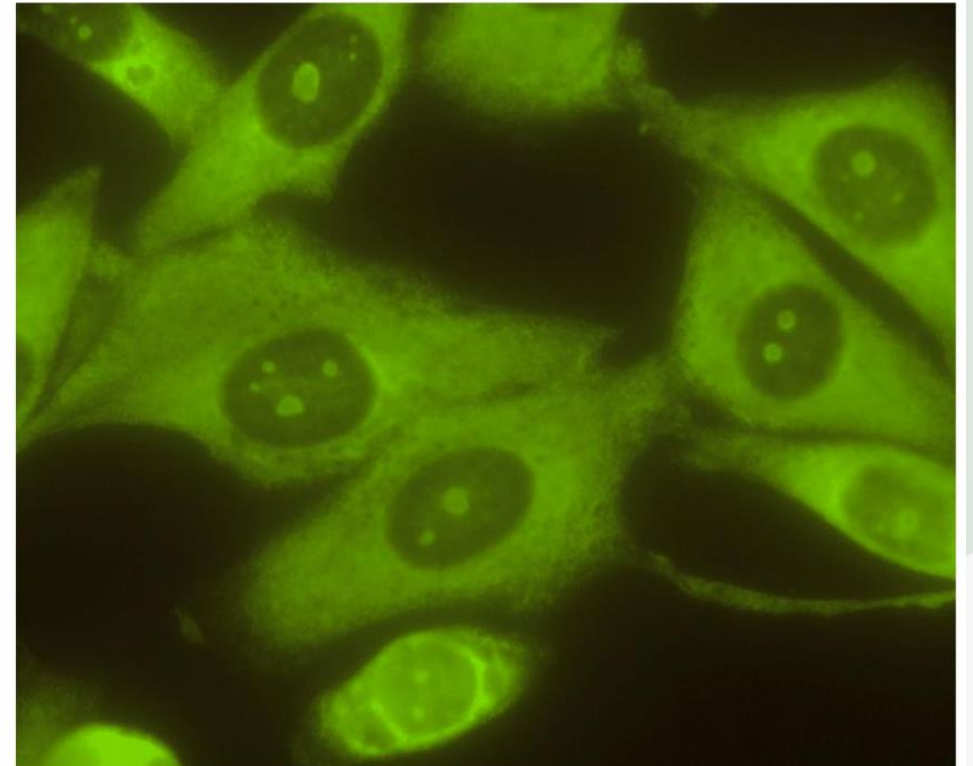
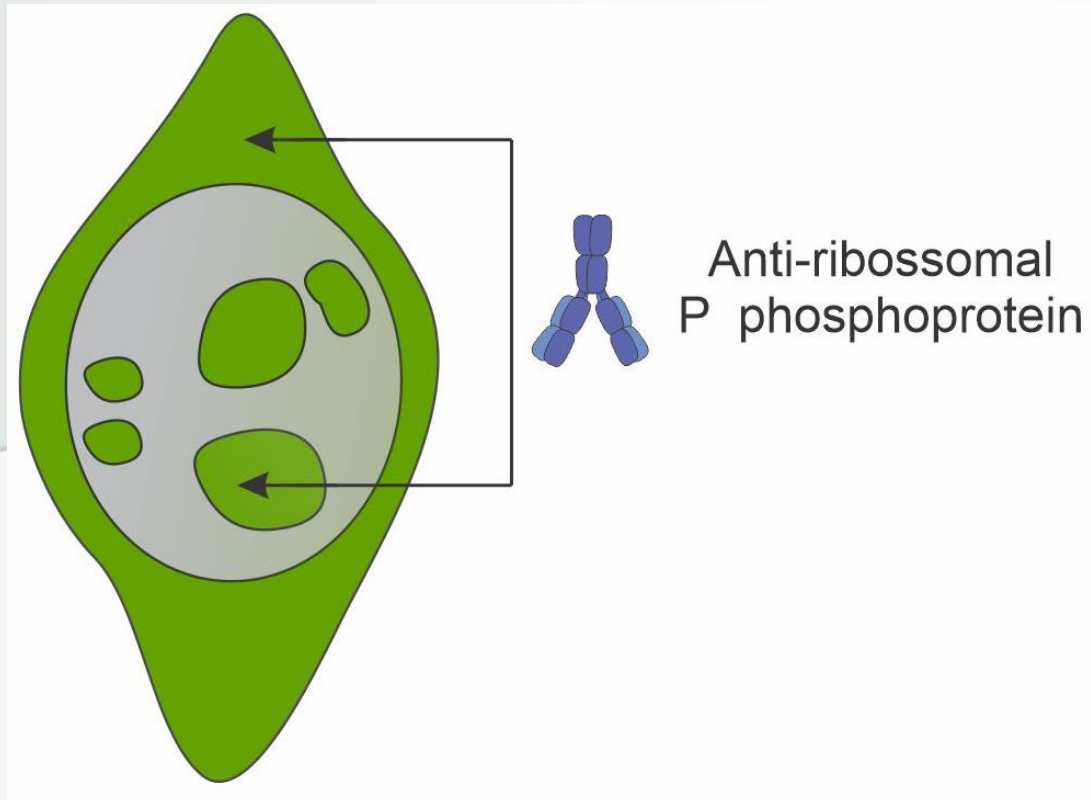
Mais de um padrão está presente mas não é possível individualiza-los.



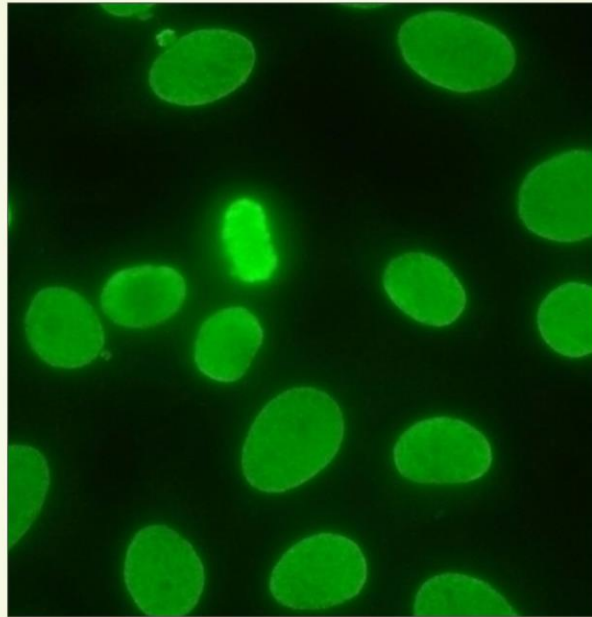
# Classificação dos padrões complexos

## PADRÃO COMPOSTO

Um único autoanticorpo causa uma combinação única de padrões elementares.  
Exemplo BAC-5.



# Recomendação para o Laudo (CBA e ICAP)



## ANA - Anti-cell antibody Test

**Method:** indirect immunofluorescence assay on HEp-2 cells (HEp-2 IFA)

**Pattern:** NUCLEAR HOMOGENEOUS (AC-1)

**Title:** 1:1280

**Nucleus:** positive

**Nuclear envelope:** negative

**Nucleoli:** not visible

**Cytoplasm:** negative

**Mitotic apparatus:** negative

**Metaphase plate:** positive

**Observation:** For more information on clinical relevance, see the pages  
[www.hep-2.com.br](http://www.hep-2.com.br) or [www.anapatterns.org](http://www.anapatterns.org)

**A**

### Sample ANA HEp-2 IIFA Report

1 **INSTITUTION:**  
e.g. Hospital for Autoimmune Diseases

2 **DEPARTMENT:**  
e.g. Immunology Laboratory, room 333, ext. # 2355

3 **REFERRAL FROM:**  
e.g. Rheumatic Diseases Clinic, Dr. Olive Doe, phone 345-3567

4 **DATE:**  
March 6, 2019 (date of ANA report)

5 **PATIENT NAME:**  
Jane Doe, PIN #12345

6 **BORN:**  
May 13, 2008

7 **ANTINUCLEAR ANTIBODY TEST (Anti-Cell Antibodies Test)**

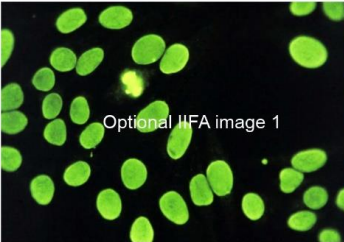
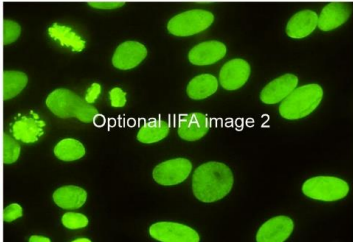
8 Indirect Immunofluorescence Assay on HEp-2 cells - serum

9 **SCREENING TITER:** 1:80

10 **RESULT:**  
Nuclear homogeneous(AC-1) 1:1,280

11 **REFERENCE RANGE:** ≤ 1:160

12 **IMAGES (from actual patient)**

13 **REMARKS:**  
AC-1 is a pattern associated with autoantibodies to dsDNA and nucleosomes. When clinically indicated, we strongly suggest testing for such specificities. Relevant information, including clinical associations, may be found at [www.anapatterns.org](http://www.anapatterns.org).

14 **SIGNATURE:** Dr. John Doe

15 **TITLE:** Head of Immunology

16 Only your health care provider may correctly interpret this laboratory test according to the clinical condition.

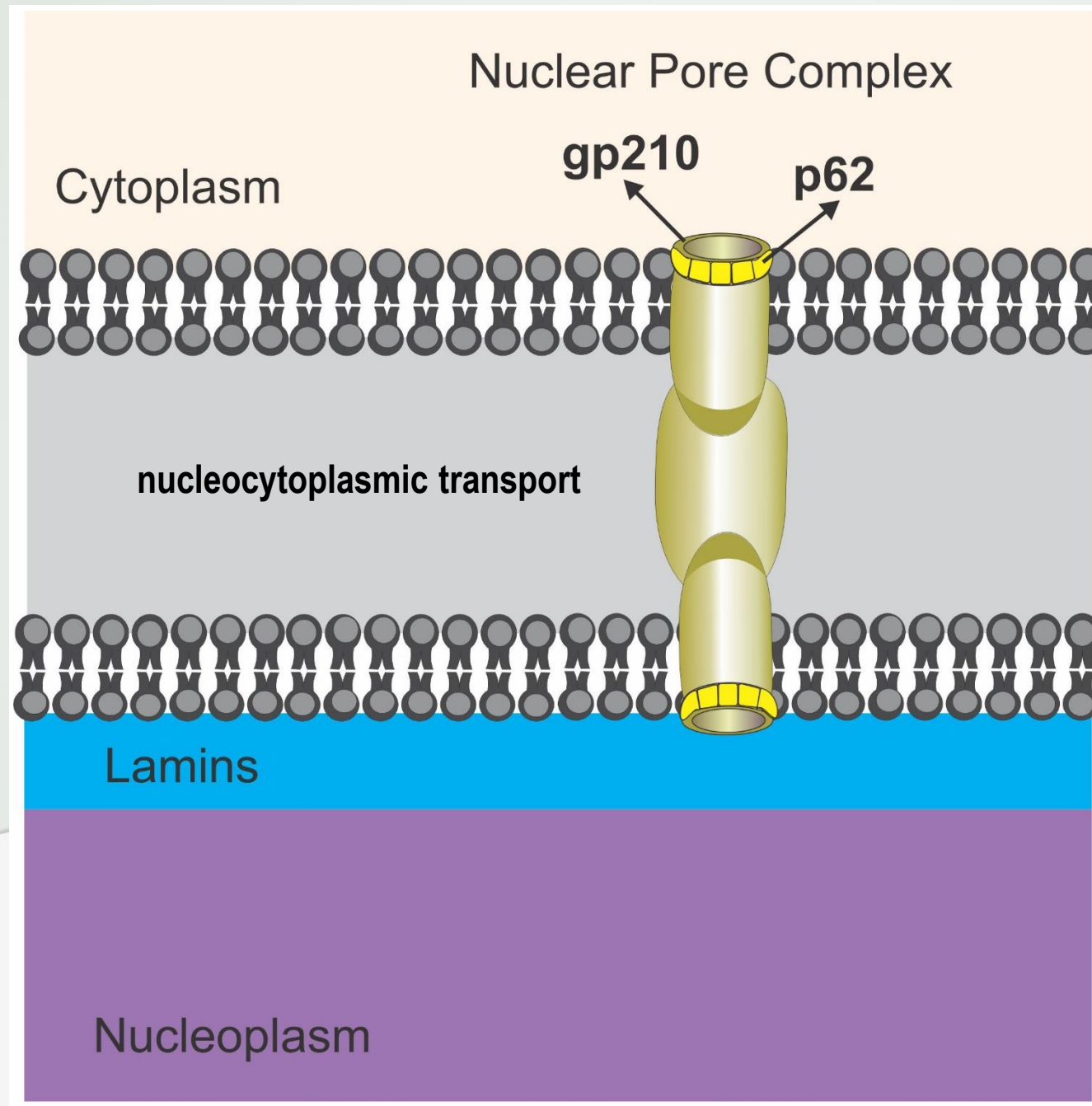


**B**

10.1 **RESULT:**

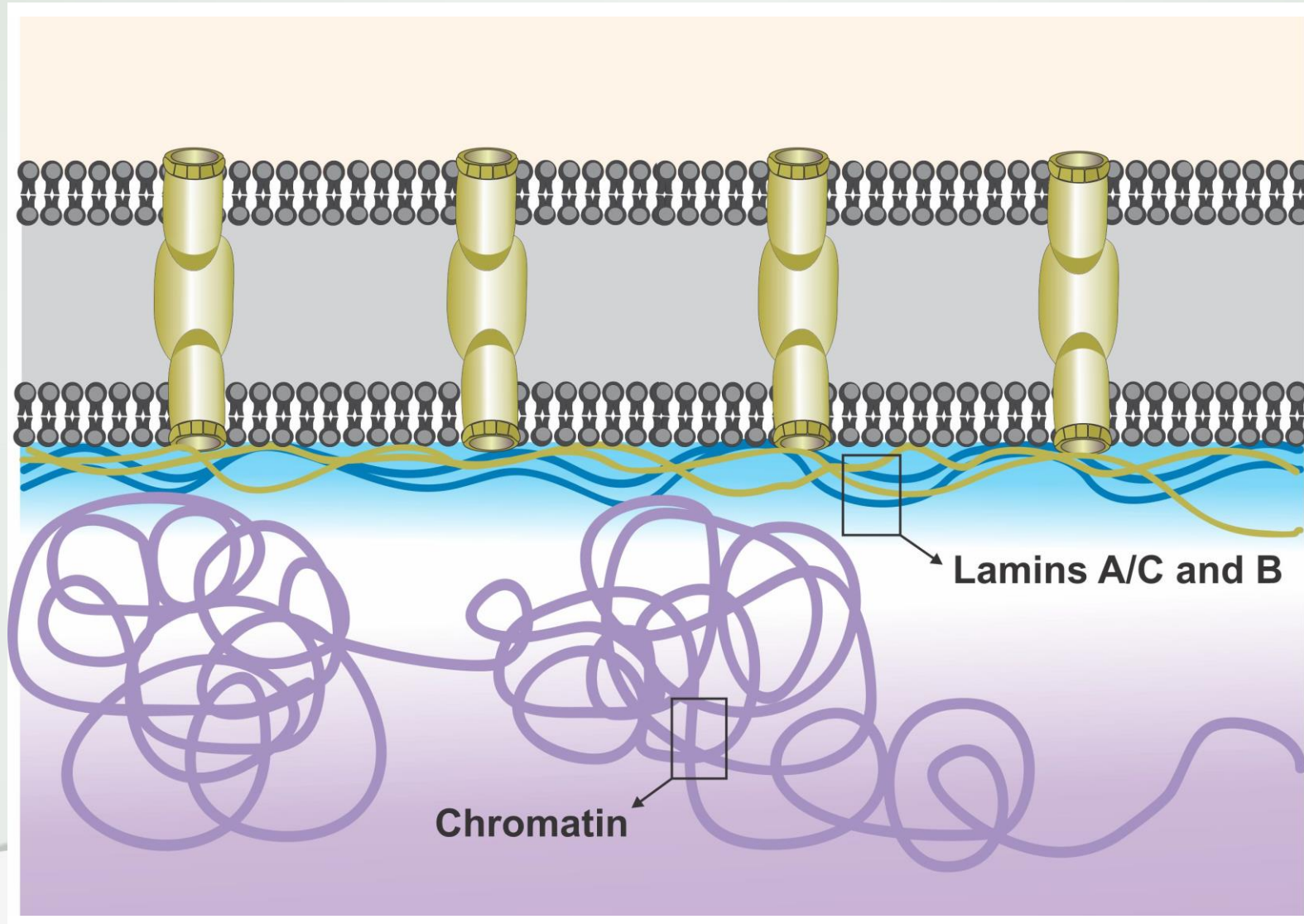
Nuclear homogeneous (AC-1)		<b>&gt;1:1,280</b>
Nucleus	++	> 1:1,280
Nucleolus	-	Negative
Cytoplasm	+	1:80
Mitotic figures	++	> 1:1,280
Mitotic Apparatus	-	Negative

von Mühlen CA, Garcia-De La Torre I, Infantino M, Damoiseaux J, Andrade LEC, Carballo OG, Conrad K, Francescantonio PLC, Fritzler MJ, Herold M, Klotz W, de Melo Cruvinel W, Mimori T, Satoh M, Musset L, Chan EKL. How to report the antinuclear antibodies (anti-cell antibodies) test on HEp-2 cells: guidelines from the ICAP initiative. Immunol Res. 2021



nuclear membranes

**Nuclear pore complexes are composed of multiple copies of approximately 30 to 50 different proteins.**



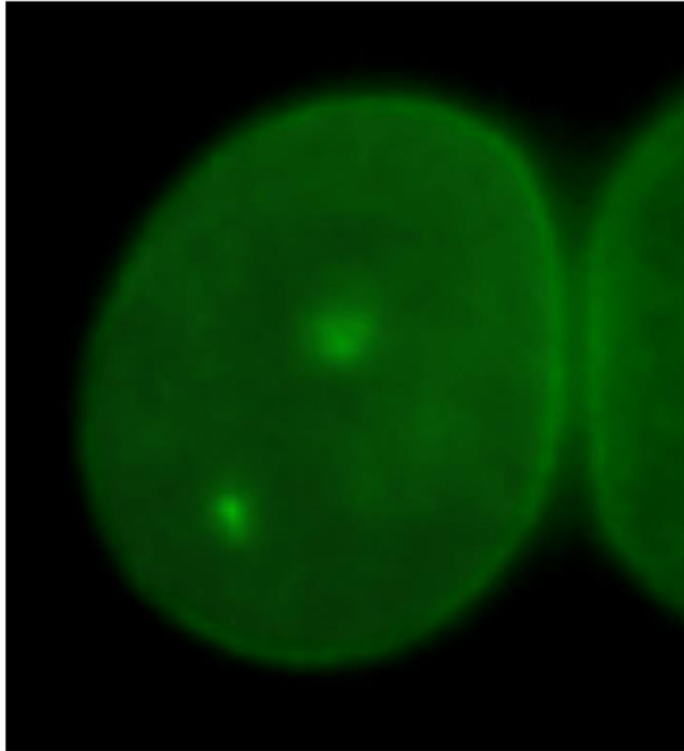
← nuclear lamina

## ❖ NUCLEAR LAMINA

- Fibrous structure underlying the inner nuclear membrane
- Structural function and transcriptional regulation during cell division, apoptosis and NP organizations

(Dechat et al., 2000;  
Gruenbaum et al., 2000;  
Worman & Courvalin, 2005).

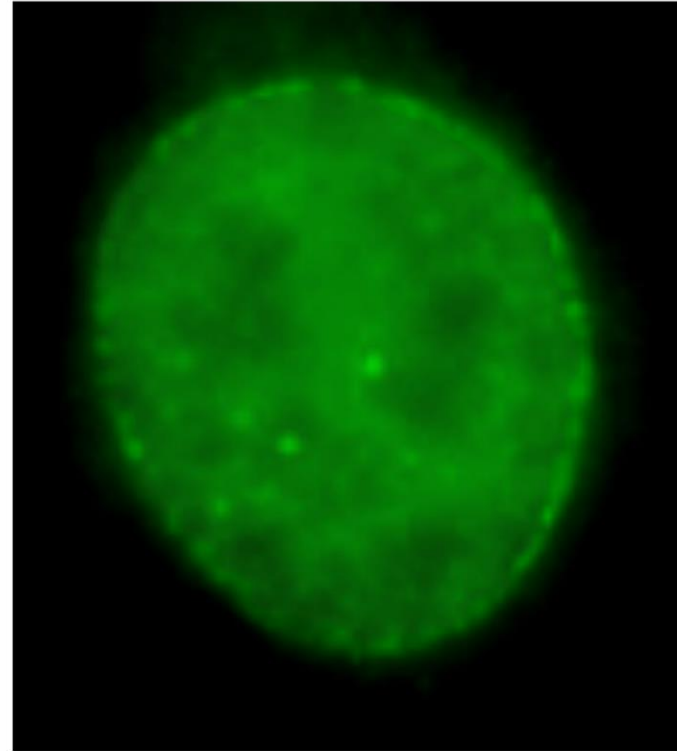
## AC-11 Smooth Nuclear Envelope



Lamins A,B,C, or lamin-associated proteins

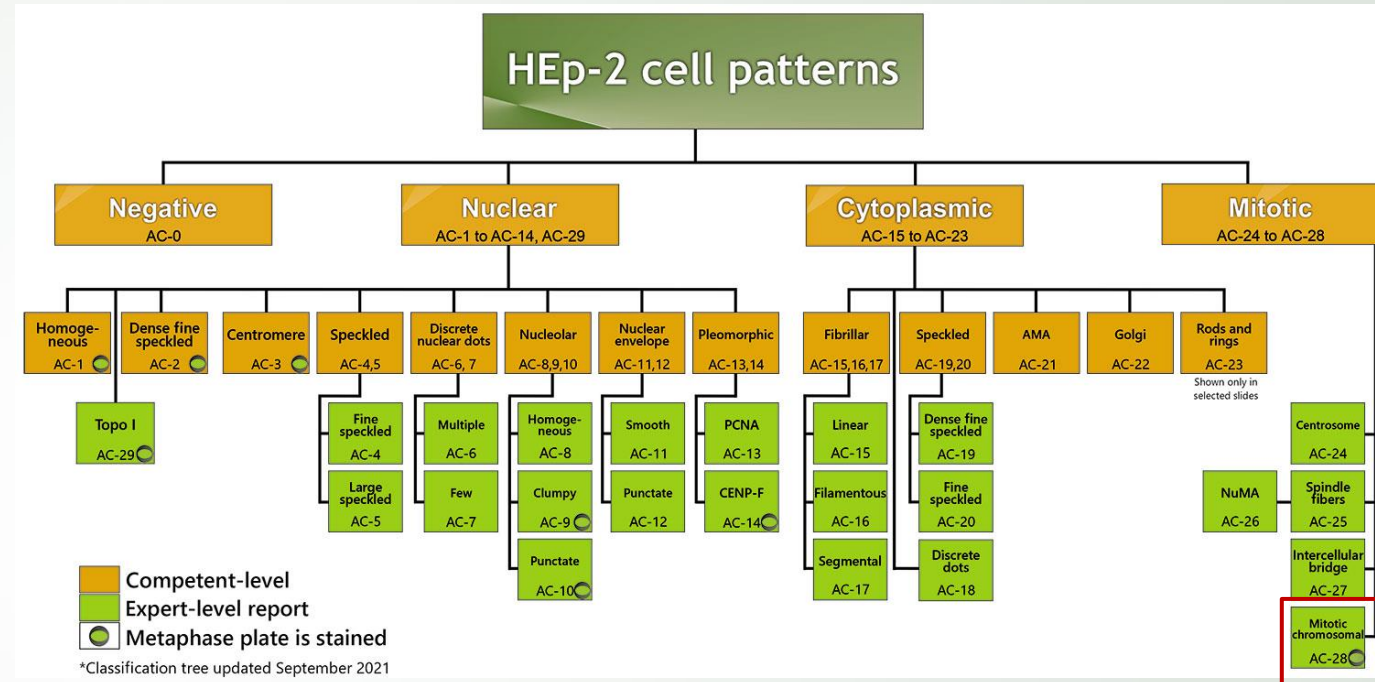
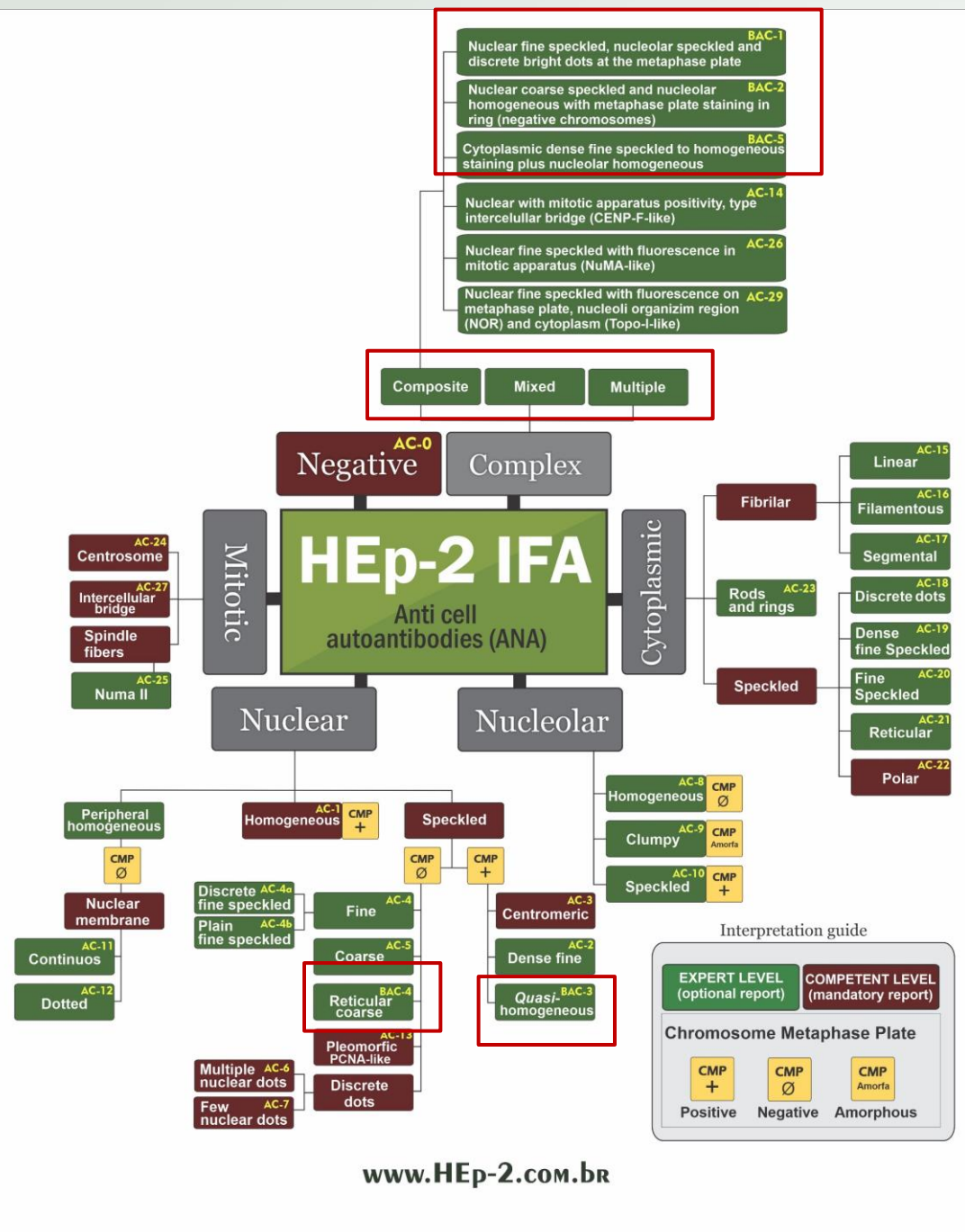
Baixa frequência na retina.  
Descrito em **citopenias autoimunes, doenças hepáticas do fígado. Escleroderma linear, APS e SARD.**

## AC-12 Punctate Nuclear Envelope



Nuclear pore complex proteins (i.e. gp210, p62)

Encontrado em pacientes com **PBC, outras doenças hepáticas autoimunes e SARD.**



Competente Expert



# Acesso às informações dos Consensos Brasileiro e Internacional



**CBA**  
Consenso Brasileiro de  
**Autoanticorpos**



PORTUGUÊS / ENGLISH

ENTRAR

Início

Publicações

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Participantes

Eventos

Apoio

Links

Contato

## Bem vindo

Consenso Brasileiro  
de Autoanticorpos

ÁRVORES DE CLASSIFICAÇÃO

PADRÕES

RELEVÂNCIA CLÍNICA

DIRETRIZES

PROFISSIONAIS DE LABORATÓRIO

MÉDICOS

PACIENTES

## APRESENTAÇÃO

Bem vindo à página do Consenso Brasileiro para pesquisa de autoanticorpos anticélulas HEp-2 (versão em revisão e avaliação). Esta página tem como finalidade disponibilizar as informações sobre Consensos Brasileiros sendo destinada à clínicos, à profissionais de laboratório e a estudantes de graduação e pós-graduação



www.ANApatterns.org

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

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 are available on the website. (For more information on the images, click here.)

The ICAP committee acknowledges the use of the term ANA 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.

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.

# Como ser um membro do ICAP?

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.
2. von Muhlen, C.A., et al., How to report the antinuclear antibodies (anti-cell antibodies) test on HEp-2 cells: guidelines from the ICAP initiative. *Immunol Res*, 2021. 69(6): p. 594-608.
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.
4. Chan, E.K.L., et al., Report of the First International Consensus on Standardized Nomenclature of Antinuclear Antibody HEp-2 Cell Patterns 2014-2015. *Front Immunol*, 2015. 6: p. 412.

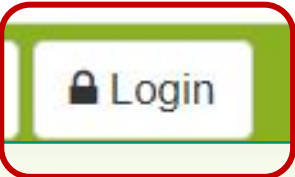
## Signup Page

Enter your data to register

<b>First Name *</b>	<b>Last Name</b>	<b>E-mail *</b>	<b>Confirm E-mail *</b>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<b>Country *</b>	<b>Organization *</b>	<b>Name of Organization *</b>	<b>Professional Information *</b>
<input type="text" value="Select"/>	<input type="text" value="Select"/>	<input type="text"/>	<input type="text" value="Select"/>
<b>Password *</b>	<b>Confirm Password *</b>		
<input type="text"/>	<input type="text"/>		

[Click here to sign up](#)

\* Required field



# Main reasons to register as an ICAP Affiliated Member

## 1. Users information helps to provide updates and new developments oriented to different profiles

TOTAL USERS : **6582**

ORGANIZATIONS	
Clinical/Diagnostic Laboratory	43,0%
Hospital/Clinic	32,0%
Academic institution	15,3%
Industry/Business	7,5%
Other	2,3%

PROFESSIONAL INFORMATION	
Physician/Clinician	46,00%
Technologist	19,11%
Other	16,00%
Student	8,00%
Researcher	6,90%
Administrator/Manager	4,03%

Immunologic Research (2021) 69:594–608  
<https://doi.org/10.1007/s12026-021-09233-0>

ORIGINAL ARTICLE

How to report the antinuclear antibodies (anti-cell antibodies) test on HEp-2 cells: guidelines from the ICAP initiative

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**Abstract**  
 Results of the anti-nuclear antibodies-indirect immunofluorescence assay (anti-cell antibodies test) on HEp-2 cell substrates should be communicated to clinicians in a standardized way, adding value to laboratory findings and helping with critical clinical decisions. This paper proposes a test report based on the practices informed by 118 laboratories in 68 countries, with recommendations from the International Consensus on ANA Patterns (ICAP) group. Major focus is placed on the report format containing endpoint titers, immunofluorescence patterns together with anti-cell (AC) nomenclature, remarks on follow-up or reflex testing, and possible other autoantibody associations. ISO 15.189 directives were integrated into the test report. Search algorithms and Manual Methods were generated. Difficulties and solutions were discussed. Laboratory Performance

## 2. Registered users have access to additional available material



Thumbnail	Title	Download	Size
	Latest ICAP Presentation and Update: International Consensus on Antinuclear Antibody Patterns (ICAP) introduction and update (Edwards K.L. Chan, Lisbon, Mar. 2018)	PDF	2,17 MB
	ICAP presentation file: Powerpoint presentation with the individual classification tree and the representative AC patterns	PDF	197 KB
	ICAP Page 1: Page with nomenclature, classification tree and patterns information (synonyms, antigen and disease associations). Recommended for printing on A4 letter compatible paper.	PDF	554,87 KB
	ICAP Page 2: Page with representative images of each pattern (AC-1 to AC-16). Recommended for printing on A4 letter compatible paper.	PDF	854,54 KB
	ICAP Page 3: Informative page with nomenclature, classification tree and representative images of each pattern (AC-1 to AC-16). Recommended for printing on A4 letter compatible paper.	PDF	2,32 MB
	ICAP Poster 4: Poster with nomenclature, classification tree and patterns information (synonyms, antigen and disease associations). Recommended for printing on A3 compatible paper.	PDF	1,76 MB

### FAQ - FREQUENTLY ASKED QUESTIONS




Submit your question to ICAP. Only confirmed users can submit a question. If you are not registered, [click here](#) questions will be routed to ICAP Coordinators Edward K. L. Chan (echan@ufl.edu) and Luis E. C. Andrade. Simple questions will be answered within 24 hours. Complex questions will be routed to several ICAP members or to provide different viewpoints and it may take 72 hours to 2 weeks for an answer. [click here](#)

# Main reasons to register as an ICAP Affiliated Member

## 3. ICAP training modules are only accessible to registered users.

ICAP Training



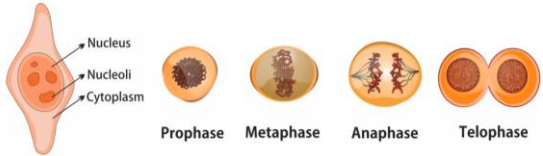
Module 1 : INTRODUCTION TO ICAP

This training presents general information about the International Consensus on ANA Patterns (ICAP), how to get the most of u

[VIEW DETAILS](#)

[VER DETALLES](#)

CELL SUBSTRATE  
Confluence of cell substrate



Interphase Prophase Metaphase Anaphase Telophase

Hep-2 cell is the most common substrate for HEp-2 IFA testing. For commercial HEp-2 slides, it is important that the distribution of cells be adequate for optimal visualization of all the cellular compartments, including the nucleus, nucleoli, cytoplasm, dividing cells, and mitotic apparatus, as well as showing all phases of the cell cycle.

ICAP INTERNATIONAL CONSENSUS ON ANA PATTERNS

www.ANApatterns.org

### CERTIFICATE OF COMPLETION

This is to certify that

**WILSON DE MELO CRUVINEL**

has participated in the educational activity titled

June 30, 2020

This Certificate of Completion has been automatically generated by anapatterns.org website. Print a copy of this certificate for your records.

Edward K. L. Chan, Ph.D.  
ICAP Coordinator

Luis Eduardo C. Andrade, M.D., Ph.D.  
ICAP Coordinator

www.anapatterns.org

- ✓ Registration and membership are free.
- ✓ The information will not share for any commercial purposes.
- ✓ If you no longer want to be a part of ICAP, your information will be deleted upon your request by email.

# ICAP TRAINING 1

## LEARNING OBJECTIVES



### Part 1: Introduction to ICAP

- Introduction to ANA
- Why do we need the ICAP consensus?
- ICAP brief history and organization
- ICAP patterns - Introduction



### Part 2: How to navigate ICAP website

- How to get the most of the ICAP website



### Part 3 Technical recommendations on how to perform the HEp-2 IFA anti-cell test

- Know the crucial steps to ensure best assay quality and reproducibility
- Learn about the HEp-2 cells substrate focusing on cell cycle and cell structures essential
- Know the technical procedure and relevant tips to get optimal results
- Establish a Standard Operating Protocol (SOP) for your laboratory

## COURSE STATISTICS

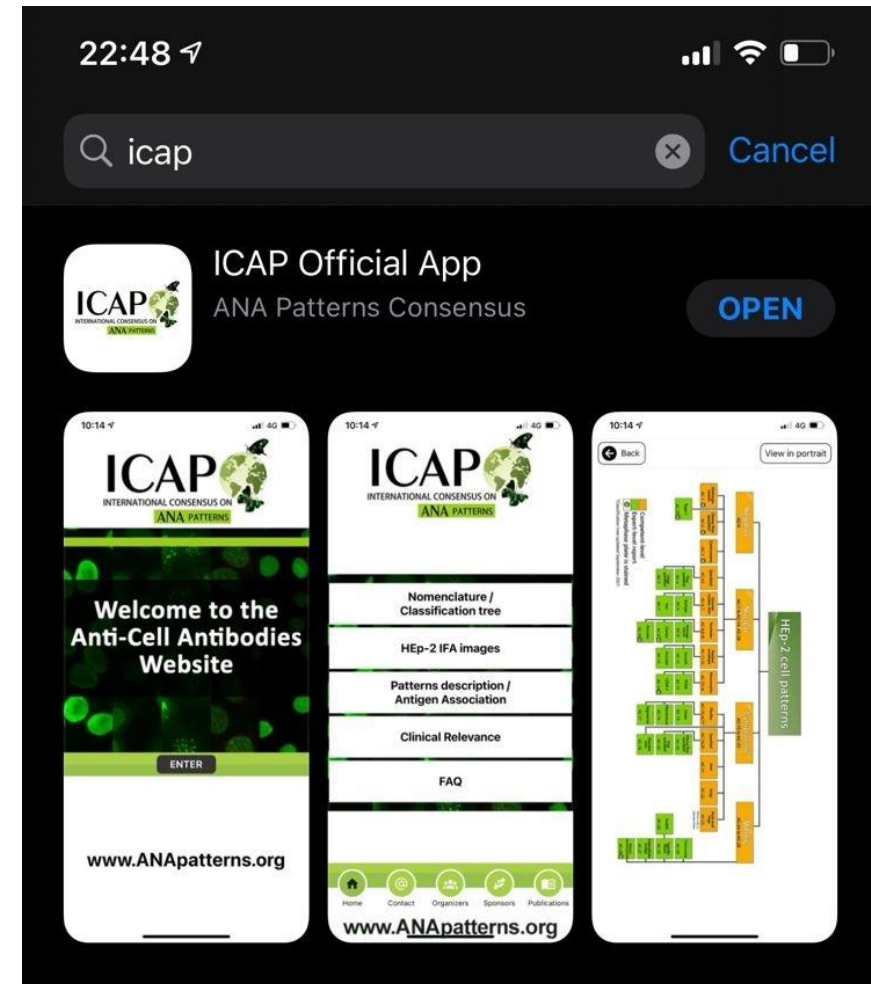
SUBSCRIBERS	CERTIFICATEDS
1409	619 (43.9%)

## COUNTRIES

India	129	5.2%
Argentina	89	6.3%
United States of America	89	6.3%
Italy	75	5.3%
Spain	74	5.3%
Mexico	71	5%
Germany	67	4.8%
Brazil	53	3.8%

# ICAP App

Já disponível em IOS  
Em breve no sistema  
Android.





# CONSIDERAÇÕES FINAIS

- ▶ Os Consensos tem subsidiado recomendações no âmbito da **realização do teste, classificação dos padrões e interpretação dos resultados.**
- ▶ As informações estão disponíveis em diferentes idiomas e formatos.
- ▶ Iniciativas de divulgação e formação são sempre bem vindas para que os objetivos sejam cumprido.

# Obrigado e até a próxima!

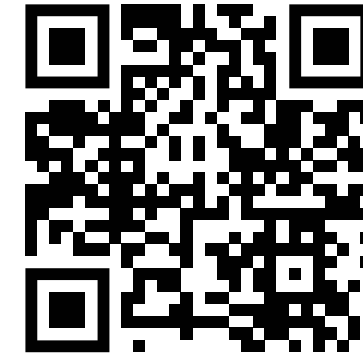
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