

# **Nouvelle nomenclature des ANA**

12th Dresden Symposium on autoantibodies

2015

Réunion GEAI

30 octobre 2015

Daniela Lakomy

# Report of the first international consensus on standardized nomenclature of antinuclear antibody HEp-2 cell patterns 2014–2015

*Edward K. L. Chan<sup>1</sup>, Jan Damoiseaux<sup>2</sup>, Orlando Gabriel Carballo<sup>3,4</sup>, Karsten Conrad<sup>5</sup>, Wilson de Melo Cruvinel<sup>6</sup>, Paulo Luiz Carvalho Francescantonio<sup>6</sup>, Marvin J. Fritzler<sup>7</sup>, Ignacio Garcia-De La Torre<sup>8</sup>, Manfred Herold<sup>9</sup>, Tsuneyo Mimori<sup>10,11</sup>, Minoru Satoh<sup>12</sup>, Carlos A. von Mühlen<sup>13</sup> and Luis E. C. Andrade<sup>14,15\*</sup>*

*<sup>1</sup> Department of Oral Biology, University of Florida, Gainesville, FL, USA, <sup>2</sup> Central Diagnostic Laboratory, Maastricht University Medical Center, Maastricht, Netherlands, <sup>3</sup> Laboratory of Immunology, Hospital Carlos G. Durand, Buenos Aires, Argentina, <sup>4</sup> Department of Immunology, Instituto Universitario del Hospital Italiano, Buenos Aires, Argentina, <sup>5</sup> Institute of Immunology, Technical University of Dresden, Dresden, Germany, <sup>6</sup> Pontificia Universidade Católica de Goiás, Goiânia, Brazil, <sup>7</sup> Department of Medicine, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada, <sup>8</sup> Department of Immunology and Rheumatology, Hospital General de Occidente, University of Guadalajara, Guadalajara, Mexico, <sup>9</sup> Department of Internal Medicine VI, Medical University of Innsbruck, Innsbruck, Austria, <sup>10</sup> Department of the Control for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, Kyoto, Japan, <sup>11</sup> Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Japan, <sup>12</sup> Department of Clinical Nursing, University of Occupational and Environmental Health, Kitakyushu, Japan, <sup>13</sup> Brazilian Society of Autoimmunity, Porto Alegre, Brazil, <sup>14</sup> Rheumatology Division, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, Brazil, <sup>15</sup> Immunology Division, Fleury Medicine and Health Laboratories, São Paulo, Brazil*

Frontiers in Immunology August 2015 / vol 6 / 1-13

[www.ANApatterns.org](http://www.ANApatterns.org)

Site ICAP (International Consensus on Antinuclear Antibody)

## But :

harmonisation et recommandations pour l'interprétation

## Méthodologie :

Session journalière Sao Paulo

66 experts, 15 pays

4 ateliers :

- Nucléaire
- Nucléolaire
- Cytoplasmique
- Mitotique

## Description aspects, synonymes, associations cliniques

Ribosomes

2009 Cy homogène – 2010 cy diffus – 2014 cy diffus – 2015 cy moucheté fin dense

Mitochondries

2009 Mitochondries – 2010 mitochondries-like – 2014 cy moucheté fin – 2015 cy réticulaire

# Autoantibody Detection Using Indirect Immunofluorescence on HEp-2 Cells

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

**TABLE 1.** Typical Nuclear and Cytoplasmic Fluorescence Patterns of Anto-Antibodies

Patterns	HEp-2 Fluorescence	Common Antigens
<b>nuclear patterns</b>		
homogeneous	homogeneous or fine granular nuclear fluorescence, chromatin in metaphase positive	dsDNA, nucleosomes, histones
fine granular	fine/intermediate granular nuclear fluorescence, negative metaphase chromatin	Ro/SS-A, La/SS-B, Ku, Mi-2
coarse granular	coarse granular nuclear fluorescence with numerous condensations, excluding nucleoli	U1-RNP, Sm
nucleolar	nucleolar fluorescence	Scl-70 (chromosomal association); PM-Scl, Fibrillarin, Th/To
centromere	dot count according to interphase chromosome number AND mitosis chromatin	CENP-B
nuclear dots	multiple nuclear dots (commonly 13 to 25 per nucleus), negative metaphase chromatin	Sp100
pleomorphic	heterogeneous staining of interphase nuclei	PCNA
<b>cytoplasmic patterns</b>		
homogeneous	cytoplasm homogeneous to fine granular	Rib-P (with positive nucleoli)
granular	fine to intermediate granular cytoplasm (or granular dots)	Jo-1
mitochondrial	Fine-stitched cytoplasmic fluorescence	AMA-M2
cytoskeletal	cytoskeleton associated fluorescence	Actin

2010

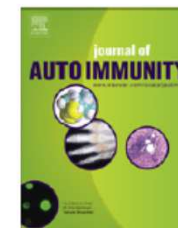
Journal of Autoimmunity 35 (2010) 276–290



Contents lists available at ScienceDirect

Journal of Autoimmunity

journal homepage: [www.elsevier.com/locate/jautimm](http://www.elsevier.com/locate/jautimm)



## Antinuclear antibodies: A contemporary nomenclature using HEp-2 cells

Allan S. Wiik<sup>a,\*</sup>, Mimi Høier-Madsen<sup>a</sup>, Jan Forslid<sup>b</sup>, Peter Charles<sup>c</sup>, Jan Meyrowitsch<sup>d</sup>

<sup>a</sup> Department of Clinical Biochemistry and Immunology, Statens Serum Institut, Artillerivej 5, 2300 Copenhagen S, Denmark

<sup>b</sup> Department of Clinical Immunology and Transfusion Medicine, Karolinska University Hospital, 171 76 Stockholm, Sweden

<sup>c</sup> Translational Research, Kennedy Institute of Rheumatology, Imperial College London, 65 Aspenlea Road, London W6 8LH, United Kingdom

<sup>d</sup> Percepton Ltd., Rialtovej 12, 2300 Copenhagen S, Denmark

Membranous nuclear patterns  
Smooth membranous nuclear  
Punctate membranous nuclear

Nucleoplasmic patterns  
Homogeneous nucleoplasmic pattern  
Large speckled nucleoplasmic  
Coarse speckled nucleoplasmic  
Fine speckled nucleoplasmic  
Fine grainy Scl-70-like nucleoplasmic  
Pleomorphic speckled (anti-PCNA)  
Centromere  
Multiple nuclear dots  
Coiled bodies (few nuclear dots)

Nucleolar patterns  
Homogeneous nucleolar  
Clumpy nucleolar  
Punctate nucleolar

Spindle apparatus patterns  
Centriole (centrosome)  
Spindle pole (NuMa) (MSA-1)  
Spindle fibre  
Midbody (MSA-2)  
CENP-F (MSA-3)

Cytoplasmic patterns  
Diffuse cytoplasmic  
Fine speckled cytoplasmic  
Mitochondrial-like  
Lysosomal-like  
Golgi-like  
Contact proteins  
Vimentin-like

Negative  
Undeterminable

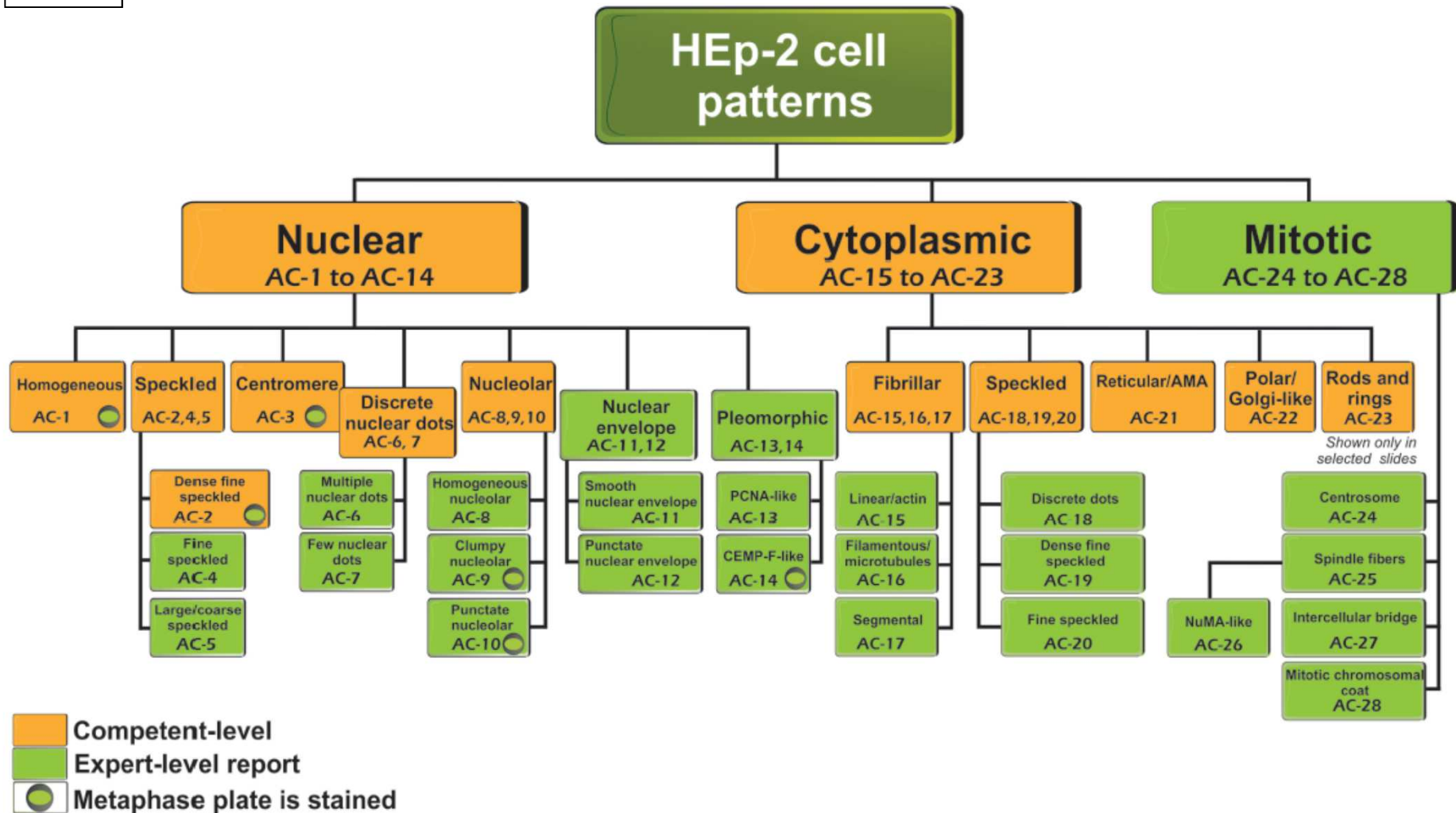
## International recommendations for the assessment of autoantibodies to cellular antigens referred to as anti-nuclear antibodies

Nancy Agmon-Levin,<sup>1,2</sup> Jan Damoiseaux,<sup>3</sup> Cees Kallenberg,<sup>4</sup> Ulrich Sack,<sup>5</sup> Torsten Witte,<sup>6</sup> Manfred Herold,<sup>7,8</sup> Xavier Bossuyt,<sup>9</sup> Lucille Musset,<sup>10</sup> Ricard Cervera,<sup>11</sup> Aresio Plaza-Lopez,<sup>12</sup> Carlos Dias,<sup>13</sup> Maria José Sousa,<sup>14</sup> Antonella Radice,<sup>15</sup> Catharina Eriksson,<sup>16</sup> Olof Hultgren,<sup>17</sup> Markku Viander,<sup>18</sup> Munther Khamashta,<sup>19</sup> Stephan Regenass,<sup>20</sup> Luis Eduardo Coelho Andrade,<sup>21</sup> Allan Wiik,<sup>22</sup> Angela Tincani,<sup>23</sup> Johan Rönnelid,<sup>24</sup> Donald B Bloch,<sup>25</sup> Marvin J Fritzler,<sup>26</sup> Edward K L Chan,<sup>27</sup> I Garcia-De La Torre,<sup>28</sup> Konstantin N Konstantinov,<sup>29</sup> Robert Lahita,<sup>30</sup> Merlin Wilson,<sup>31</sup> Olli Vainio,<sup>32</sup> Nicole Fabien,<sup>33</sup> Renato Alberto Sinico,<sup>34</sup> Pierluigi Meroni,<sup>35</sup> Yehuda Shoenfeld<sup>1,2,36</sup>

**Table 2** IIFA nuclear/cytoplasmic patterns detected on HEp-2 substrates and related antigens/diagnosis

Most commonly recognised patterns		
Nuclear patterns	Related antigens	Related diagnosis
Homogeneous	dsDNA, histones, chromatin/nucleosomes, HMG	SLE, drug induced SLE/vasculitis, JIA
Coarse speckled	U1-SnRNP, U2-6 snRNP (Sm), nuclear matrix	MCTD, SLE, Raynaud, SSc, SS, UCTD
Fine speckled	SSA/Ro, SSB/La, Topo-1, common to many antigens	SLE, SS, SSc, IM, MCTD
Centromere	Kinetochores: CENP-A, B, C, F	SSc (limited), Raynaud's
Nucleolar	PM/Scl, RNA-polymerase, URNP, U3-RNP, To/Th, B23 phosphoprotein/numatrin	SSc, Raynaud's, IM, overlap
Cytoplasmic patterns		
Nuclear patterns	Related antigens	Related diagnosis
Diffuse	RibP, Jo-1, other tRNA synthetases, SRP	SLE, IM
Fine speckled	Jo-1, SRP, PDH (mitochondria)	IM, DM, PBC, interstitial lung disease
Less commonly recognised patterns		
Nuclear patterns	Related antigens	Related diagnosis
Peripheral/rim or nuclear envelope	Lamins, LAP1/2 gp210, nucleoporin p62; nuclear envelope and nuclear pore complex antigens	SLE, RA, PBC, IM autoimmune liver diseases
Dense fine speckled	DFS70/LEDGF-P75	Healthy subjects and other inflammatory conditions
Pleomorphic cell cycle speckled (PCNA)	Auxiliary protein proliferating cell nuclear antigen: elongation factor of DNA polymerase delta	SLE, lymphoproliferative diseases, SS
Nucleolar (clumpy)	U3-SnRNP (fibrillarin)	SSc
Multiple/few nuclear dots	Sp100, PML bodies, p80-coilin	PBC, CAH, SS
Centrosome/centriole (formerly:spindle apparatus)	Enolase, ninein, pericentrin	SSc, Raynaud's, inflammatory disease
MSA (mitotic spindle)	NuMA/centrophilin	RA, inflammatory conditions; pneumonia (mycoplasma)
Cytoplasmic patterns		
Nuclear patterns	Related antigens	Related diagnosis
Discrete speckled	Endosome (early endosome antigen 1), GW/Processing bodies, multivesicular bodies/lysosomes	Neurological conditions, SS, SLE, RA, PBC, UCTD
Golgi complex	Golgi proteins/golgins: giantin, golgin 245, golgin 110, golgin 97, golgin 95, others	SLE, SS, RA, overlap syndromes, cerebellar ataxia
Cytoplasmic fibres	Actin, cytokeratin, tropomyosin, vimentin	CAH, DM, infections and other inflammatory diseases





**FIGURE 1 | Nomenclature and classification tree for nuclear, nucleolar, cytoplasmic, and mitotic IIF staining patterns on HEp-2 cell substrates.**

This is a summary of the International Consensus on Antinuclear antibody Pattern (ICAP) meeting and subsequent discussion, debate, and dialog. Patterns are shown from AC-1 to AC-28. Examples of some of the major

patterns are shown in **Figures 2 and 3**, while additional images of each are depicted in a web page linked to the ANA ICAP website ([www.ANAPatterns.org](http://www.ANAPatterns.org)). Boxes with amber background are recommended as competent-level reporting, whereas those with olive green background are considered for expert-level reporting. AC, anti-cell.

- Aspects techniques dans un rapport à part
- Tous les aspects ne figurent pas pour l'instant
  - aspects rares
  - aspects mixtes
  - aspects composés
- Si fluorescence cytoplasmique ou mitotique : rendre ANA pos
- Si forte corrélation entre aspect IFI et la cible : utiliser terme « like » mais une caractérisation ultérieure reste nécessaire (ex-PCNA-like)
- Tous les aspects connus doivent être rendus (préciser la signification clinique)