HEp-2 CIC PROJECT

CLINICAL AND IMMUNOLOGICAL CHARACTERIZATION OF HEP-2 PATTERNS FREQUENCY OF NUCLEAR PATTERNS IN HEp-2 IFA DIFFER IN LABORATORIES WORLDWIDE

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Background and Aims:

The International Consensus on ANA Patterns (ICAP) launched the HEp-2/CIC project aiming to collect information on methodology/reporting of HEp-2 IFA tests in laboratories worldwide.

Methods:

Laboratories were selected according to geographical representation, expertise, scientific productivity, and/or recommendation by ICAP. Laboratories provided HEp-2 IFA results for all samples without disclosure of personal identification data. Patterns were converted into ICAP AC-codes in consensus with local participants.

Top five nuclear patterns

	AC-1 (Homogeneous)	AC-2 (Dense fine speckled)	AC-3 (Centromere)	AC-4 (Fine speckled)	AC-5 (Large speckled)	AC-4/5 (Speckled)
Laboratories reporting	100%	83%	100%	50%	50%	50%
Minimum frequency	6%	1%	1%	3%	1%	3%
Maximum frequency	64%	33%	10%	86%	40%	94%
Average frequency	28%	7%	4%	39%	7%	45%

Figure 1. Five top nuclear patterns: frequency of laboratories reporting and the frequency of each pattern (Data based on 464,161 HEp-2/IFA results from 42 laboratories in 30 countries and 5 continents)

Results:

Most laboratories report AC-1, AC-2 and AC-3 patterns, but only 50% distinguished AC-4 and AC-5 (Table 1). The frequency of patterns across laboratories varies considerably, especially for AC-1. Of interest, laboratories not reporting AC-2 had increased frequencies of AC-1 and AC-4/5. Distinction between discrete nuclear dots AC-6 and AC-7 was reported by 62% of the laboratories; among nucleolar patterns AC-8, AC-9 and AC-10 by 33%; between nuclear envelope AC-11 and AC-12 by 42% of the laboratories (with frequency <2%); and between pleomorphic patterns AC-13 and AC-14 by 67% of the laboratories (with frequency <2%).

Cytoplasmic patterns (AC-15 to AC-23)

	AC-15 (Fibrillar linear)	AC-16 (Fibrillar Filamen.)	AC-17 (Fibrillar Segmental)	AC-18 (Discrete dots)	AC-19 (DFS)	AC-20 (Fine Spk.)	AC-21 (AMA)	AC-22 (Golgi)	AC-23 (RR)	AC-15 to AC-23
Laboratories reporting	40%	43%	28%	63%	60%	55%	73%	60%	35%	13%
Maximum frequency	4%	4%	1%	9%	9%	9%	22%	1%	22%	23%

Figure 2. Cytoplasmic patterns: frequency of laboratories reporting and the frequency of each pattern

Mitotic patterns (AC-24 to AC-28)

	AC-24 (Centrosome)	AC-25 (Spindle fibers)	AC-26 (NuMA)	AC-27 (Intercellular Bridge)	AC-28 (Mitotic chromosomal)
Laboratories reporting	70%	60%	60%	63%	28%
Maximum frequency	3%	1%	1%	5%	1%

Figure 3. Mitotic patterns: frequency of laboratories reporting and the frequency of each pattern

Results:

The most reported cytoplasmic patterns were AC-18, AC-19 and AC-22. In this group the AC-21 was the most frequent pattern. Despite being reported in more than half of the laboratories, the AC-22 pattern was rather rare (1% of the positive samples). Some laboratories (13%) assumed not to differentiate between the different cytoplasmic patterns.

All the mitotic patterns were reported in more than 60% of the participating laboratories, except for the AC-28 that was reported in just 28% of the laboratories. The mitotic sub-group of patterns had low frequency (<5%).

Preliminary conclusions

Competent-level patterns (AC-1, AC-3, AC-4/5) have larger worldwide inter-laboratory consistency than non-competent-level patterns. Differentiation of speckled (AC-4/5) nucleolar (AC-8/9/10) and envelope (AC-11/12) patterns are not available in many laboratories. The non-recognition of AC-2 caused a putatively misrepresented high frequency in AC-1 and AC-4/5 patterns in some laboratories.

In comparison with the nuclear patterns, cytoplasmic and mitotic patterns were less frequently reported in the participating laboratories and represented a lower fraction of the positive cases, especially the mitotic patterns. The AC-21 pattern had a frequency higher than that expected for anti-mitochondria autoantibodies.

There is an urgent need for worldwide harmonization and training in the interpretation/reporting HEp-2 IFA patterns.