IFA

CytoBead®

For manual and automated assessment

MEDIPAN

GA Generic Assays

Multiparameter IFA Technology

Product Highlights

- Second generation IFA by combining of screening and confirmation
- Multiplex analysis capability
- Integration with automated evaluation systems

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Over 30 Years of Experience, 150 Partners in more than 100 Countries

CytoBead® Technology

Next Generation Multiparameter IFA Technology

CytoBead® Technology

The CytoBead® technology is an innovative approach in the analysis of autoantibodies (AAb) associated with autoimmune diseases. It facilitates the interpretation of indirect immunofluorescence (IFA) on cellular and tissue substrates and quantitative multiplex analysis of AAb using addressable microbead immunoassays within a single reaction environment. Fundamentally, the CytoBead® technology integrates two crucial components of autoantibody analysis:

1. Screening of Autoantibodies: By employing cell- or tissue-based immunofluorescence tests (IFA), the CytoBead® technology allows for the screening of AAb in patient samples. This initial screening phase enables the identification of potentially positive samples containing autoantibodies targeting various cellular components.

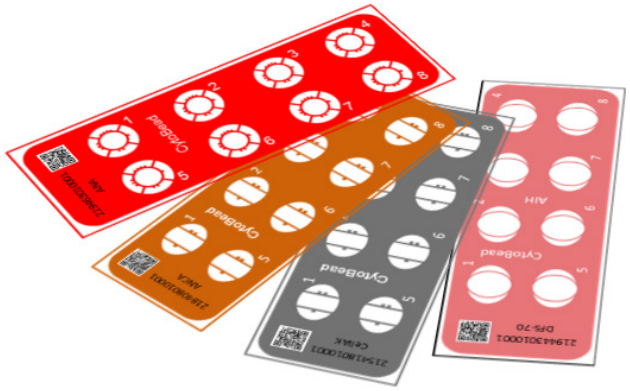
2. Confirmation of Autoantibodies: Through the use of microbead immunoassays, the CytoBead® technology facilitates the differentiation of AAb and determination of their specificity.

By combining screening and confirmation into a single step, the CytoBead® technology significantly enhances the efficiency and accuracy of autoimmune disease diagnosis. Moreover, it enables multiplex analysis, allowing for the simultaneous detection of multiple AAb within a single sample.

The utilization of specialized automated platforms such as AKLIDES® or akiron® systems complements the CytoBead® technology by facilitating the automated interpretation of results. These systems leverage advanced algorithms and software to interpret fluorescence patterns and quantify the presence of AAb in patient samples.

With the CytoBead® technology, laboratories can streamline their analysis processes, resulting in faster turnaround times, increased accuracy, and reduced variability in result interpretation. Ultimately, this integration enhances the efficiency and reliability of autoimmune disease diagnosis and management.[1]

CytoBead®



Available for:

ANA/ANA 2 | ANCA | CeliAK | DFS-70

[1] Sowa M., Hiemann R., Schierack P., Reinhold D., Conrad K., Roggenbuck. D.: Next-Generation Autoantibody Testing by Combination of Screening and Confirmation—the CytoBead® Technology Clinic Rev Allerg Immunol 2017, 53:87–104.

CytoBead® Technology

CytoBead® Technology

1 - Step Strategy

Screening & Confirmation 1.5 - 2h

Confirmed Results

Save Time

Save Material

Save Costs

Standard workflow in Autoimmune Diagnostics

2 - Step Strategy

1.5 - 2h

1. Screening test

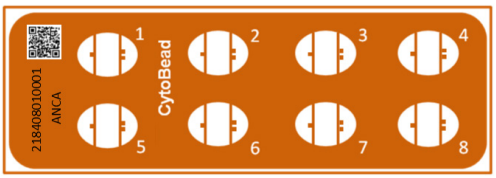
1.5 - 2h

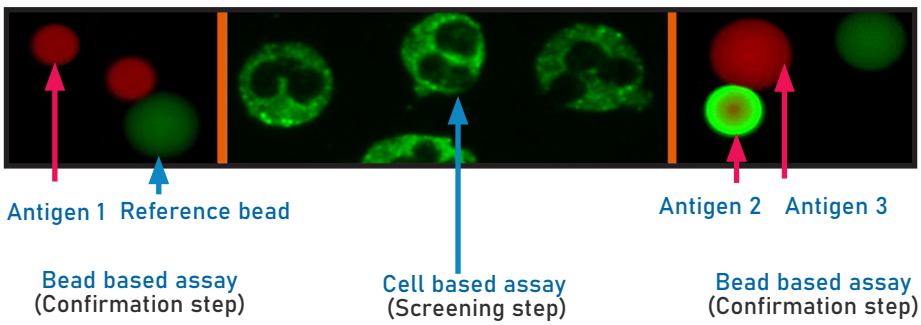
2. Confirmation test

> 4h

Results

How do CytoBead® assays work?





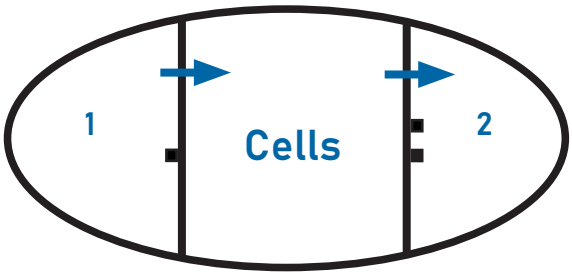
Compartmented slide well:

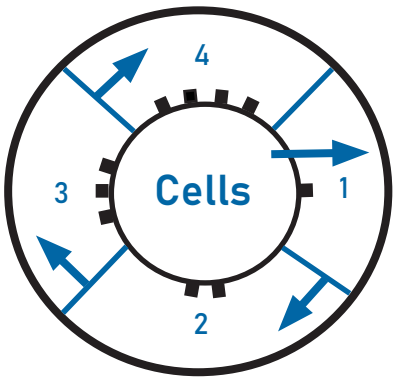
- Screening on cells (classic IFA) in the central compartment
- Confirmation with a bead based assay in the side compartments

Manual CytoBead® Evaluation

Manual Evaluation using the CytoBead® Technology

Bead compartment guides for better orientation (two variants)





Reading direction →

Compartment 1 to cells to compartment 2

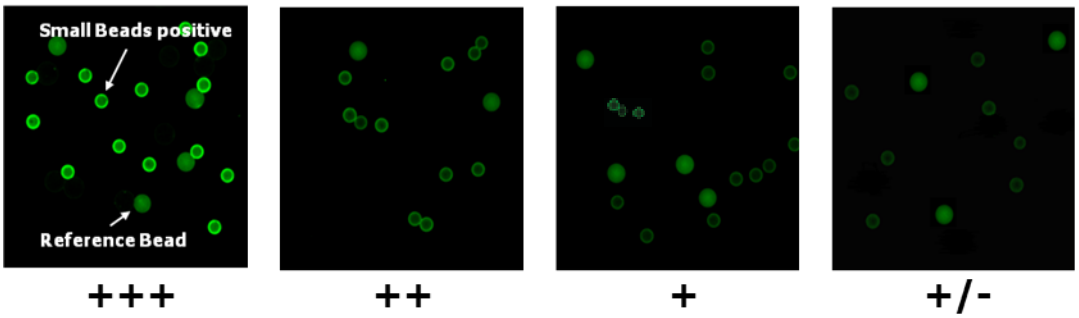
- Compartment marker

Reading direction →

Cells to compartment 1 to 2 to 3 to 4

- Compartment marker

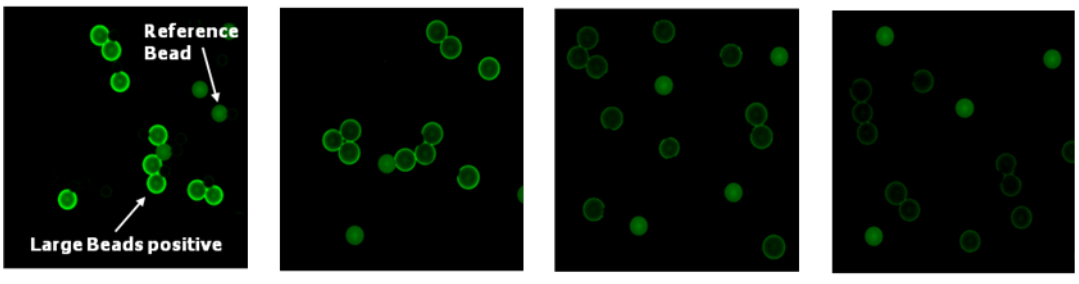
Semi-quantitative evaluation of fluorescence intensity



+++ ++ + +/-

small beads

(= smaller than reference beads)



+++ ++ + +/-

large beads

(= larger than reference beads)

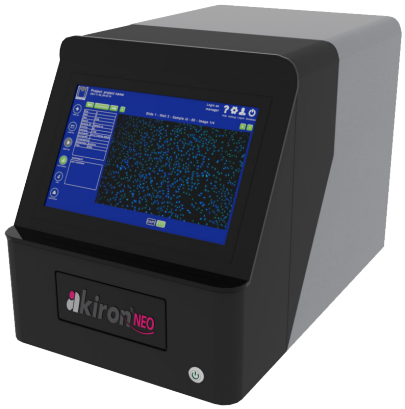
Enlarged images (10x objective)

Automatic CytoBead® Evaluation

Evaluation by akiron® NEO

akiron® NEO

The akiron® NEO is a compact benchtop IFA analyzer for automated digital imaging of processed immunofluorescence slides to support the diagnosis of autoimmune diseases. The akiron® NEO software based on artificial intelligence (AI) allows for an objective ANA / ANCA pattern recognition and intensity evaluation in about 35 seconds*. Validated akiron® NEO assays support the standardized evaluation of a variety of immunofluorescence assays ranging from the determination of antibodies against HEp-2 cells (ANA), granulocytes (ANCA), *Crithidia luciliae* (CLIFT, dsDNA), several tissues as well as against specific antigens using the CytoBead® technology. The powerful easy-to-use akiron® NEO with a small footprint is indispensable for all routine diagnostic services in rheumatology and gastroenterology and not only for laboratories with limited bench space.



Product Highlights

- Automated digital benchtop IFA analyzer with small footprint
- ANA / ANCA pattern recognition and intensity evaluation of processed slides
- AI-based software
- ANA / ANCA titer determination from only one standard sample dilution
- CLIFT for determination of antibodies against dsDNA
- Quantification of antibody activities in U/mL or IU/mL using the CytoBead® technology
- Imaging of tissue sections (e.g. EmA, ...)
- Results in 35 seconds*
- User-friendly touch screen monitor
- Archiving of results for quality assured data management
- Export of all relevant results in pdf- or xls-file format
- LIS Connectivity

* ANA / ANCA / CLIFT

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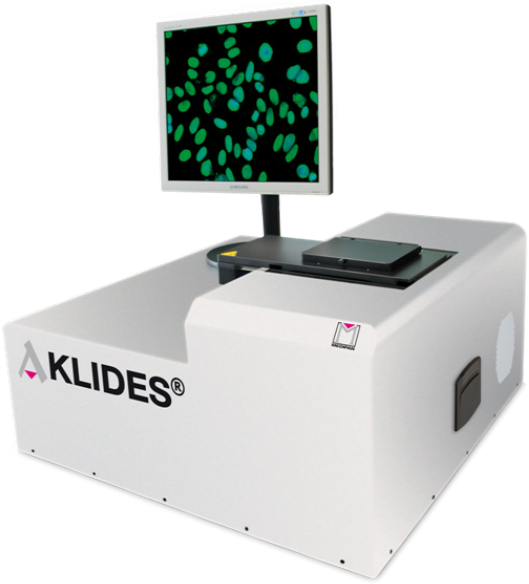
Automatic CytoBead® Evaluation

Evaluation with the Technology Platforms AKLIDES®

AKLIDES®

The AKLIDES® system was the world's first automated IFA analyzer for standardized, digital imaging of processed IFA slides in the market to support the diagnosis of autoimmune diseases. It allows the analysis of up to five slides or 60 samples for a high sample throughput. The user-friendly AKLIDES® software enables objective ANA / ANCA pattern recognition in approx. 35 seconds* per sample (ANA/ANCA/CLIFT). The simultaneous recording of the fluorescence intensity allows the determination of the end-titer from just one standard sample dilution, making the analysis of complex and cost-intensive dilution series obsolete. Validated protocols and AKLIDES® assay files support the standardized evaluation of a large number of immunofluorescence analyzes for the determination of antibodies against HEp-2 cells (ANA), granulocytes (ANCA) and *Crithidia luciliae* (CLIFT, dsDNA), various tissue sections and against specific antigens using the CytoBead® technology. The powerful AKLIDES® system is easy and intuitive to use and indispensable for all diagnostic routine services in the fields of rheumatology and gastroenterology.

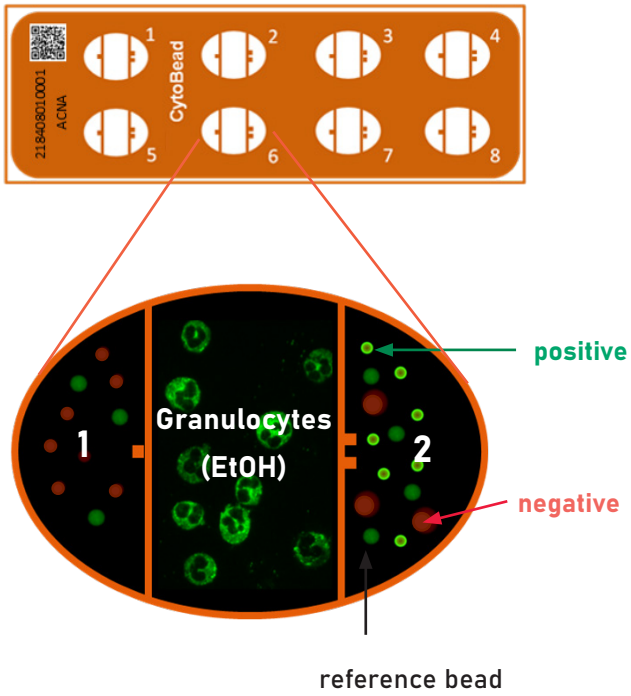


Product Highlights

- Automated IFA analyzer for high sample throughput
- Digital imaging of processed IFA slides
- ANA / ANCA pattern recognition and intensity evaluation
- ANA / ANCA titer determination from only onestandard sample dilution
- CLIFT for determination of antibodies against dsDNA
- Quantification of antibody activities in U/mL or IU/mL using CytoBead® technology
- Imaging of tissue sections (e.g. EmA, ...)
- Results in 35 seconds*
- Archiving of results for quality assured data management
- Export of all relevant results in pdf- or xls-file format
- LIS Connectivity

* ANA / ANCA / CLIFT

CytoBead® ANCA



Fast and easy ANCA diagnostics

ANCAs (Anti-Neutrophil Cytoplasmic Antibodies) play an important role in the diagnosis of ANCA associated vasculitides (AAV). According to international guidelines ANCA screening is performed using immunofluorescence (IFA) with ethanol-fixed granulocytes, whereby cytoplasmic (cANCA; antigen PR3) and perinuclear (pANCA; antigen MPO) IFA patterns can be differentiated.

Unique combination of HEp-2 cells with antigen coated microbeads

Advantages of CytoBead® ANCA

- Screening with standardized ethanol fixed granulocytes
- Confirmation of 3 ANCA-specific antigens

CytoBead® ANCA

Tissue pattern	Compartment	Bead (positive)	Quantification	Antigen	Clinical relevance
honeycomb pattern of muscularis mucosa	1		U/mL	tTG	Celiac disease, dermatitis herpetiformis
	1		U/mL	DG	
	2		U/mL	Anti-IgA	IgA deficiency

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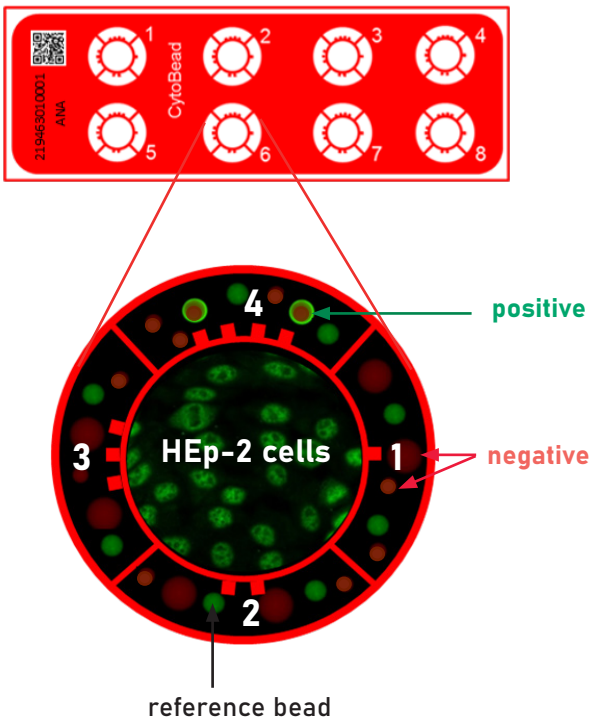
CytoBead® ANA / ANA 2



Fast and easy ANA diagnostics

ANA (Anti-Nuclear Antibodies) are autoantibodies which recognize conserved nuclear antigens. ANA show a characteristic staining of nuclear structures with indirect immunofluorescence on human epithelial cells (HEp-2). The confirmation of ANA is done in accordance to the target antigens.

Unique combination of HEp-2 cells with antigen coated microbeads

Advantages of CytoBead® ANA / ANA 2

- Screening with standardized HEp-2 cells
- Confirmation of 8 ANA-specific antigens

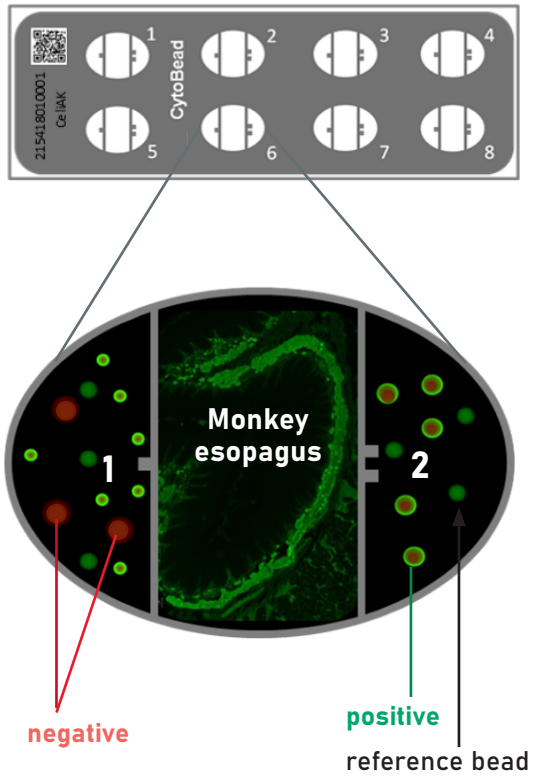
CytoBead® ANA / ANA 2

HEp-2 cell pattern	Compartment	Bead (positive)	Quantification	Antigen	Clinical relevance
Homogeneous	**3**		IU/mL	dsDNA	Systemic lupus erythematosus (SLE)
			U/mL	Scl-70	Marker for progressive systemic sclerosis (PSS)
Speckled	**2**		U/mL	Sm	Sm antibodies highly specific for SLE; high anti-nRNP titers specific for mixed connective tissue disease (MCTD) together with other ANAs in rheumatoid arthritis (RA), SLE, PSS
			U/mL	nRNP	
	4		U/mL	Ro60/SS-A	Often in primary Sjögren's syndrome, anti-SS-A often in neonatal lupus
			U/mL	Ro52/SS-A	
	1		U/mL	La/SS-B	
Centromere	**1**		U/mL	CENP-B	Marker for CREST syndrome, rarely in diffuse scleroderma and Raynaud's phenomenon

CytoBead® ANA 2, Jo-1 microbead replaces CENP-B microbead

Cytoplasmic	**1**		U/mL	Jo-1	Polymyositis, dermatomyositis

CytoBead® CeliAK



Fast and easy diagnostics of celiac disease or dermatitis herpetiformis and detection of IgA deficiency

Celiac disease (gluten induced enteropathy) is an intolerance to gluten. This intolerance leads to extended lesions of the mucous membranes, which manifests as a "flat" mucosa. Gliadin, the alcohol-soluble fraction of gluten, is responsible for the emergence of celiac disease. Gliadin induces inflammatory processes in the small intestinal mucosa as part of the humoral and cellular immune processes. The diagnosis of celiac disease is characterized through highly specific autoantibodies against transglutaminase 2 (tissue transglutaminase, tTG) and deamidated gliadin (DG). Endomysial antibodies (EmA) are directed against extracellular tTG. Celiac specific antibodies are usually of IgA class but in patients with IgA deficiency the IgG class is of diagnostic significance.

Unique combination of esophageal tissue with antigen coated microbeads

Advantages of CytoBead® CeliAK

- Screening with standardized monkey esophageal tissue
- Confirmation of 3 celiac-specific antigens

CytoBead® CeliAK

Tissue pattern	Compartment	Bead (positive)	Quantification	Antigen	Clinical relevance
honeycomb pattern of muscularis mucosa	1		U/mL	tTG	Celiac disease, dermatitis herpetiformis
	1		U/mL	DG	
	2		U/mL	Anti-IgA	IgA deficiency

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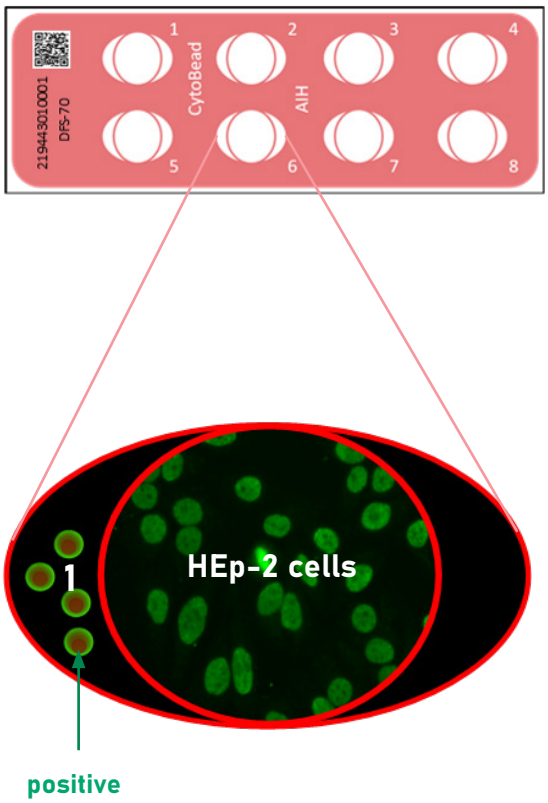
CytoBead® ANA DFS-70



Exclusion of „false positive“ ANA results

Up to 20 % of positive patterns in indirect immunofluorescence on HEp-2 cells may be caused by antibodies to DFS-70, confusing the assignment of positive results to systemic rheumatic diseases. These antibodies show dense fine speckled nuclear pattern combined with speckled mitotic chromatin zone. Fluorescence staining also on the added DFS-70 beads allows the exclusion of these results from rheumatologic screening.

Unique combination of HEp-2 cells with DFS-70 coated microbeads
Advantages of CytoBead® ANA DFS-70 · ANA screening with standardized HEp-2 cells · Exclusion of non-related patterns using the DFS-70 beads

CytoBead® ANA DFS-70

HEp-2 cell pattern	Compartment	Bead (positive)	Quantification	Antigen	Clinical relevance
Dense fine speckled	1		Not available yet	DFS-70	Very rare in systemic rheumatic diseases, found in different autoimmune diseases and malignancies, also present in healthy people
Other patterns					See CytoBead® ANA and ANA 2

CytoBead® Literature

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2. **Investigation of dense fine speckled pattern and anti-dense fine speckled 70 antibody by a single step assay.** Onarer P, Mutlu E, Öngüt G, Gültekin M. J Microbiol Methods 2022, 203:106606.

3. **Frequency of positive ANCA test in a population with clinical symptoms suggestive of autoimmune disease and the interference of ANA in its interpretation.** Romero-Sánchez C, Benavides-Solarte M, Galindo-Ibáñez I, Ospina-Caicedo AI, Parra-Izquierdo V, Chila-Moreno L, Villa Amanda, Casas-Gómez MC, Angarita I, Bautista-Molano W, Romero-Álvarez V, Bello-Gualteroa JM. Reumatología Clínica 2020, 473-479.

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5. **The Discrepancy of ANA and Compartment Bead Patterns Suggestive of a Neuropsychiatry Systemic Lupus Erythematosus (NPSLE).** Fitriah M, Rahmawati LD, Wulanda IA, Susianti H, Tambunan BA., Case Rep Psychiatry 2023, 5260208.

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7. **Next-Generation Autoantibody Testing by Combination of Screening and Confirmation– the CytoBead® Technology.** Sowa M, Hiemann R, Schierack P, Reinhold D, Conrad K, Roggenbuck D. Clinic Rev Allerg Immunol 2017, 53:87-104.

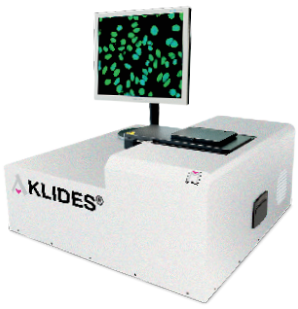
8. **Second generation analysis of antinuclear antibody (ANA) by combination of screening and confirmatory testing**. Scholz J, Grossmann K, Knütter I, Hiemann R, Sowa M, Röber N, Rödiger S, Schierack P, Reinhold D, Bogdanos DP, Meroni PL, Radice A, Conrad K, Roggenbuck D. Clin Chem Lab Med 2015, 53(12): 1991-2002.

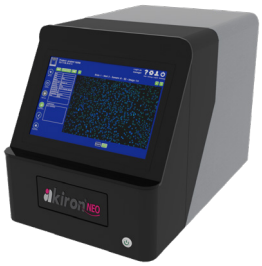
9. **Simultaneous automated screening and cofirmatory testing for vasculitis-specific ANCA**. Sowa M, Grossmann K, Knütter I, Hiemann R, Röber N, Anderer U, Csernok E, Bogdanos DP, Borghi MO, Meroni PL, Schierack P, Reinhold D, Conrad K, Roggenbuck D. PLoS One 2014, 16;9(9).

10. **The CytoBead assay - a novel approach of multiparametric autoantibody analysis in the diagnostics of systemic autoimmune diseases**. Sowa M, Grossmann K, Scholz J, Röber N, Rödiger S, Schierack P, Conrad K, Roggenbuck D, Hiemann R. J Med Lab 2014, 38:309-17.

CytoBead Assays® - Order Information

Automated Assays





Manual Assays

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Automated CytoBead® Assays for AKLIDES® & akiron® NEO

Test	Reference	Determinations
AKLIDES® CytoBead® ANA	4272	80 (10 x 8)
AKLIDES® CytoBead® ANA 2	4277	80 (10 x 8)
AKLIDES® CytoBead® ANCA	4270	48 (6 x 8)
AKLIDES® CytoBead® CeliAK	4271	48 (6 x 8)
CE certified		

Manual CytoBead® Assays

Test	Reference	Determinations
CytoBead® ANA	8065	80 (10 x 8)
CytoBead® ANA 2	8220	80 (10 x 8)
CytoBead® ANCA	8063	48 (6 x 8)
CytoBead® CeliAK	8064	48 (6 x 8)
CE certified		
CytoBead® ANA DFS-70	8260	80 (10 x 8)
For research use only		

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