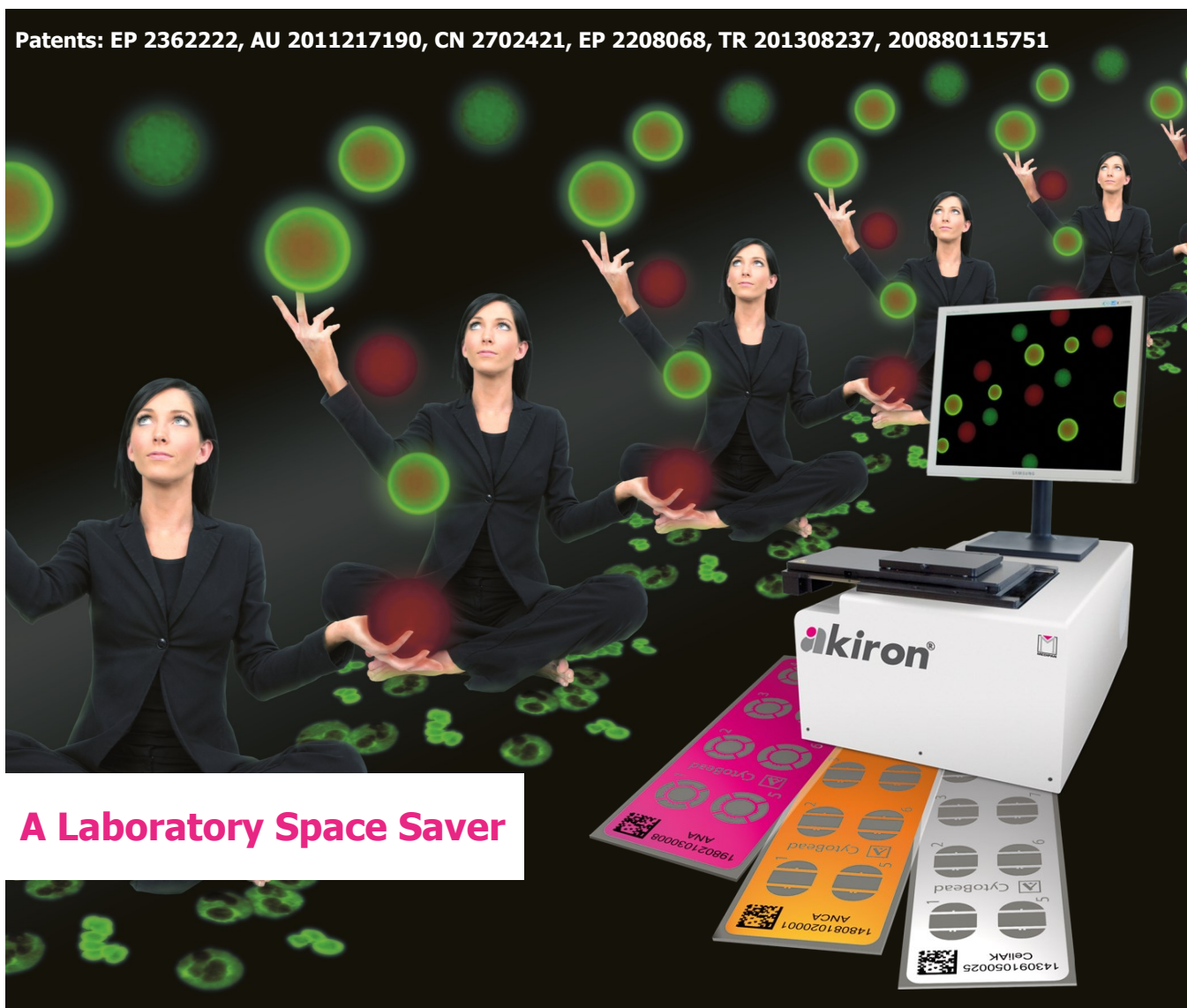


ikiron[®]

The Automated Way of CytoBead[®] Assays

Patents: EP 2362222, AU 2011217190, CN 2702421, EP 2208068, TR 201308237, 200880115751



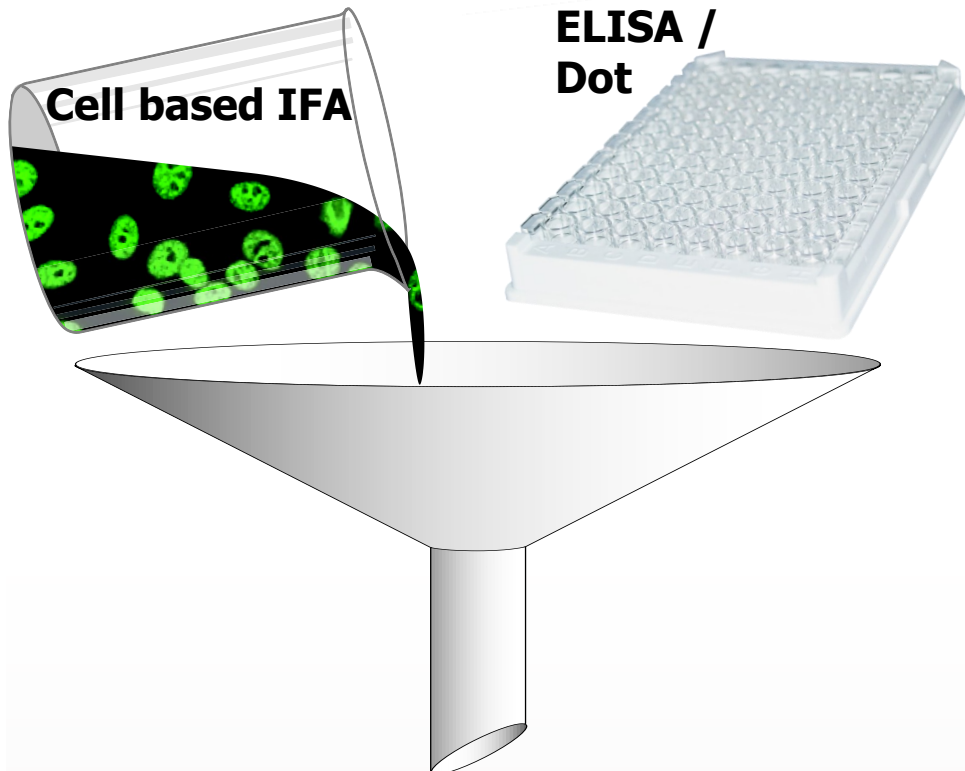
A Laboratory Space Saver

Classical Handling of Autoimmune Diagnostics

2-Step
Diagnostics

1st Screening

2nd Confirmation



1-Step
Diagnostics

Next Generation IFA

CytoBead® Technology

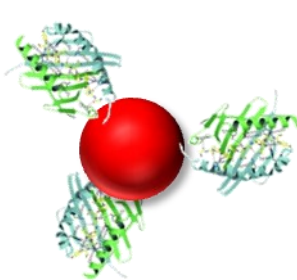
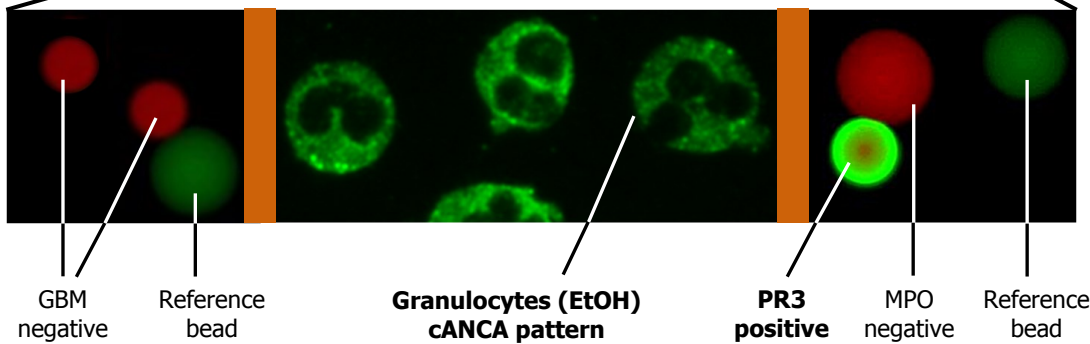
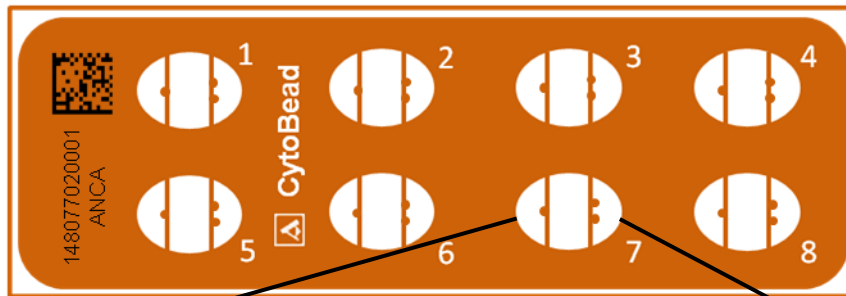
- ANA / ANA 2
- ANCA / RPGN
- CeliAK

Automated evaluation!

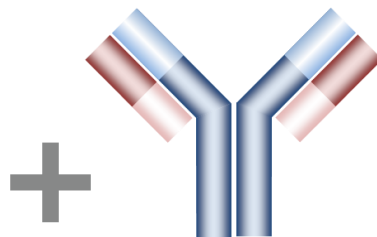


Screening and Confirmation at once!
One Well - One Step - One Assay

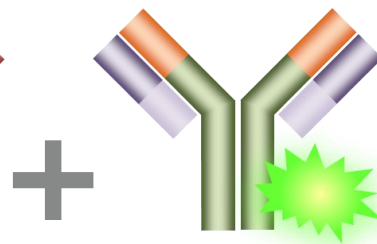
Example AKLIDES® CytoBead® ANCA



Antigen coated bead (e.g. PR3)



Primary antibody (patient sera)



Secondary antibody fluorochrome labeled



AKLIDES® CytoBead® is time saving and economical.

Quantitative determination of autoantibodies with akiron® or AKLIDES® system.

Evaluation with akiron® system

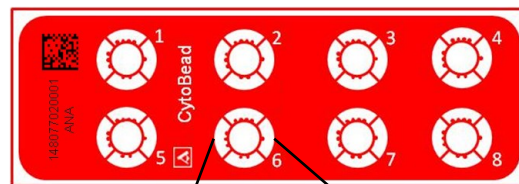
- Fully automated screening and objective evaluation of cells and tissues as well as automated microbead identification and measurement of the ligand fluorescence intensity of the beads
- Standardized and reliable results between different instruments due to intensity calibration
- ELISA typical quantification of antibodies in U/ml or IU/ml with lot specific standard curves using 4 point calibration
- Automatic titer prediction → only one sample dilution is required
- Overall report of all relevant quantitative results in pdf- and xls-format
- Single well report in pdf-format (including cell images)

Slide Report

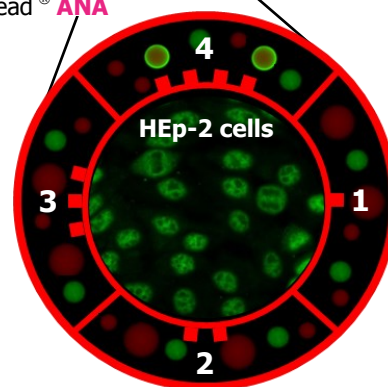
	OT: 652 Project: 15427001		Lot: 15427001		1 / 1	
	Test: 4270 CytoBeadANCA quant 08 Data measured: 2015-05-28 12:10:59 (qc) Data confirmed: 2015-05-28 12:18:03 (qc) Institute: Login: qc Design:	5 ID: MPO Dilution: 1/160 Cells + Intensity 569.00 Pattern + pANCA Titer 640 Beads + PR3 - 1.4 IU/ml MPO + 70.2 IU/ml GBM - 4.6 U/ml		1 ID: Control (CII) Dilution: Cells + Intensity 579.00 Pattern + pANCA Titer 2560 Beads + PR3 + >100.0 IU/ml MPO + >100.0 IU/ml GBM + 20.9 U/ml		
		6 ID: dsDNA Dilution: 1/20 Cells + Intensity 489.00 Pattern + nuclear Titer 80 Beads - PR3 - 1.4 IU/ml MPO - 2.8 IU/ml GBM - 2.2 U/ml		2 ID: Control (CIII) Dilution: Cells + Intensity 560.00 Pattern + cANCA Titer 2560 Beads + PR3 + >100.0 IU/ml MPO - 2.2 IU/ml GBM - 3.0 U/ml		
		7 ID: GBM Dilution: 1/20		3 ID: Control (CI) Dilution:		
						

Fast and easy ANA Diagnostics

ANA (Anti-Nuclear Antibodies) are autoantibodies (AAB) 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.



CytoBead[®] ANA



Unique Combination of HEp-2 Cells with antigen coated Microbeads

Advantages of the CytoBead[®] ANA / ANA 2

- **Screening** with standardized HEp-2 cells
- **Confirmation** of 8 ANA specificities with microbeads

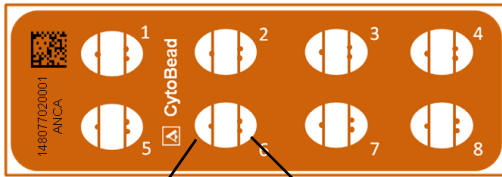
CytoBead[®] ANA / ANA 2

HEp-2 cell pattern	Com-part-ment	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	1		U/ml	La/SS-B	
Centromere	1		U/ml	CENP-B	Marker for CREST syndrome, rarely in diffuse scleroderma and Raynaud's phenomenon

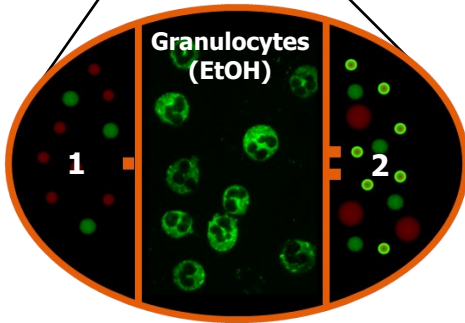
CytoBead[®] ANA 2, Jo-1 microbead replaces CENP-B microbead

Cytoplasmic	1		U/ml	Jo-1	Polymyositis, dermatomyositis
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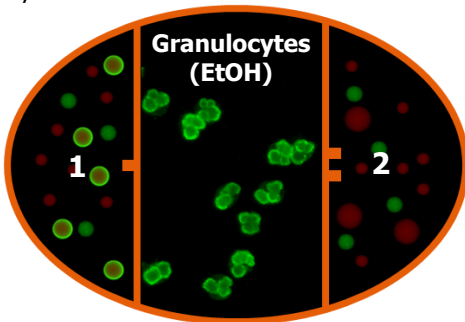
- Small bead: negative
 Large bead: negative
 Reference bead in each compartment



CytoBead[®] ANCA



CytoBead[®] RPGN



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 indirect immunofluorescence (IIF) with ethanol fixed granulocytes, whereby cytoplasmic (cANCA; antigen PR3) and perinuclear (pANCA; antigen MPO) IIF patterns can be differentiated.

Unique Combination of Ethanol fixed Granulocytes with antigen coated Microbeads

Advantages of the CytoBead[®] ANCA

- **Screening** with standardized ethanol fixed granulocytes
- **Confirmation** of 3 antibody specificities with microbeads

RPGN (Rapidly Progressive Glomerulo-Nephritis)

Especially for Use in Emergency Situations

Advantages of the CytoBead[®] RPGN

- **Screening** with standardized ethanol fixed granulocytes
- **Confirmation** of 4 antibody specificities with microbeads

CytoBead[®] ANCA / RPGN

Cell pattern	Compartment	Bead (positive)	Quantification	Antigen	Clinical relevance
negative	1		U/ml	GBM	Goodpasture syndrome
cytoplasmic	2		IU/ml	PR3	Granulomatosis with polyangiitis
perinuclear	2		IU/ml	MPO	Microscopic polyangiitis, eosinophilic granulomatosis with polyangiitis, polyarteritis nodosa

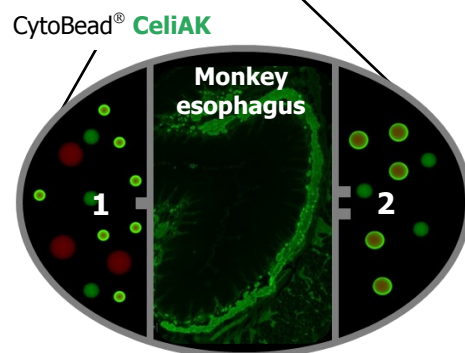
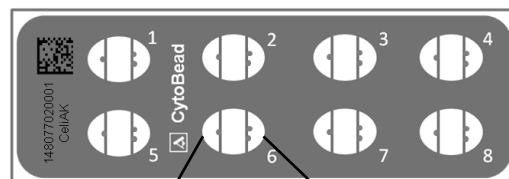
Additionally in CytoBead[®] RPGN

nuclear	1		IU/ml	dsDNA	Lupus nephritis
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- Small bead: negative
 Large bead: negative
 Reference bead in each compartment

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 (AAB) against transglutaminase 2 (tissue transglutaminase, tTG) and deamidated gliadin (DG). Endomysial antibodies (EmA) are directed against extracellular tTG. Celiac specific antibodies are typically of IgA class. In celiac patients with IgA deficiency, antibodies of the IgG type form the basis of diagnostics.



Unique Combination of esophageal Tissue with antigen coated Microbeads

Advantages of the CytoBead[®] CeliAK

- **Screening** with standardized monkey esophageal tissue
- **Confirmation** of 3 antibody specificities with microbeads

CytoBead[®] CeliAK

Pattern Tissue	Com-part-ment	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	IgA	IgA deficiency

Small bead: negative

Large bead: negative

Reference bead in each compartment

akiron[®] instrument (4296)

- Motorized fluorescence microscope with 20x objective
- LED-Light source with 3 wavelengths (400 nm DAPI, 470 nm FITC, 635 nm APC)
- Motorized x-y-stage for 5 slides and multiwell plates
- High quality grey scale camera (1.5 megapixel)

akiron[®] software

4308	akiron[®]	System software license
4309	akiron[®]	Database license
4312	akiron[®]	CytoBead [®] ANCA / RPGN evaluation software license
4313	akiron[®]	CytoBead [®] ANA / ANA 2 evaluation software license

CytoBead[®] Assays

4272	AKLIDES[®]	CytoBead[®]	ANA	CE
4277	AKLIDES[®]	CytoBead[®]	ANA 2	CE
4270	AKLIDES[®]	CytoBead[®]	ANCA	CE
4281	AKLIDES[®]	CytoBead[®]	RPGN	CE
4271	AKLIDES[®]	CytoBead[®]	CeliAK	CE



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