

BytoBead[®] Assays

Patents: EP 2362222, AU 2011217190



**New
Combinations**

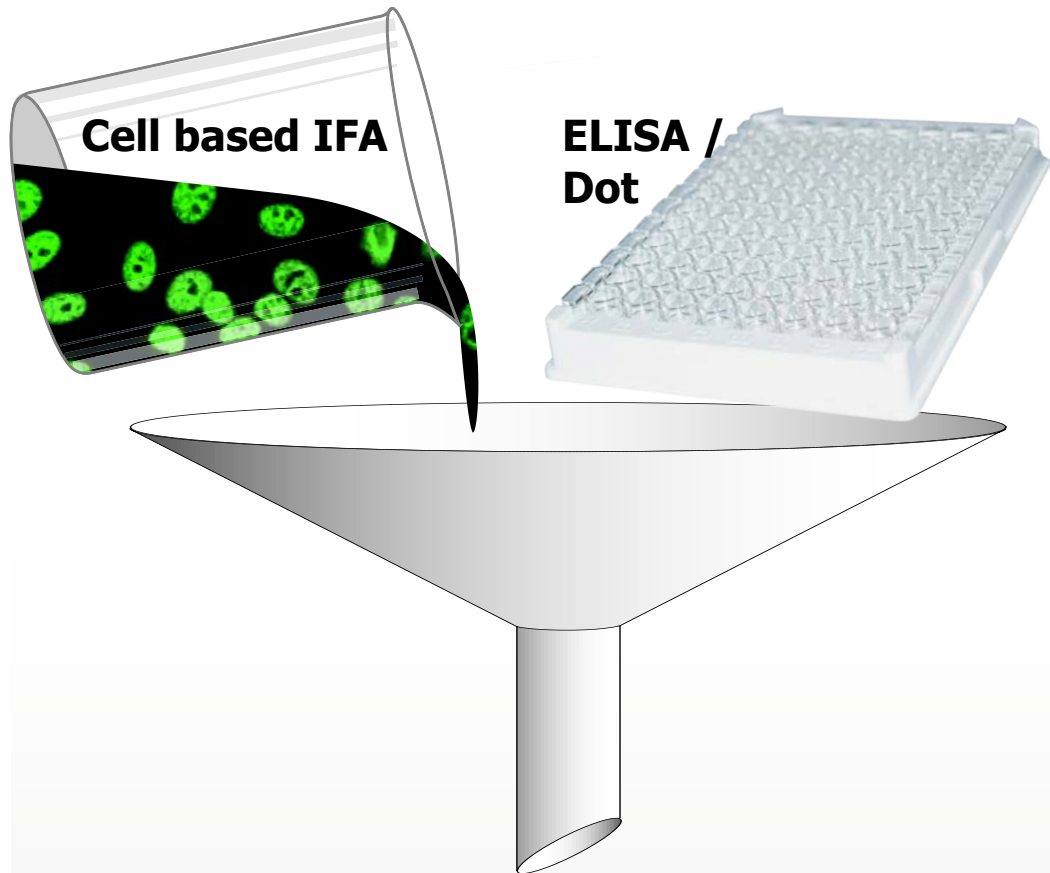
**New
Possibilities**

Classical Handling of Autoimmune Diagnostics

**2-Step
Diagnostics**

1st Screening

2nd Confirmation



**1-Step
Diagnostics**

Next Generation IFA

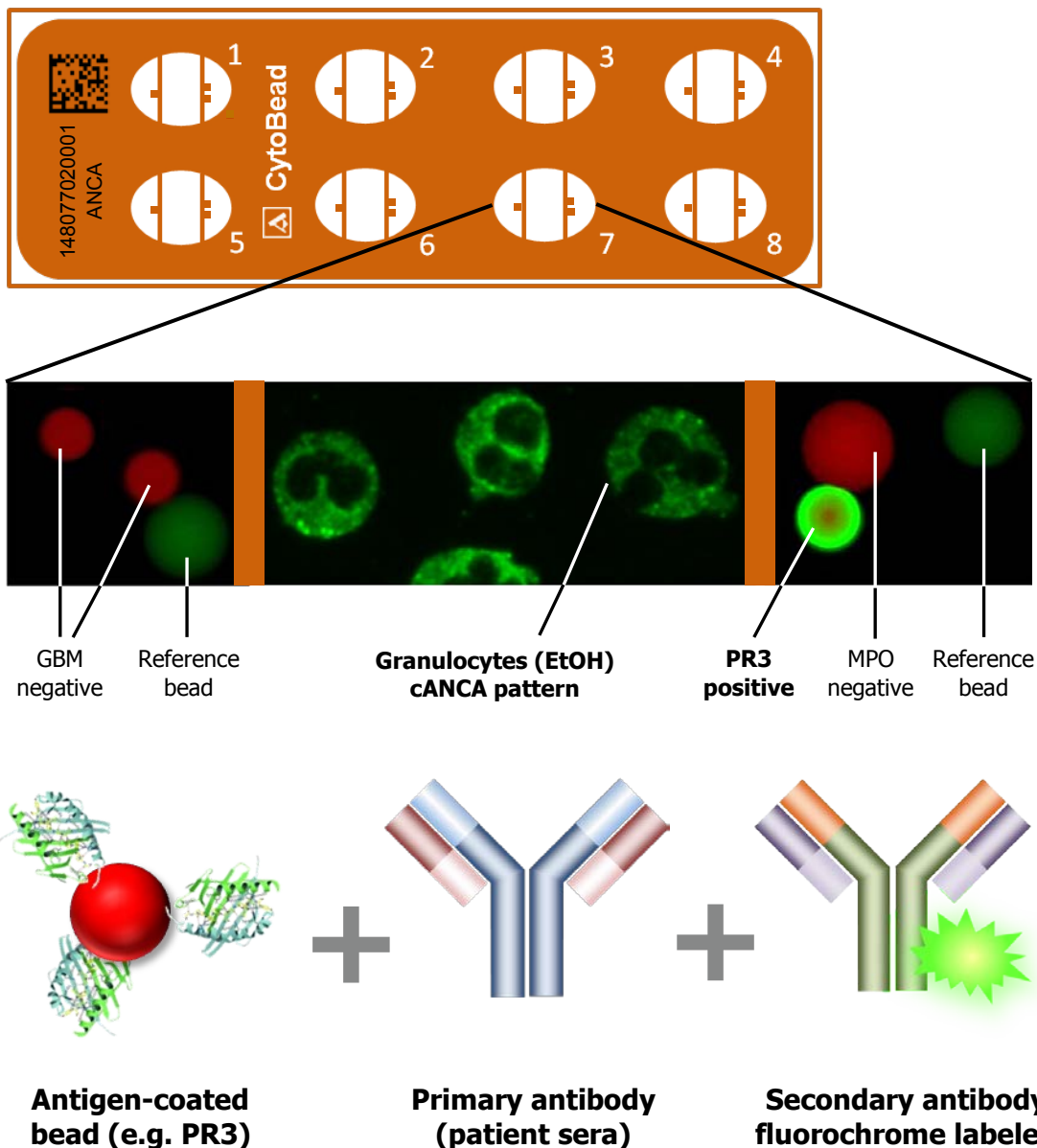
**ANA / ANA 2
ANCA / RPGN
CeliAK**

BytoBead[®] - **Technology**

Suitable for all manual fluorescence microscopes!

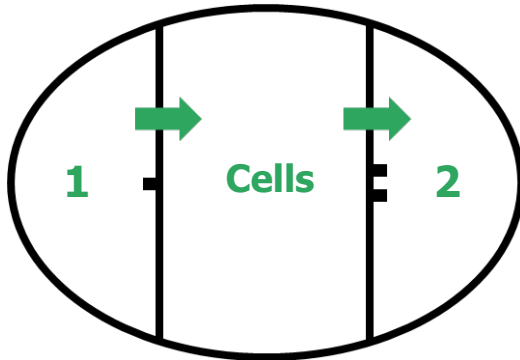
Screening and Confirmation at once! One Well - One Step - One Assay

Example CytoBead[®] ANCA



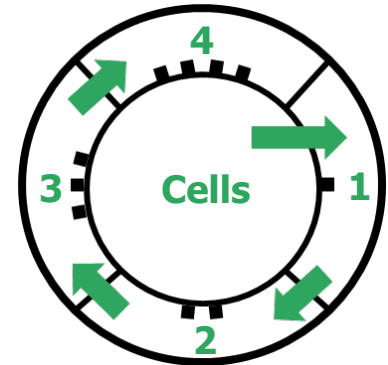
CytoBead[®] is time saving and economical.

Bead Compartment Markers for better Orientation



Reading direction →
 Compartment **1** to **cells** to compartment **2**
 ■ Compartment marker

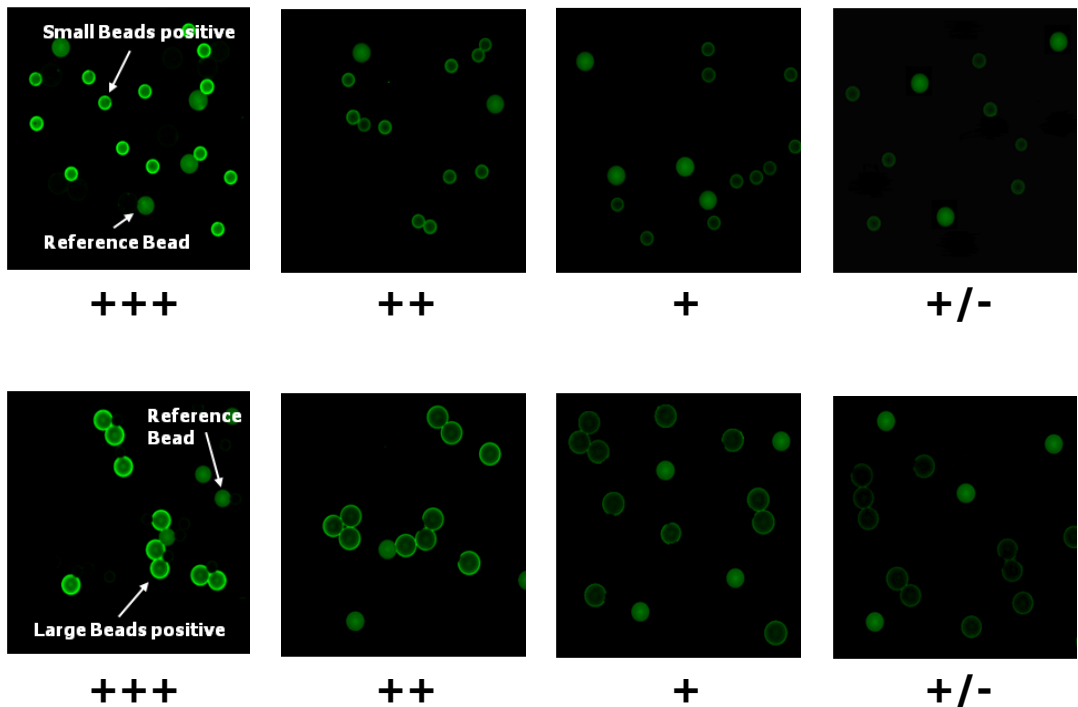
Assays: ANCA, RPGN, CeliAK



Reading direction →
Cells to compartment **1** to **2** to **3** to **4**
 ■ Compartment marker

Assays: ANA, ANA 2

Evaluation of Fluorescence Intensity (semi-quantitative)



Enlarged images (10x objective, obtained with AKLIDES®, MEDIPAN GMBH)

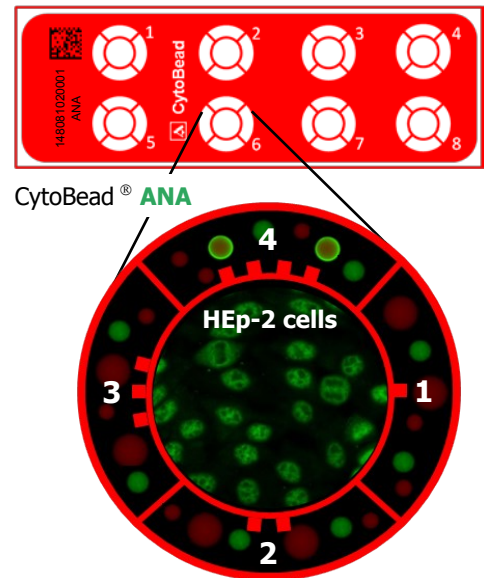
Fast and easy ANA Diagnostics

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.

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



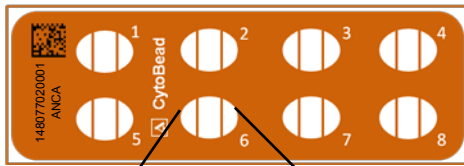
CytoBead® ANA / ANA 2

HEp-2 cell pattern	Compartment	Bead (positive)	Possible beadfluorescence	Possible antigens	Clinical relevance	
Homogenous	3		dsDNA	dsDNA	Systemic lupus erythematosus (SLE)	
			Scl-70	Scl-70	Marker for progressive systemic sclerosis (PSS)	
Speckled	2		Sm	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	
			RNP-Sm	nRNP		
	4		Ro60	Ro60/SS-A		Often in primary Sjögren's syndrome, anti-SS-A often in neonatal lupus
			Ro52	Ro52/SS-A		
1		La	La/SS-B			
Centromere	1		CENP-B	Centromeric proteins of the chromosomes	Marker for CREST syndrome, rarely in diffuse scleroderma and Raynaud's phenomenon	

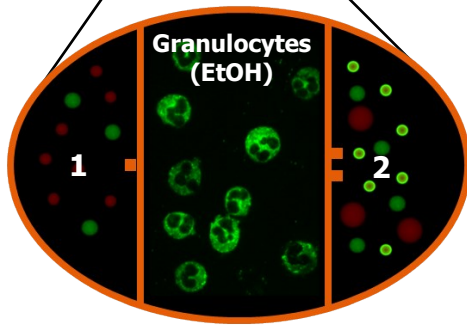
CytoBead® ANA 2, Jo-1 microbead replaces CENP-B microbead

Cytoplasmic	1		Jo-1	Jo-1 (PL-7, PL-12)	Polymyositis, dermatomyositis
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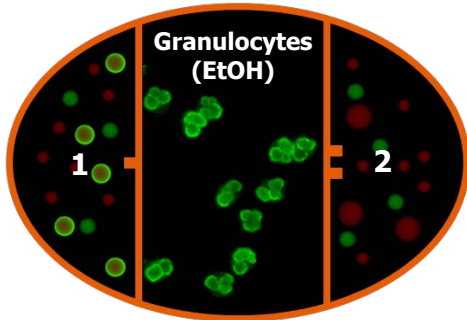
● Small bead: negative
 ● Large bead: negative
 ● Reference bead in each compartment



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 (Rapid 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	Com-part-ment	Bead (positive)	Possible be-adfluorescence	Possible antigens	Clinical relevance
negative	1		GBM	GBM	Goodpasture syndrome
cytoplasmic	2		PR3	PR3	Granulomatosis with polyangiitis
perinuclear	2		MPO	MPO	Microscopic polyangiitis, eosinophilic granulomatosis with polyangiitis, polyarteritis nodosa

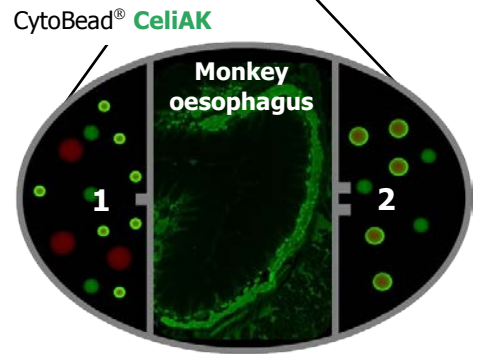
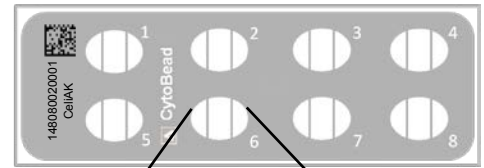
Additionally in CytoBead® RPGN

nuclear	1		dsDNA	dsDNA	Systemic lupus erythematosus, pathogenesis of 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 AAB against transglutaminase 2 (tissue transglutaminase, tTG) and deamidated gliadin (DG). Endomysial antibodies (EmA) are directed against extracellular tTG. Celiac 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	Compart-ment	Bead (positive)	Possible be-adfluorescence	Possible antigens	Clinical relevance
honeycomb pattern of muscularis mucosa	1		tTG	tTG	Celiac disease Dermatitis herpetiformis
	1		DG	DG	
	2		IgA	IgA	IgA deficiency

Small bead: negative
 Large bead: negative
 Reference bead in each compartment

Order information

CytoBead® ANA	Order no. 8065	€
CytoBead® ANA 2	Order no. 8220	€
CytoBead® ANCA	Order no. 8063	€
CytoBead® RPGN	Order no. 8066	€
CytoBead® CeliAK	Order no. 8064	€

Literature

Simultaneous detection of celiac disease-specific IgA antibodies and total IgA.

Grossmann K, Röber N, Hiemann R, Rödiger S, Schierack P, Reinhold D, Laass M.-W., Conrad K, Roggenbuck, D.
Auto Immun Highlights. 2016 Dec, 7(1): 2.

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.

Simultaneous automated screening and confirmatory 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, 9(9):e107743.

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.



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