

Multi analyte testing in autoimmunity:

From early days to modern technologies

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Scientific & Clinical Affairs Manager, R&D, Autoimmunity

12th International Autoimmunity Seminar, Vilnius

Agenda

PAST
PRESENT
FUTURE

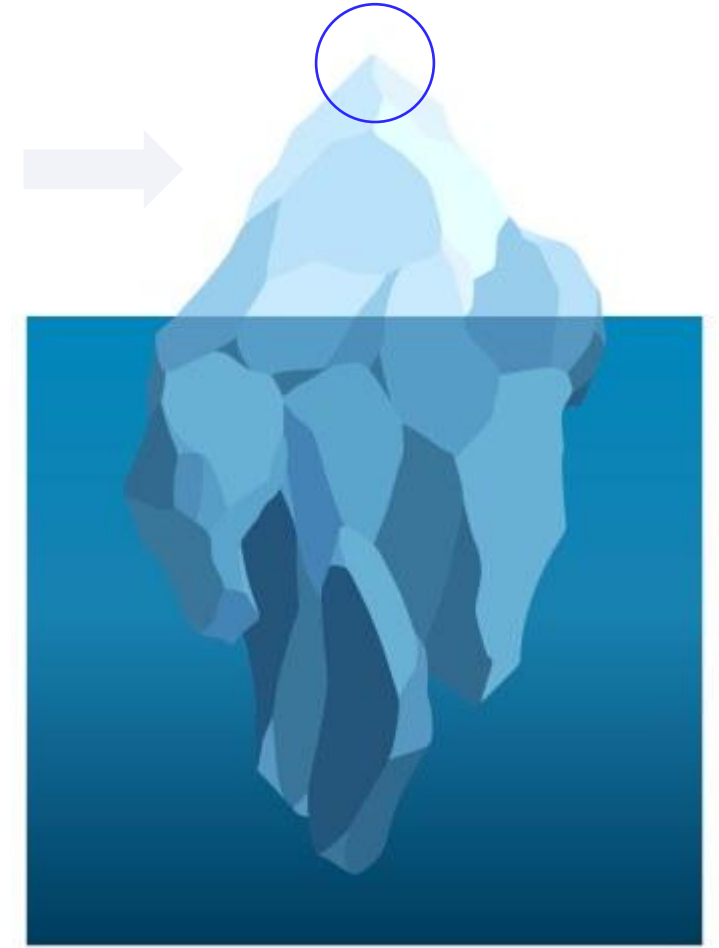
Introduction

Introduction

The early days of autoimmunity

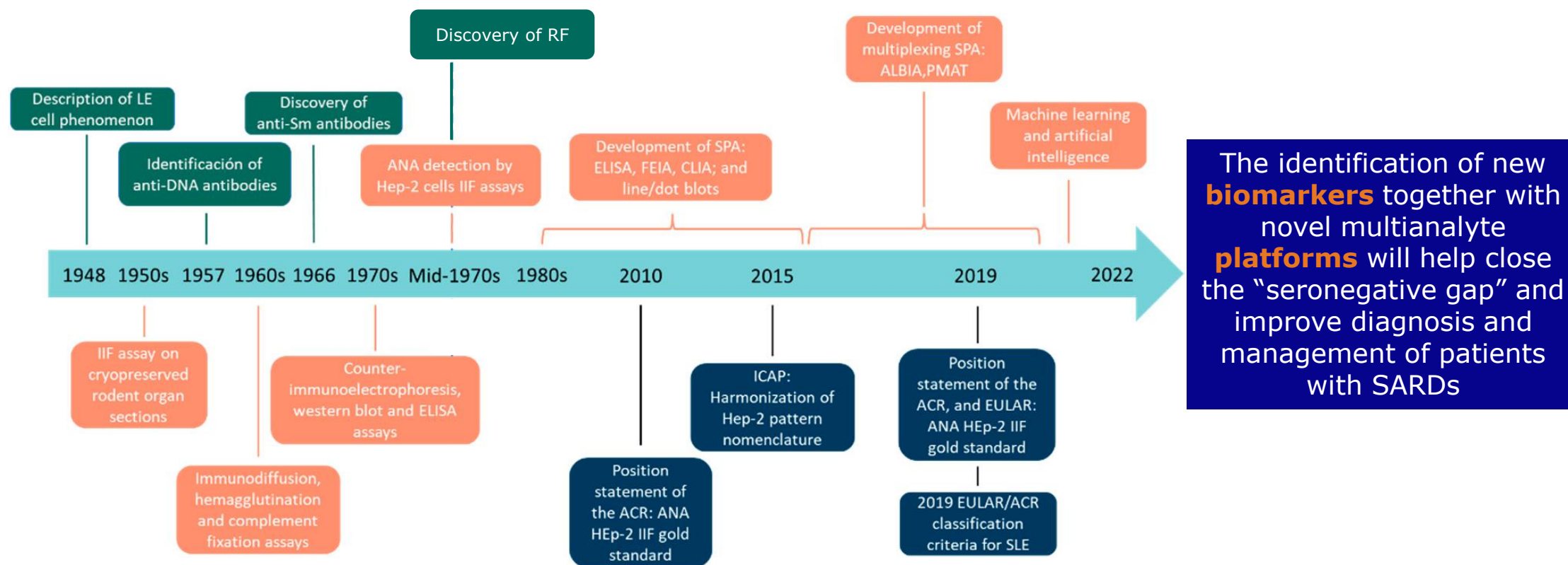
- **1940s** - Concept of immunological self versus non-self first proposed
 - Paul Ehrlich theories - "*Horror autotoxicus*"
 - **1948** - Discovery of the Lupus Erythematosus (LE) cell phenomenon by Hargraves et al
 - **1950s-1960s** - Renaissance of interest in autoimmunity and in the mechanisms of regulation of tolerance
 - **1957** - Holborow et al. - ANA with IIF, anti-dsDNA antibodies
 - **1959** - Extractable nuclear antigens (ENAs)
 - **1966** - Discovery of anti-Sm antibodies
-
- **Clinical immunologists and immunology laboratories are the "James Bond of medical researchers"**

Silverstein, A. M. Chapter 2 - **Autoimmunity: A History of the Early Struggle for Recognition**, Editor(s): Noel R. Rose, Ian R. Mackay, The Autoimmune Diseases (Sixth Edition), Academic Press, 2020, Pages 9-16, ISBN 9780128121023. Linklater S. **Defining autoimmunity: an epistemological history**. *The Lancet*, 2025. Mackay, Ian R. and Warwick Anderson. **Intolerant Bodies: A Short History of Autoimmunity**. Johns Hopkins University Press, 2014. Project MUSE.



Introduction

Past, present and future

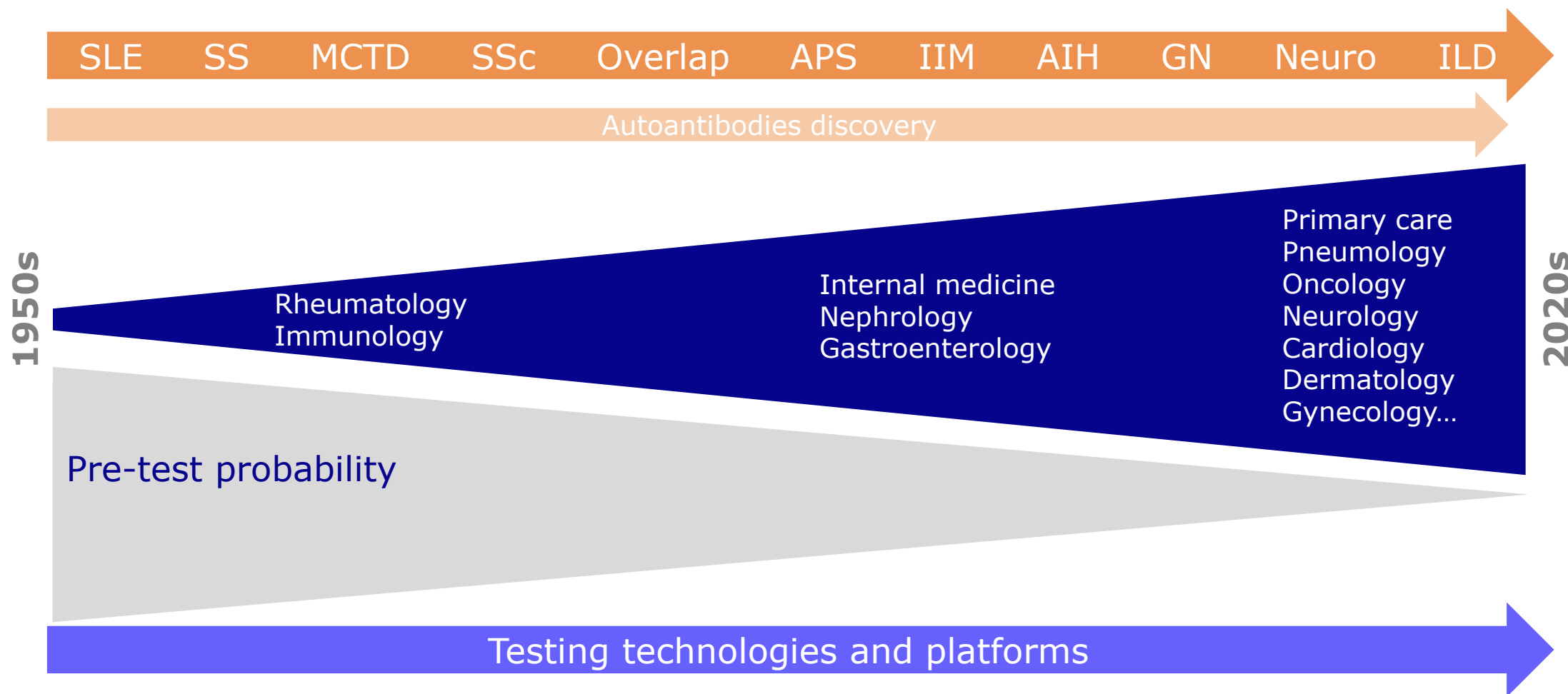


- No single technique can correctly identify all patients with ANA associated SARDs, so it is essential to combine the results obtained by various techniques to provide the most clinically valuable information

Modified from Irure-Ventura, J.; López-Hoyos, M. **The Past, Present, and Future in Antinuclear Antibodies (ANA)**. *Diagnostics* 2022;**12**:647.

Introduction

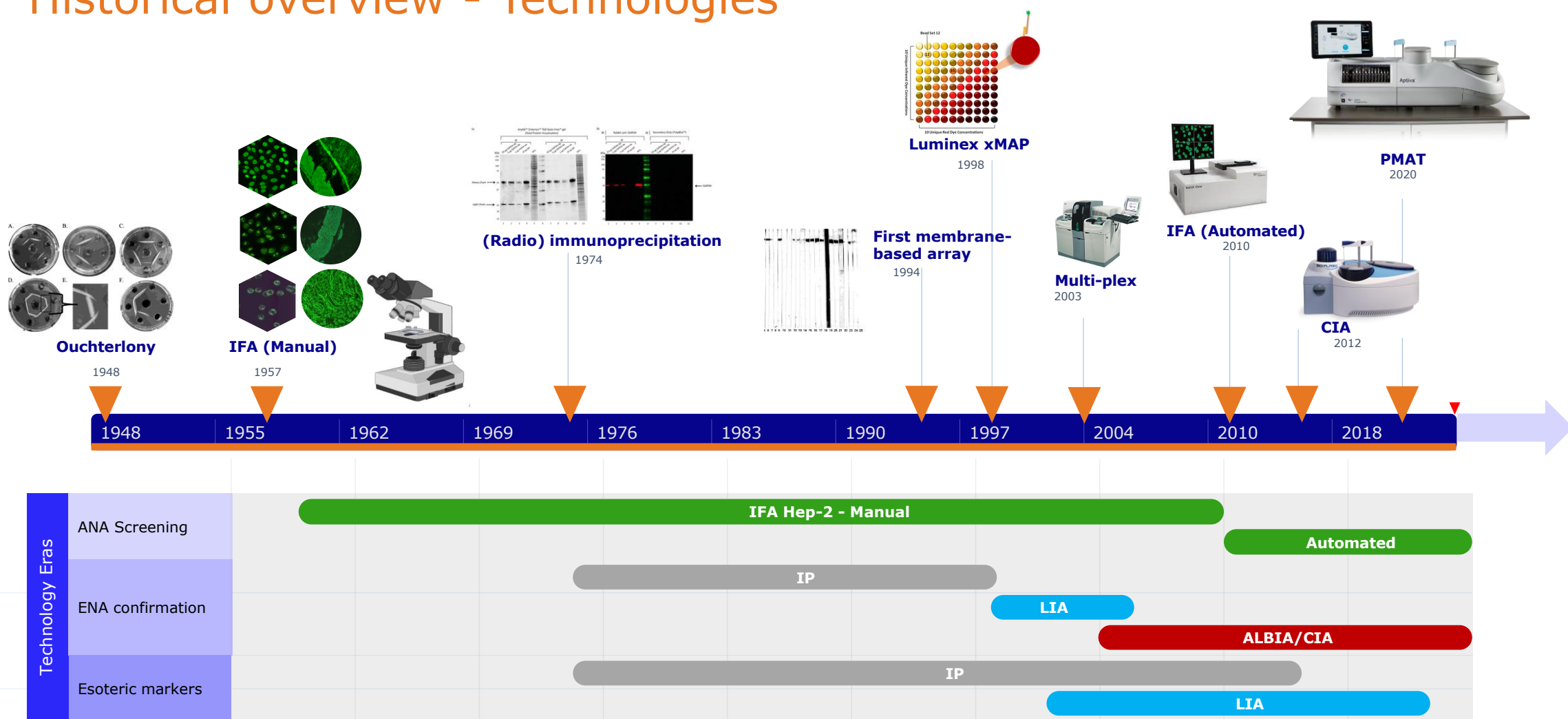
Evolution of autoantibody testing requests



Modified from Irure-Ventura, J.; López-Hoyos, M. **The Past, Present, and Future in Antinuclear Antibodies (ANA)**. *Diagnostics* 2022;**12**:647.

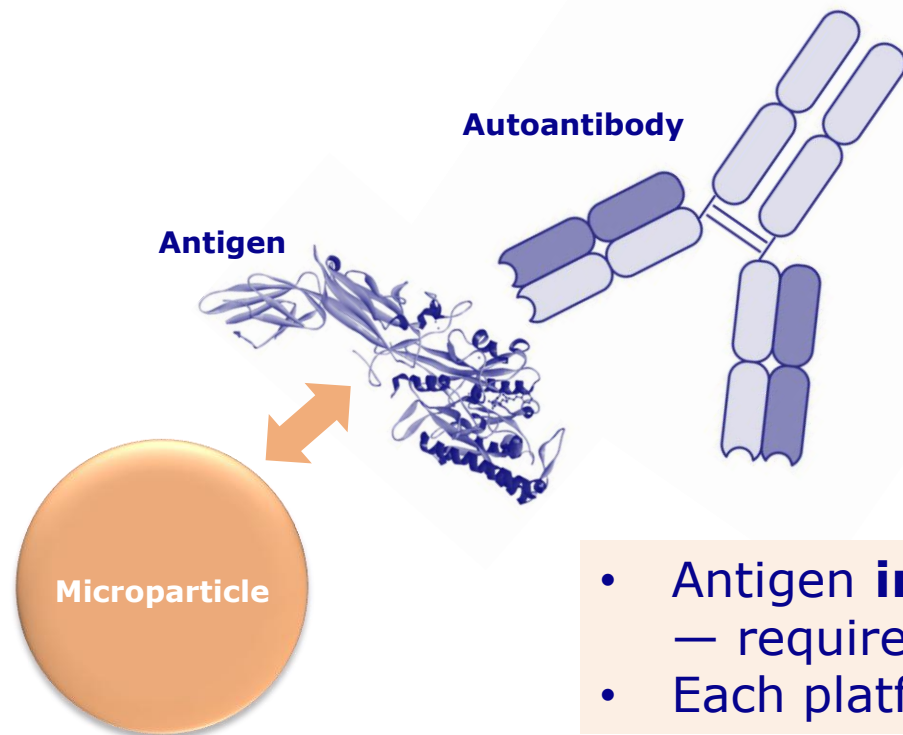
Introduction

Historical overview - Technologies



Introduction Considerations

- The **antigens** are central to autoantibody detection and assay development
 - Design, source, expression, purification → Folding, conformation and epitope exposure and recognition for antibody binding
 - Direct impact in assay performance (sensitivity and specificity, stability, etc)



- Cellular location → solubility
- Epitope mapping; linear vs conformational epitopes → Full length vs truncated proteins or peptides
- "Simple" proteins vs complexes

- Antigen **immobilization** onto solid phase — slides, beads, etc — requires robust and targeted conjugation strategies
- Each platform presents with unique limitations and challenges

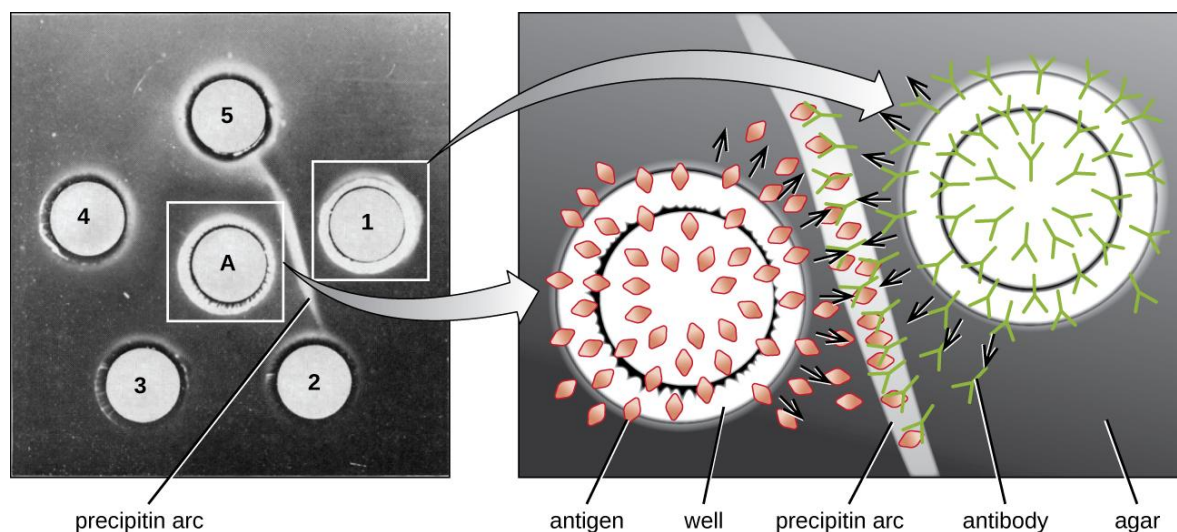
The past



The past Immunodiffusion

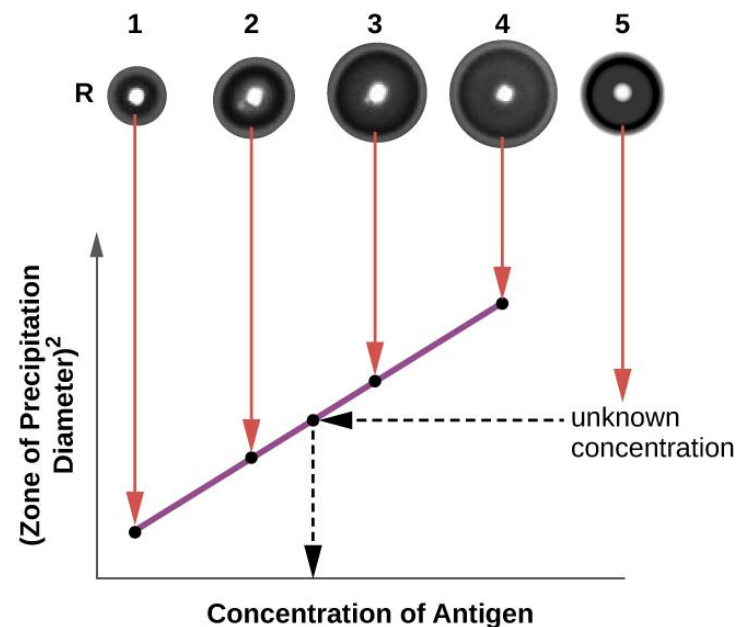
1948 - Ouchterlony (Double immunodiffusion)

- Based on precipitation of ab/ag interaction
 - Antigen (A) and antisera (1-5) in a gel
 - Antibodies and antigen diffuse through the gel, causing a precipitin arc to form at the zone of equivalence



1965 - Radial immunodiffusion (RID) assay

- Original method qualitative, 2nd Generation (semi)-quantitative
- Antiserum + agar
 - Ag solutions in increasing concentrations (1-4)
 - Ag solution of an unknown concentration (5)

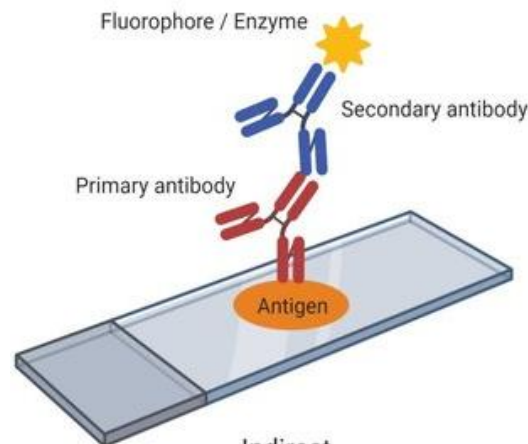


<https://openstax.org/books/microbiology/pages/20-2-detecting-antigen-antibody-complexes>

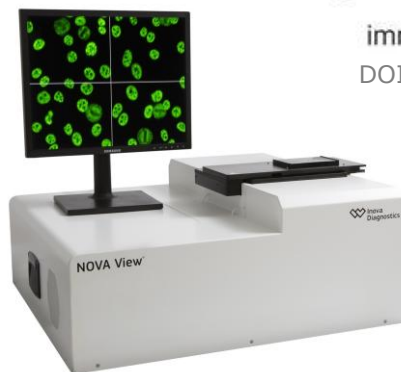
The past (*present and future*)

Indirect immunofluorescence (IIF, IFA)

1957 – Anti-nuclear antibodies on HEp-2 cells
(Coons, Miescher, Friou)



Indirect
immunofluorescence assay
DOI: [10.3384/diss.diva-170740](https://doi.org/10.3384/diss.diva-170740)



Acta Allergologica, 1963, XVIII, 489-494

From the Courtauld Institute of Biochemistry, Middlesex Hospital
Medical School, London W. 1.

METHODS FOR THE DETECTION OF AUTO-ANTIBODIES

By
G. TORRIGIANI

Although the concept of auto-immunisation is by no means new in the history of medicine (as early as 1900, Metalnikoff had shown that guinea pigs, when injected with homologous spermatozoa formed antibodies capable of reacting even with their own spermatozoa), nevertheless it is only in recent years that extensive research has been carried out in this field.

The methods used to reveal the presence of auto-antibodies consist in the main of precipitation, agglutination, complement fixation reactions and immunofluorescence.

PRECIPITATION REACTIONS

The precipitin reactions were those first used by Roitt et al. in detecting antithyroglobulin antibodies. Although they are not very sensitive, they continue to be used because they are very easy to conduct.

It is possible to perform this reaction by bringing the antigen and the serum containing the antibodies into contact in small test tubes and studying the precipitation which occurs at the liquid-liquid interphase. However, best results are obtained when the antigen-antibody contact occurs in an agar gel. In this case, there is an easily perceptible precipitate.

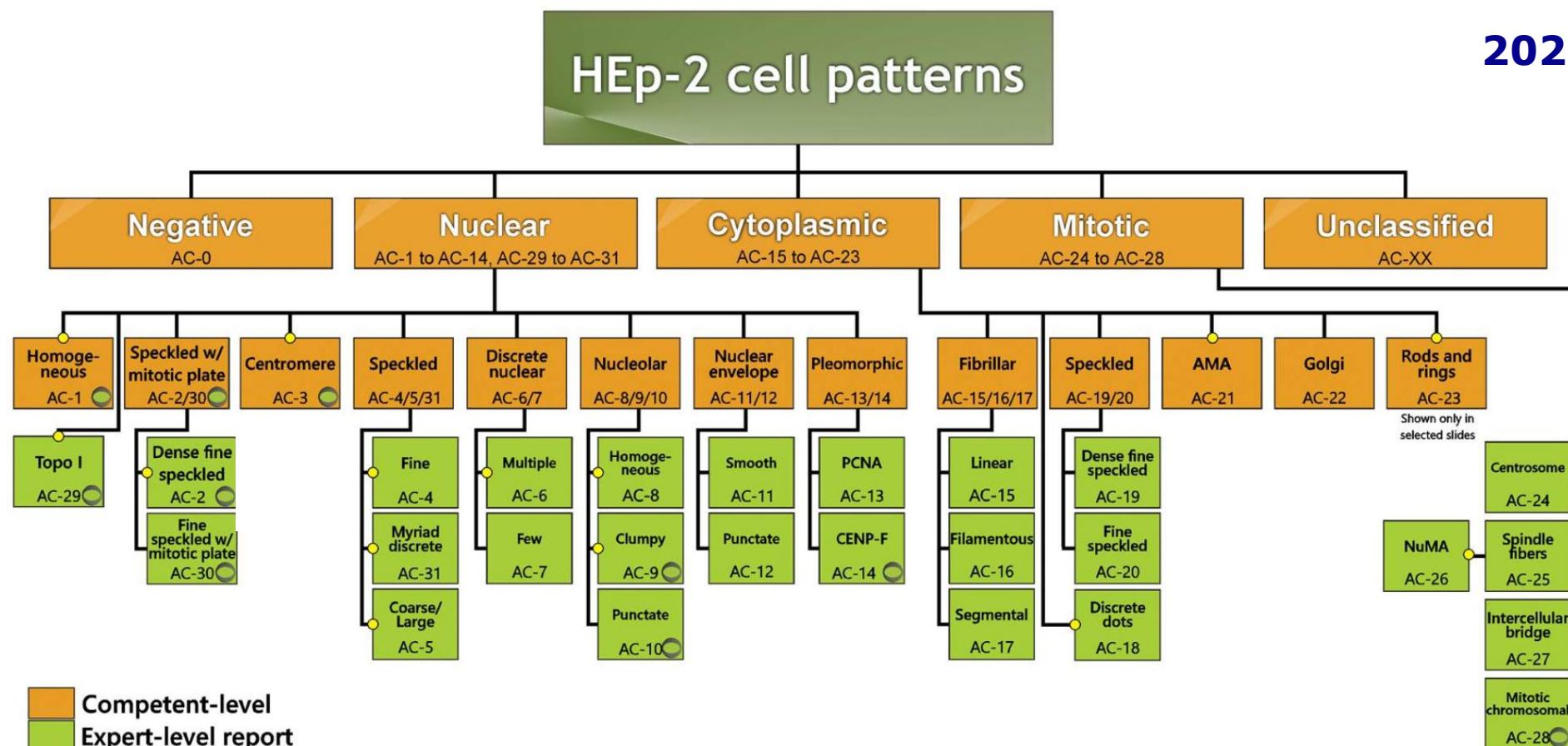
In performing these gel reactions, it is possible to use either the Oudin method in which the reaction takes place in test tubes or the Ouchterlony method, in which the reaction occurs

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The past (*present and future*)

Indirect immunofluorescence (IIF, IFA)

2025



<https://anapatterns.org/trees.php>

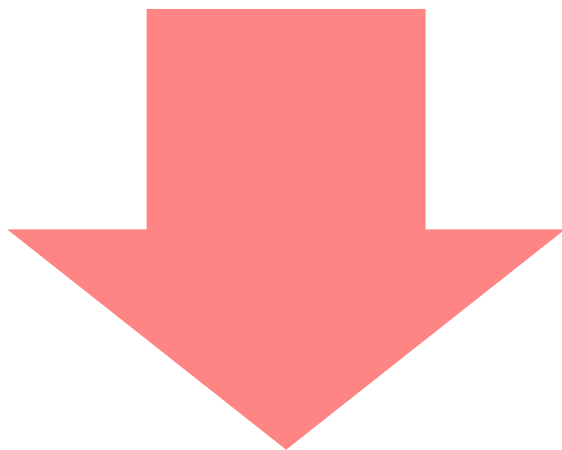
The past (*present and future*)

Indirect immunofluorescence (IIF, IFA)

INDIRECT IMMUNOFLUORESCENCE (IIF, IFA)



- Variety and number of autoantigens (>100)
- Screening and confirmatory tool
- Discovery tool for novel autoantibodies
- Useful for a spectrum of autoimmune diseases
- Automation tools (slides processing and loading, image acquisition)

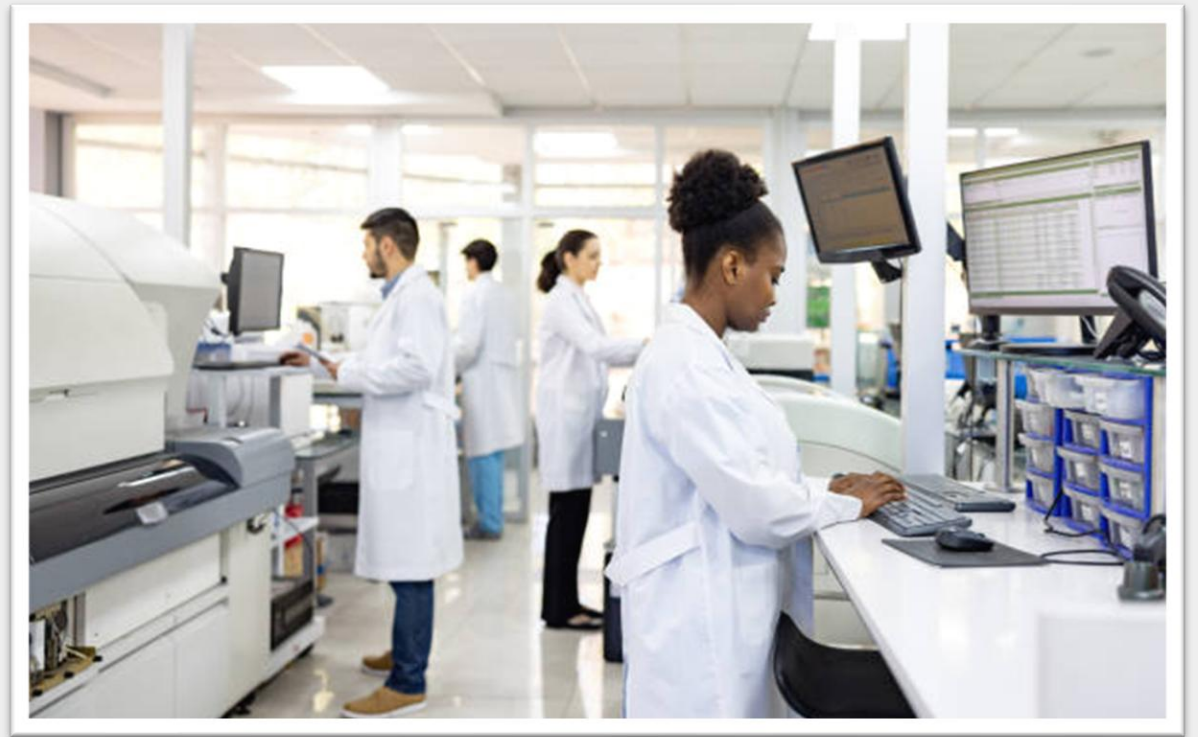


- Subjectivity; poor standardization and harmonization
- Labor intensive; requires training and expertise
- Low sensitivity for certain clinically important autoantibodies, especially antigens with low local density (i.e.: anti-Ro, some MSA, ribosomal P)
- Although patterns are indicative for some aabs, few patterns are very specific (e.g. centromere)

<https://www.aacc.org/cln/articles/2014/june/ana-testing>

Buchner C, Bryant C, Eslami A, Lakos G. **Anti-nuclear antibody screening using HEp-2 cells.** *J Vis Exp.* 2014;**88**:e51211.

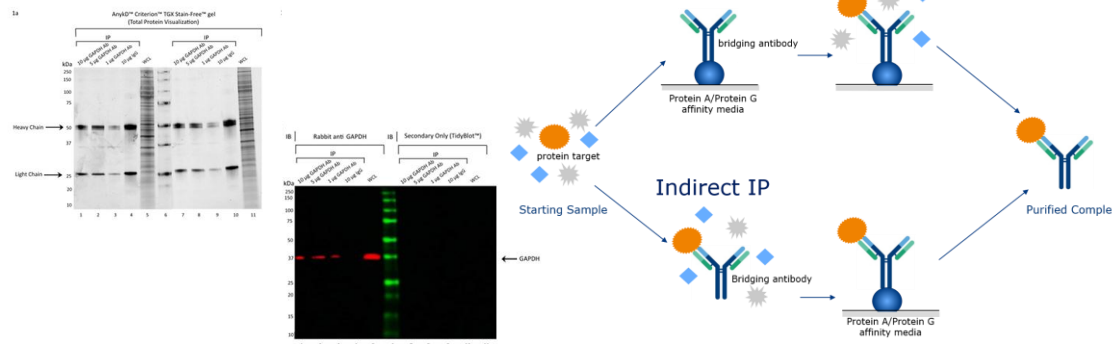
The present



The present

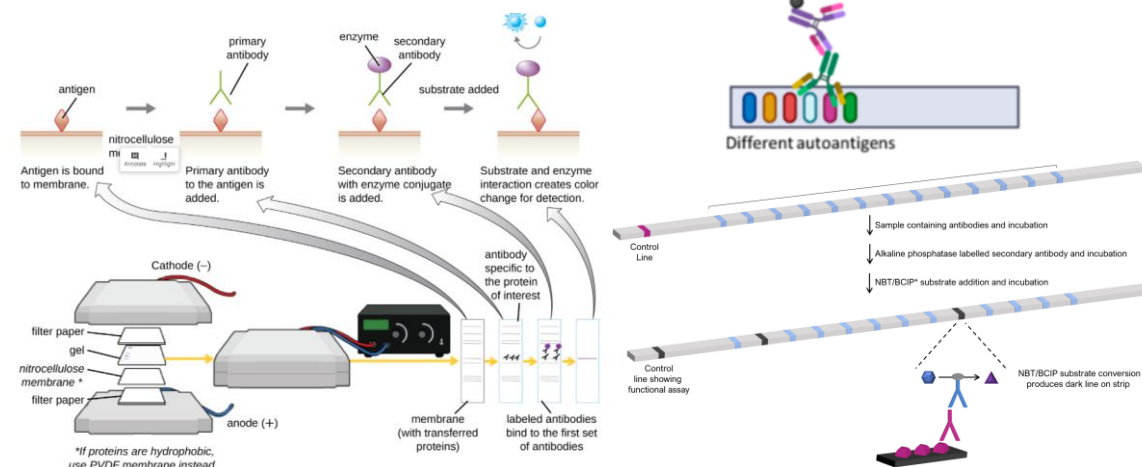
Immunoprecipitation (IP)

- Incubation of cellular extracts with patient sample leads to precipitation of proteins or protein complexes (including RNA)
- Detects antibodies to many antigens
- Highly specific → Still considered 'gold standard' for several autoantibodies
- Limitations
 - No standardization of protocol
 - No comparison data available
 - No regulatory clearance (LDT)



Membrane-based assays

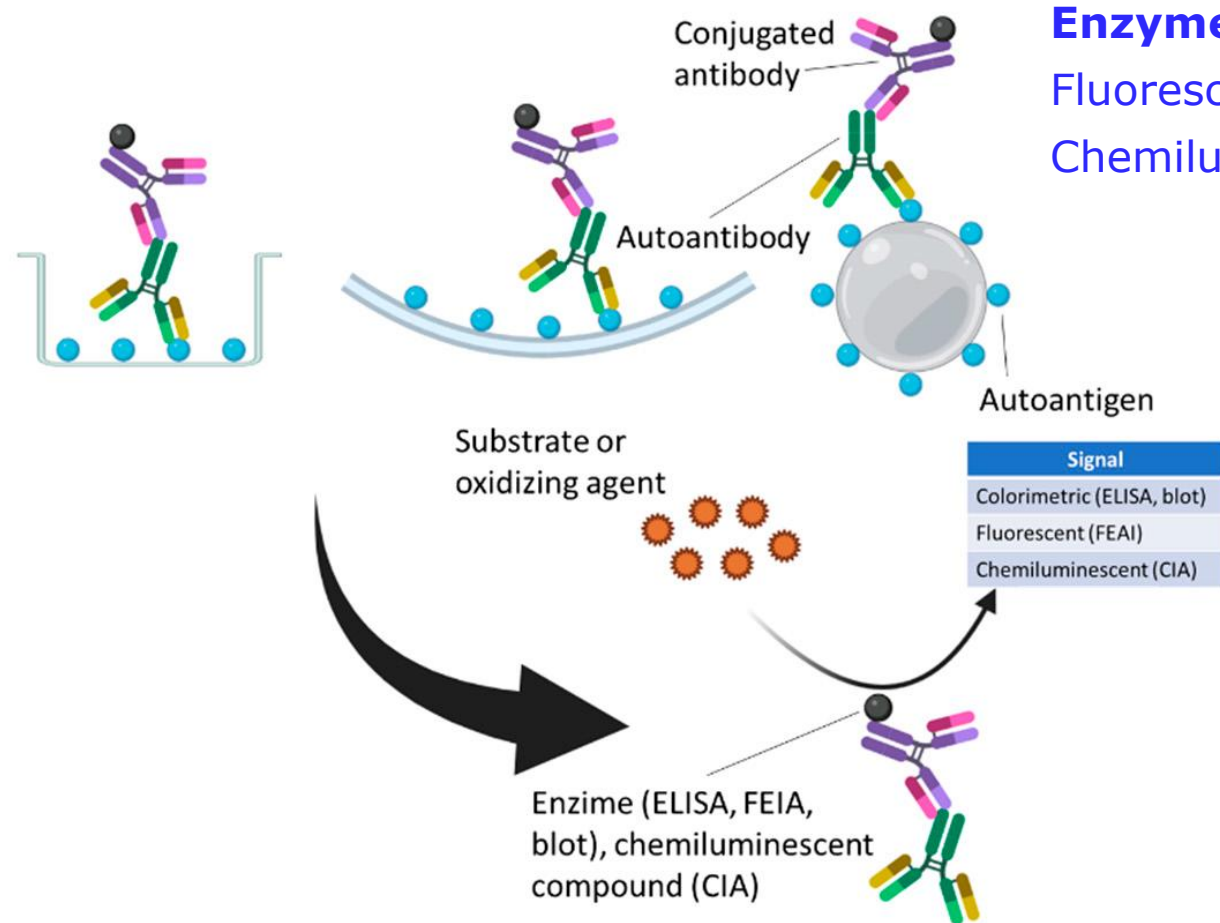
- **Western blot (WB)** using HEp-2 or HeLa extracts or purified antigens often used in research and were also commercialized (mostly replaced by LIA)
- Several **Line immunoassays (LIA)** developed and commercially available for autoantibodies detection
 - Automation and semi-quantitative solutions
- Today, commonly used for myositis, SSc and autoimmune liver disease testing



Olsen NJ, Choi MY, Fritzler MJ. **Emerging technologies in autoantibody testing for rheumatic diseases.** *Arthritis Res Ther.* 2017;**19**:172.
<https://mitogendx.com/technologies/>

The present

Solid-phase *single-analyte* assays



Enzyme Linked Immunosorbent Assay (ELISA)

Fluorescence enzyme immunoassay (FEIA)

Chemiluminescent immunoassay (CIA)

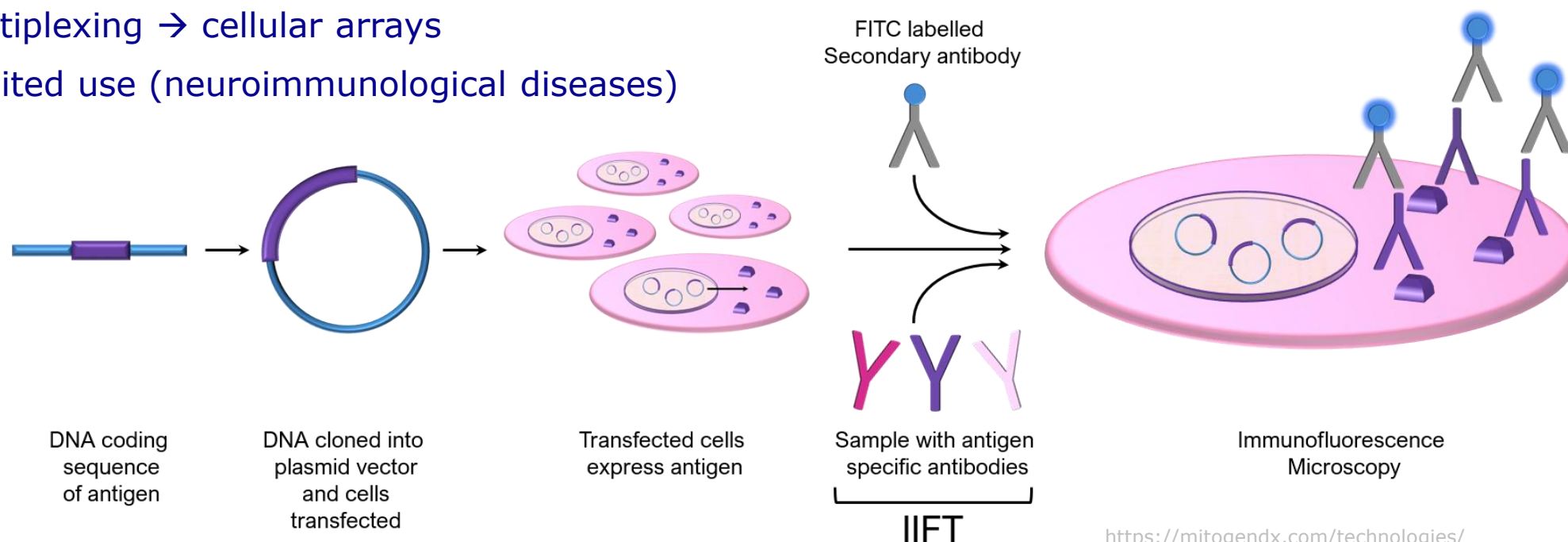
- Detection and quantification of antigen specific autoantibodies
- Increased sensitivity and specificity compared to LIA
- Less subjective than IP
- Higher throughput compared to IP, can be automated
- Quantitative or semi-quantitative, can follow titers
- Antigen conformation and epitope exposure on the solid phase

Irure-Ventura, J.; López-Hoyos, M. **The Past, Present, and Future in Antinuclear Antibodies (ANA)**. *Diagnostics* 2022;**12**:647.

The present

Cell-based assays (CBAs)

- Based on IIF protocols using cells that are transfected with cDNA of a specific antigen that is subsequently over expressed → Transfected cells = IIF substrate
- Advantages: in vivo expression, conformational epitopes, no antigen purification requirements, and flexibility in the choice of antigen expressed
- Limitations: resource-intensive, expression, standardization and harmonization...
- Multiplexing → cellular arrays
- Limited use (neuroimmunological diseases)

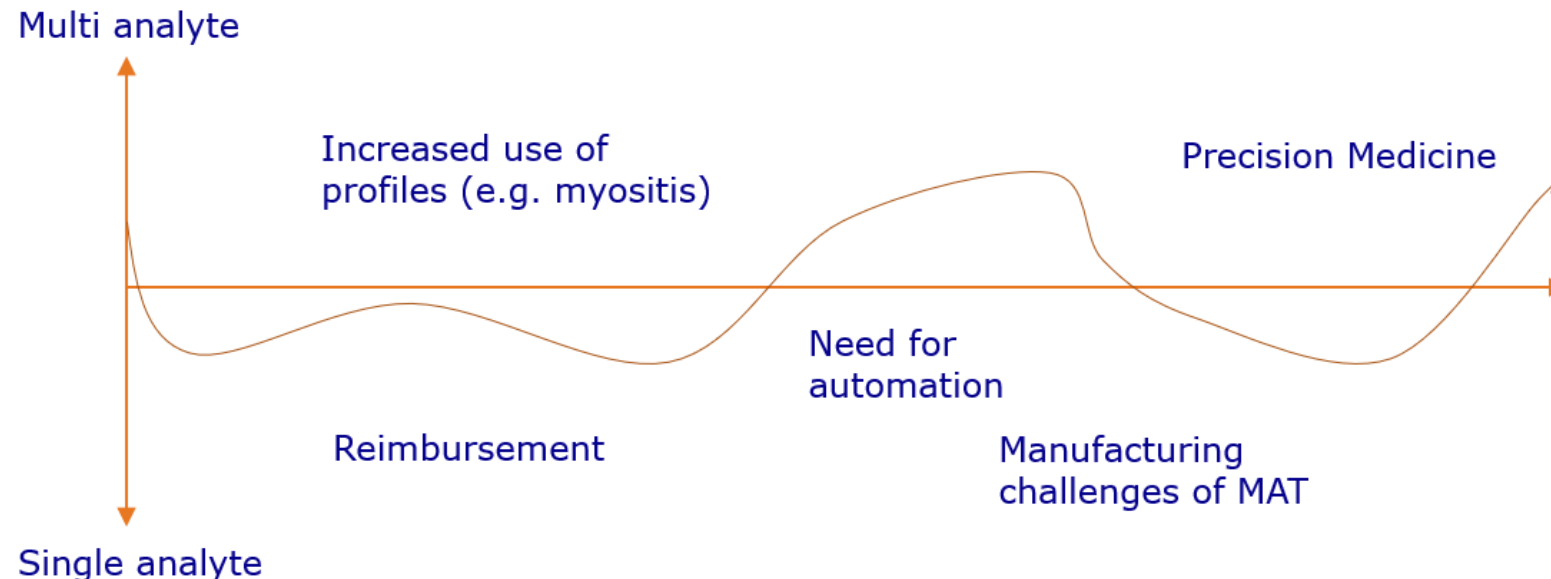


<https://mitogendx.com/technologies/>

The present

The desire for multi-analyte testing

- Most autoimmune diseases are characterized by **multiple antibodies** which triggered the desire to measure multiple autoantibodies at the same time
 - **Infectious disease**: One marker, one disease
 - **Autoimmunity**: Many markers, one syndrome (SLE: >180 autoab)
- Need for multi-analyte testing in AID dates to the early days; challenged by lack of automation
- Significant interest increase associated to patient stratification and precision medicine

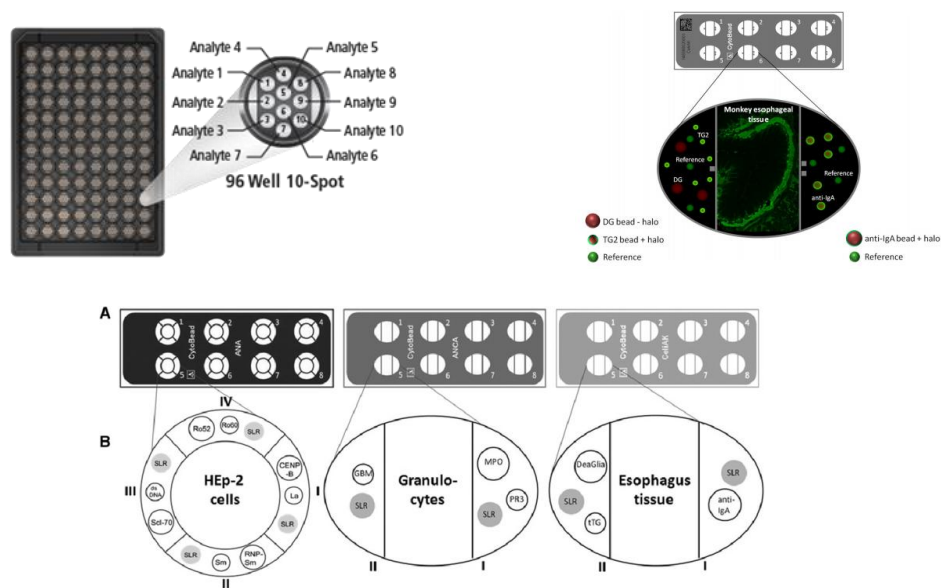


Yaniv G, Twig G, Shor DB, Furer A, Sherer Y, Mozes O, Komisar O, Slonimsky E, Klang E, Lotan E, Welt M, Marai I, Shina A, Amital H, Shoenfeld Y. **A volcanic explosion of autoantibodies in systemic lupus erythematosus: a diversity of 180 different antibodies found in SLE patients.** *Autoimmun Rev* 2015 **14**:75-9.

The present Multi-analyte assays

- Two very different concepts (planar vs. particle-based arrays)

Planar arrays



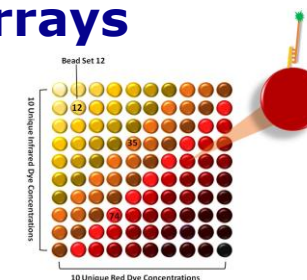
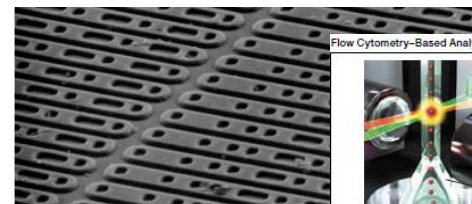
Particle-based arrays

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ANNALS NEW YORK ACADEMY OF SCIENCES

Determination of ANA Specificity Using the UltraPlex™ Platform

JODIE SMITH, DAVID ONLEY, CAROLINE GAREY, STUART CROWTHER, NICHOLAS CAHIR, ADAM JOHANSON, SIANIE PAINTER, GRANT HARRADENCE, RICARDO DAVIS, AND PETER SWARBRICK
SmartBead Technologies Limited, Babraham, Cambridge CB2 4AT, United Kingdom



Flow Cytometry-Based Analysis – Traditional xMAP Technology (Bio-Plex 200, Bio-Plex 3D Systems)

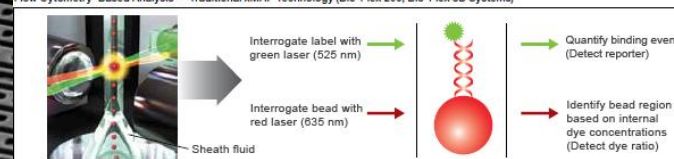
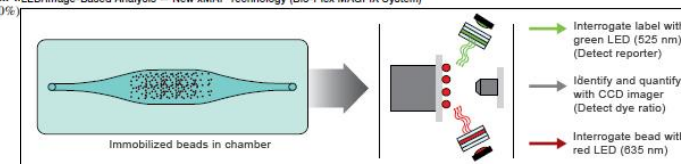


FIGURE 1. Electron micrograph showing aluminum release (original magnification: ×67; figure reduced to 40%)

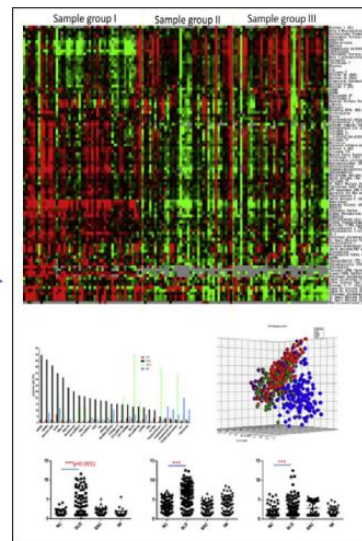
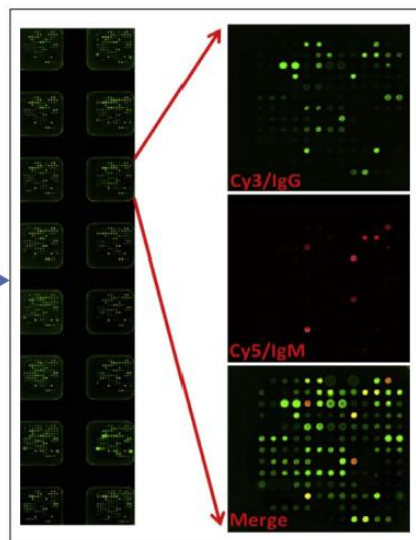
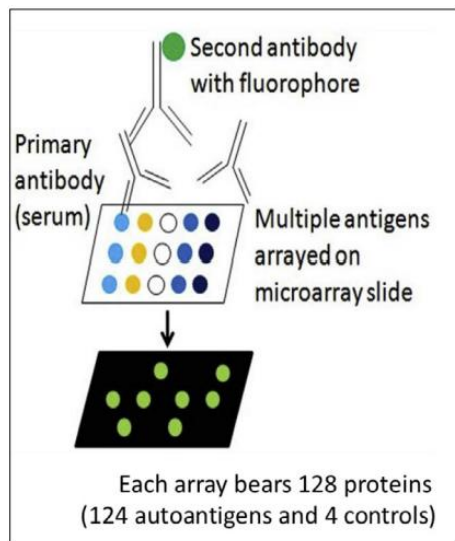


Keij JF, Steinkamp JA. Flow cytometric characterization and classification of multiple dual-color fluorescent microspheres using fluorescence lifetime. *Cytometry* 1998, 33:318-23. Sowa M, et al. Next-Generation Autoantibody Testing by Combination of Screening and Confirmation-the CytoBead® Technology. *Clin Rev Allergy Immunol* 2017, 53:87-104.

The present Multi-analyte assays

PLANAR ARRAYS

- One of first studies describing microarray on membranes →
 - **1994:** semi-quantitative assay for the detection of IgG antibodies to 42 antigens



Journal of Immunological Methods 169 (1994) 183–193

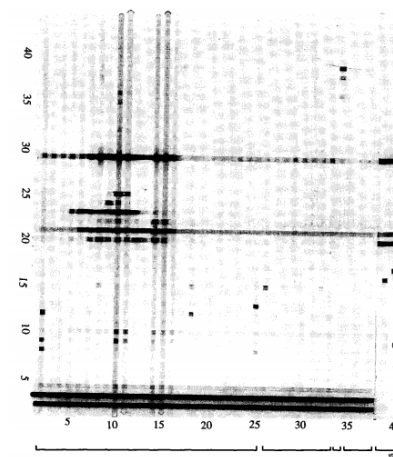
JOURNAL OF
IMMUNOLOGICAL
METHODS

A rapid and semi-quantitative method for the detection of autoantibodies by multiple spot immunoassay

Bo Baslund *, Jörgen Wieslander

Department of Autoimmune Serology, Statens Serum Institute, Artillerivej 5, DK-2300 Copenhagen, Denmark

(Received 21 June 1993, revised received 31 August 1993, accepted 12 October 1993)



Baslund B, Wieslander J. **A rapid and semi-quantitative method for the detection of autoantibodies by multiple spot immunoassay.** *J Immunol Methods* 1994; **169**:183-93.
Zhu H, et al. **Autoantigen Microarray for High-throughput Autoantibody Profiling in Systemic Lupus Erythematosus.** *Genomics Proteomics Bioinformatics* 2015; **13**:210-8.

The present Multi-analyte assays

PLANAR ARRAYS

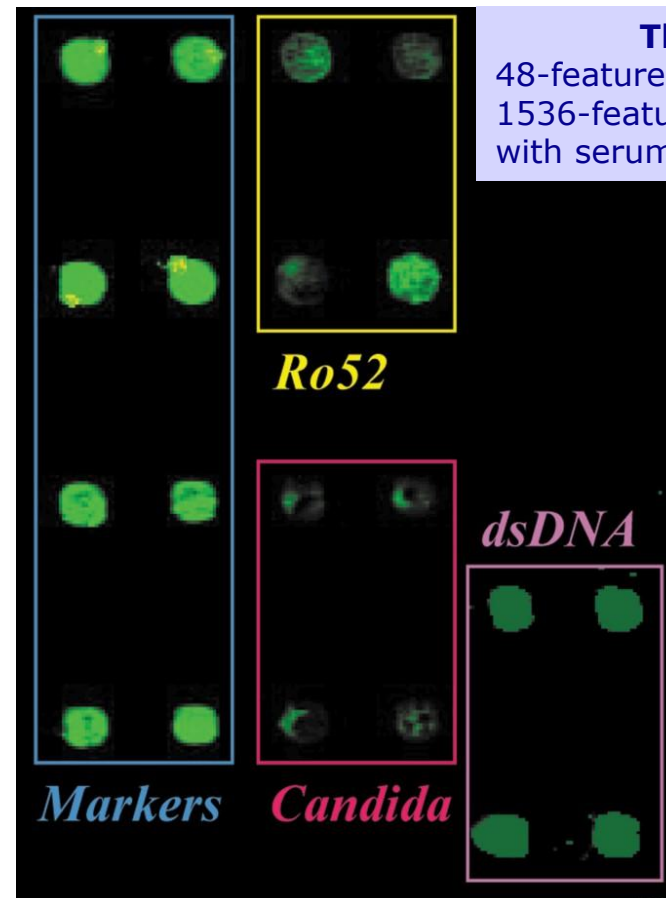
Proteomics technologies for autoantibody profiling: selected published studies

System	Assay format	Detection	Antigens tested in citation(s)	Estimated capacity per array	Comments	Reference
Antigen microarrays	Robotic attachment of antigens in ordered arrays on membranes and derivatized microscope slides	Secondary antibody; chemiluminescence	18	5000+	Demonstrate sensitive and specific detection of autoantibodies in serum on planar arrays	[16]
Protein microarrays	Robotic attachment of antigens in ordered arrays on derivatized microscope slides	Direct labeling of samples with fluorescent markers for comparative analysis	115	10,000+	Comparative analysis requires fluorescent labeling of individual samples; 50% of antigens detected	[7]
Antigen microarrays	Robotic attachment of antigens on derivatized microscope slides	Secondary antibody; fluorescence; comparative analysis with direct fluorescent labeling of samples	196	10,000+	Detection of autoantibodies characteristic of eight autoimmune rheumatic diseases, including autoantibodies against proteins, peptides, nucleic acids, and macromolecular complexes	[17]
Bead microarrays (LabMAP™; cytometric bead array)	Antigens conjugated to sets of spectrally resolvable fluorescent beads	Fluorescence; analysis of individual beads using a flow cytometer	16	64 per well; 5000+ per 96-well plate	Fluid-phase; commercial development by Luminex, and Becton-Dickinson	[35]
Nanobarcode™ particle technology	Attachment of antigens to addressable multimetal microrods encoded with submicrometer metal stripes	Light microscopy; fluorescence; mass spectrometry	2	80,000 using three distinct metals	Fluid-phase; Commercial development by SurroMed	[8]
Arrayed proteins from cDNA expression libraries	Expression and purification of polypeptides encoded in a cDNA expression library in microtiter plates, followed by robotic attachment to PVDF filters	Chemiluminescence	4800	10,000+	Performing autoantigen discovery; bacterial expression of autoantigens does not confer post-translational modifications	[13,14]
Protein <i>in situ</i> array	Protein array generated <i>in situ</i> using PCR and a cell-free transcription/translation expression system	Colorimetric	15	96 per plate	Probably less robust than other systems	[36]
Photolithography-generated peptide arrays	<i>In situ</i> synthesis of peptides by photolithography	Fluorescence		10,000+	Linear peptide epitopes only; not under active development	[4]
Microarrays of cells expressing defined cDNAs	Robotic printing of cDNA in expression vectors on slides followed by incubation with adherent mammalian cells	Fluorescence	192	10,000+	Mammalian expression system confers certain post-translational modifications	[9]
Protein arrays of living transformants; modified yeast two-hybrid screen	Robotic delivery of yeast transformants expressing yeast open reading frames fused to an activating domain	Colorimetric	6000	Performed in 384-well microtiter plates	Arrays of yeast expressing fusion proteins	[10]
'Line immunoassay'	Electrophoresis of antigens and transfer to nitrocellulose membranes (western blot of purified antigens)	Chemiluminescence	15	< 50	Not high-throughput; commercial development by Innogenetics	[12]
'Universal protein array'	Dot-blots of purified antigens on nitrocellulose membranes	Secondary antibody; radioactivity	48	< 200	Requires large quantities of purified antigen and serum samples	[11]
'Lab-on-a-chip', microfluidics	Microchannels etched in solid supports; electrokinetic, electro-osmotic, electrophoretic, or pressure-driven flow	Fluorescence; UV light absorption	Limited	N/A	Fluid-phase assay; low-affinity binding detectable; kinetics can be calculated; commercial development by Caliper, Aclara, and Fluidigm	[37]
Peptides on pins (Multipin™)	<i>In situ</i> synthesis of peptides on polyethylene pins	Colorimetric	96	96 per plate	Linear epitopes only; strip and re-use peptides on pins for subsequent experiments	[1,2]

N/A, not applicable; PCR, polymerase chain reaction; PVDF, polyvinylidene difluoride. For manufacturer details, please see text.

Hueber W, et al. **Autoantibody profiling for the study and treatment of autoimmune disease.** *Arthritis Res.* 2002;**4**:290-5.

Robinson WH, et al. **Autoantigen microarrays for multiplex characterization of autoantibody responses.** *Nat Med* 2002;**8**:295-301.



The 'CTD' array
48-feature collage derived from a 1536-feature 'CTD' array probed with serum from an SLE patient

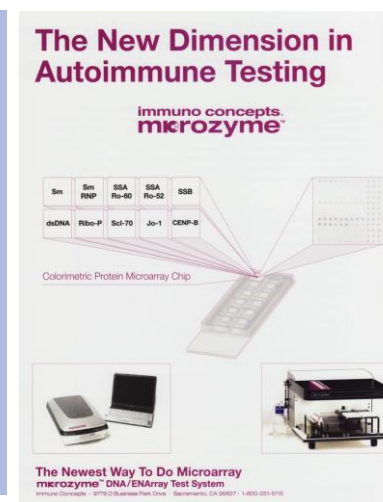
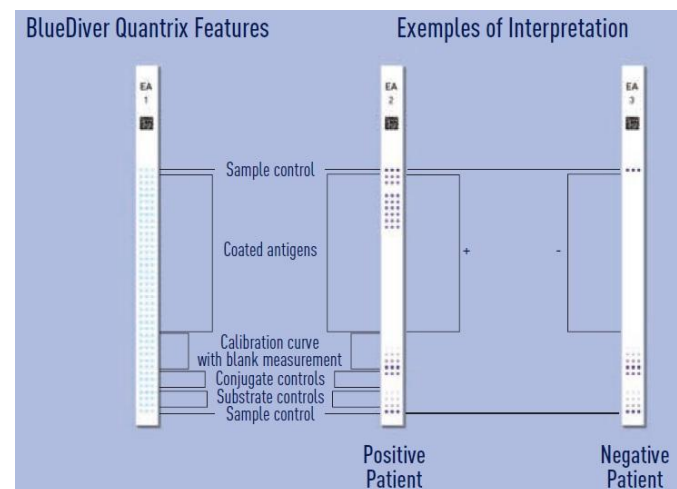
The present Multi-analyte assays

PLANAR ARRAYS

- Hype from DNA microarrays (chips) and the promise from research triggered commercial attempts for planar arrays for autoantibodies
- Several companies have developed or launched planar arrays, but so far no mainstream adoption
- Either lack of automation of manufacturing challenges have tempered the success



Olsen NJ, Choi MY, Fritzler MJ. **Emerging technologies in autoantibody testing for rheumatic diseases.** *Arthritis Res Ther* 2017, 19:172. He L, et al. **High-Throughput Multiplex Electrochemiluminescence Assay Applicable to General Population Screening for Type 1 Diabetes and Celiac Disease.** *Diabetes Technol Ther* 2022, 24:502-509.

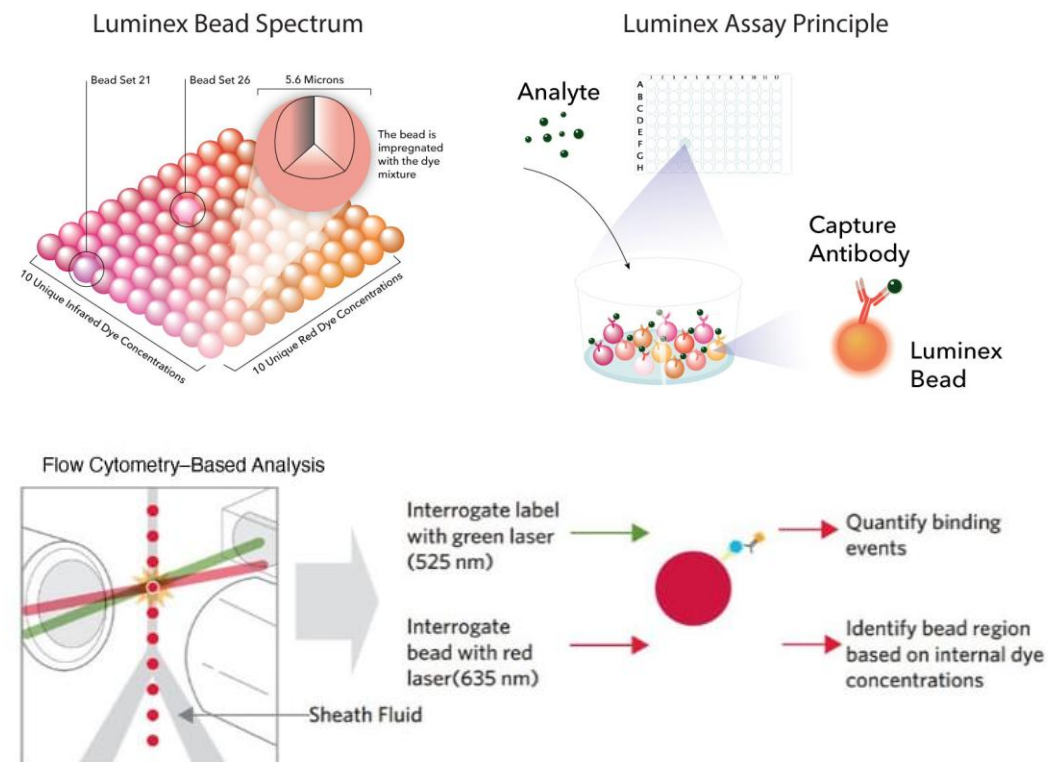
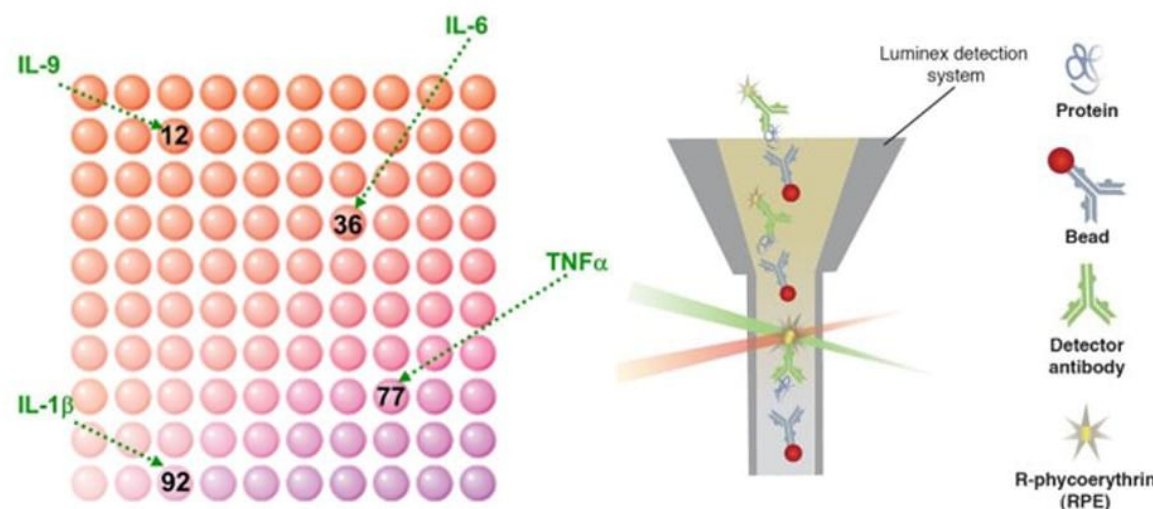


The present Multi-analyte assays

PARTICLE-BASED ASSAYS

Luminex technologies

- xMAP → Dallas, 1994: family, friends and tacos
- 1st described scientifically in 1998
- Recognition of colors of particles real time



https://www.rndsystems.com/what-luminex-assay?gclid=Cj0KCQjwTJKqBhCaARIsAN_yS_kVaUaV7w1AkcrTHhbR8cdFvTF3O6vi6NoRV6lYGif-0My-e4hQmhMaAgndEALw_wcB&gclid=aw.ds

Keij JF, Steinkamp JA. Flow cytometric characterization and classification of multiple dual-color fluorescent microspheres using fluorescence lifetime. *Cytometry* 1998;33:318-23. Vignali DA. Multiplexed particle-based flow cytometric assays. *J Immunol Methods* 2000;243:243-55. Graham H, Chandler DJ, Dunbar SA. The genesis and evolution of bead-based multiplexing. *Methods* 2019;158:2-11.

The present Multi-analyte assays

PARTICLE-BASED ASSAYS

- First, Luminex 100/200 were developed, later Luminex MagPix and FlexMAP
- QUANTA Plex (Inova Diagnostics) was first FDA cleared Luminex (xMAP) product (in 2001)
- Several similar products followed
 - AtheNA (Zeus Scientific)
 - FIDIS (BMD) (ALBIA)
- Analytical unit of Luminex 100 became core of the BioPlex 2200
- Widely used on clinical routine for autoantibodies for (ANA, ANCA, Celiac Disease, APS)



510(k) Premarket Notification

510(k) | Define | Registration & Listing | Adverse Events | Results | PMA | HDE | Classification | Standards
CFR Title 21 | Radiation-Emitting Products | X-Ray Assembler | Mammography Reports | CLIA | TPLC

[New Search](#) [Back To Search Results](#)

Device Classification Name	extracable antinuclear antibody and/or control
510(k) Number	K011440
Device Name	QUANTA PLEX ENA PROFILE 4
Applicant	INOVA DIAGNOSTICS, INC. 10180 SCRIPPS RANCH BLVD. SAN DIEGO, CA 92131
Applicant Contact	BRYN C MYERS
Correspondent	INOVA DIAGNOSTICS, INC. 10180 SCRIPPS RANCH BLVD. SAN DIEGO, CA 92131
Correspondent Contact	BRYN C MYERS
Registration Number	886.5100
Classification Product Code	LLL
Date Received	04/13/2001
Decision Date	07/27/2001
Decision	Substantially Equivalent (SESE)
Regulation Medical Specialty	Immunology
510k Review Panel	Immunology
Type	Traditional
Reviewed by Third Party	No
Combination Product	No



xMAP INTELLIFLEX DR-SE System



xMAP INTELLIFLEX System



FLEXMAP 3D System

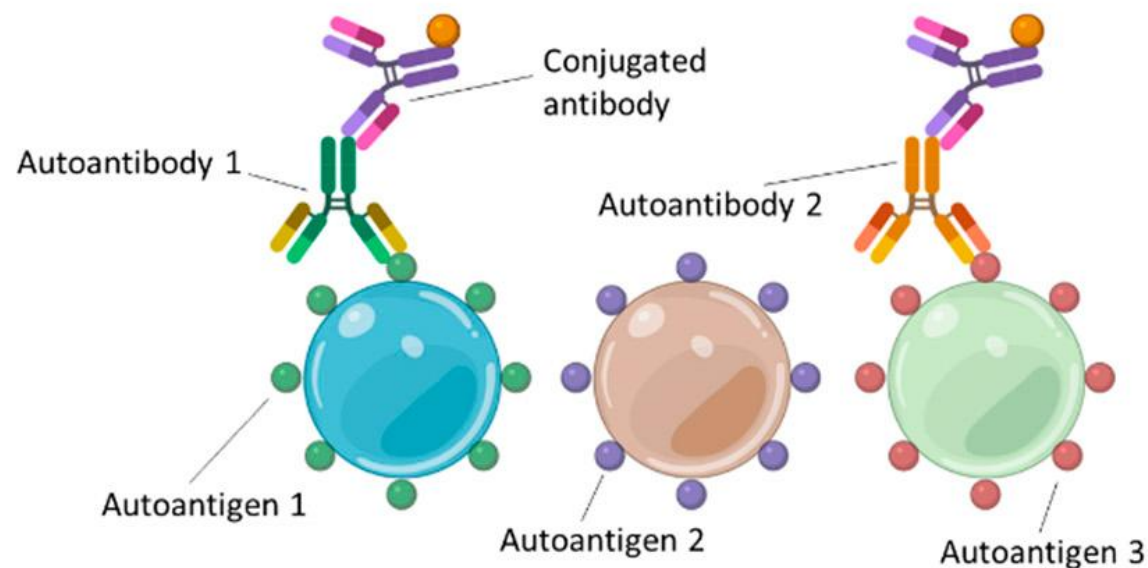


Luminex 200 System

Rouquette AM, Desgruelles C, Laroche P. **Evaluation of the new multiplexed immunoassay, FIDIS, for simultaneous quantitative determination of antinuclear antibodies and comparison with conventional methods.** *Am J Clin Pathol* 2003, 120:676-81.

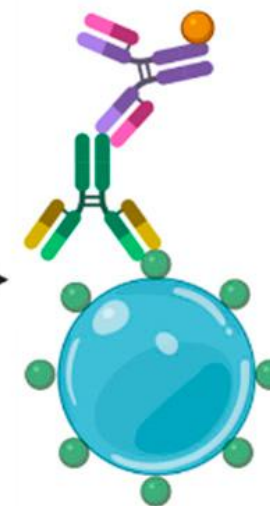
The present Multi-analyte assays

PARTICLE-BASED ASSAYS (ALBIA, PMAT)



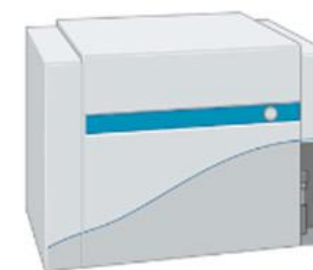
Different beads (ALBIA) or particles (PMAT) with a unique intrinsic fluorescent signal (ALBIA) or signature (PMAT)

Addressable laser bead immunoassays (ALBIA)



Particle-based multi-analyte technology (PMAT)

Detección by flow cytometry (ALBIA)



Detection by digital camera (PMAT)



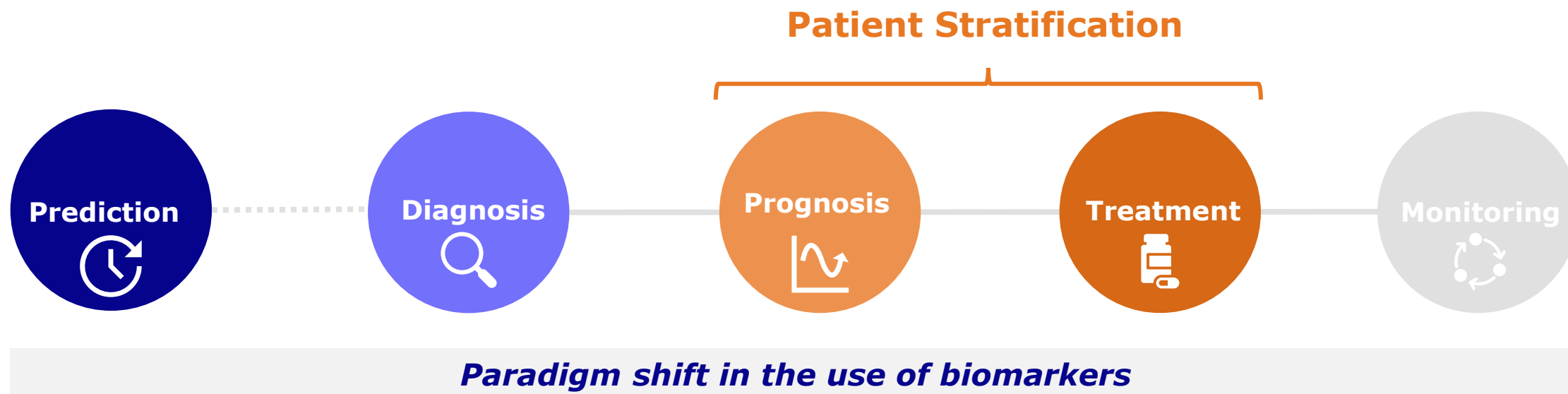
Irure-Ventura, J.; López-Hoyos, M. **The Past, Present, and Future in Antinuclear Antibodies (ANA).** *Diagnostics* **2022**, *12*, 647.

4. The future

4. The future is here

The future is here

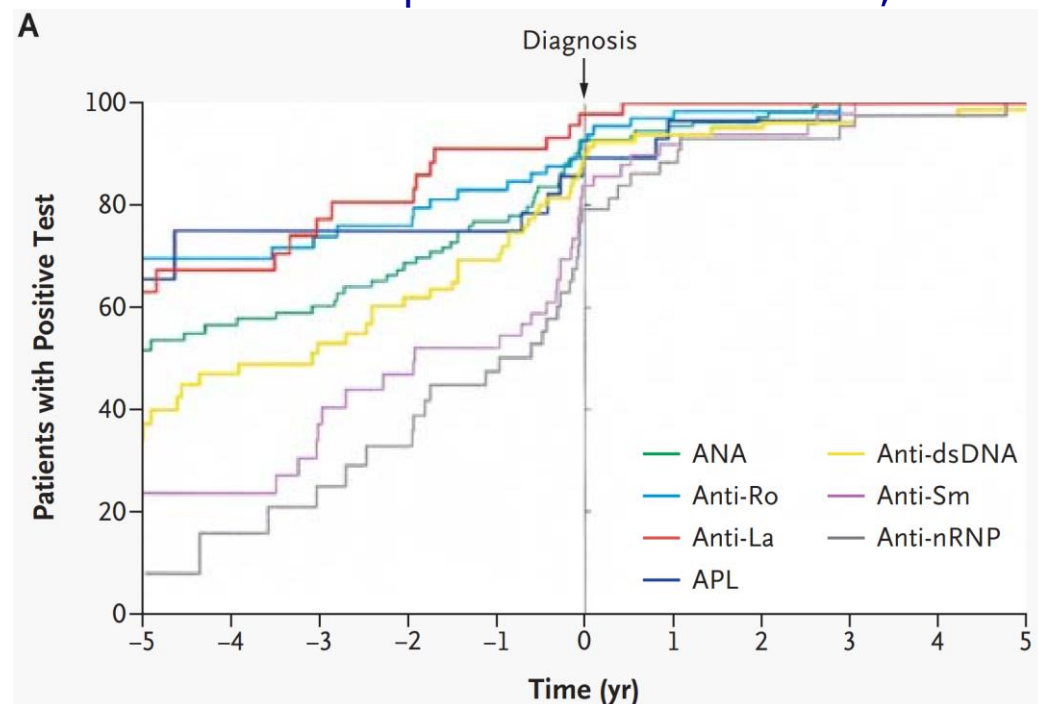
Towards precision medicine in autoimmunity



The future is here

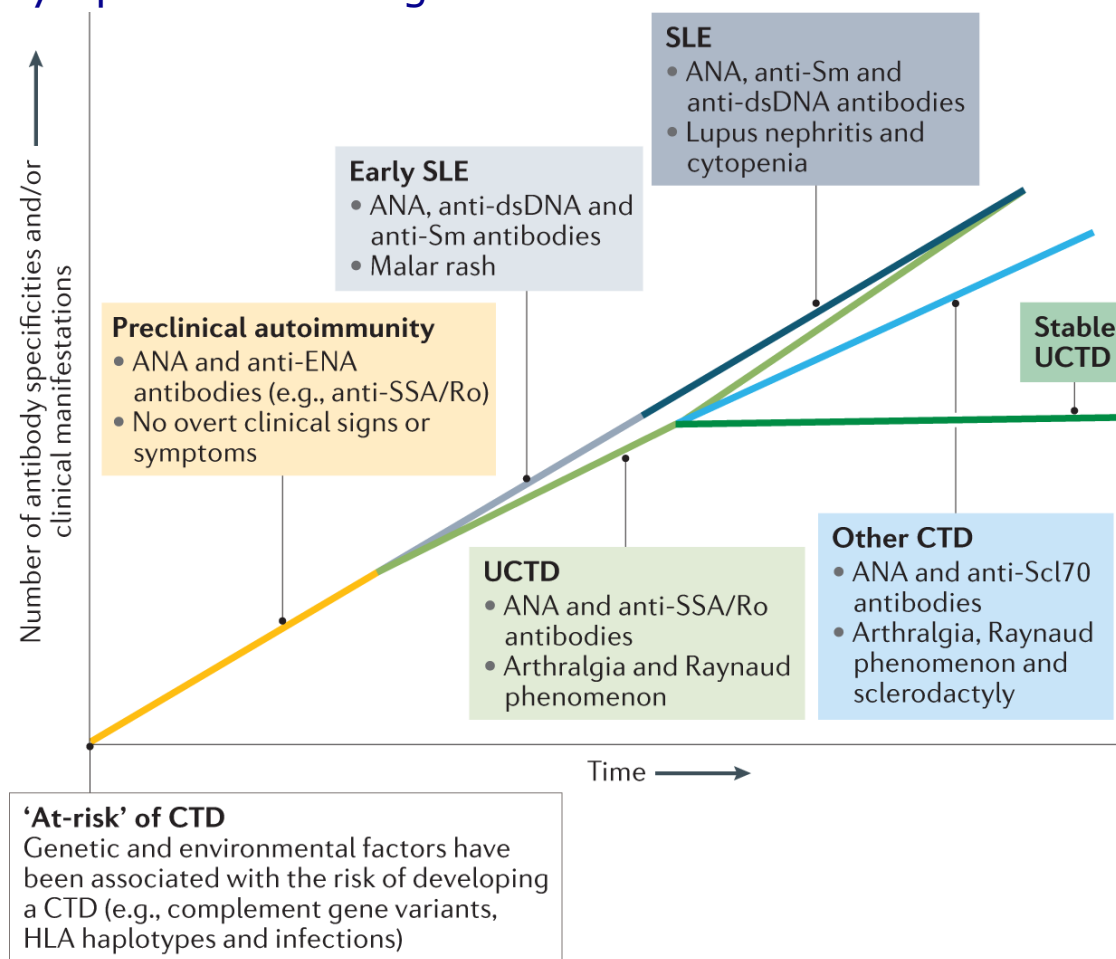
Autoantibody profiling – Prediction and early diagnosis

- Autoantibodies precede disease onset, clinical symptoms and diagnosis



Arbuckle MR, McClain MT, Rubertone MV, Scofield RH, Dennis GJ, James JA, Harley JB. Development of autoantibodies before the clinical onset of systemic lupus erythematosus. *N Engl J Med*. 2003;349:1526-33.

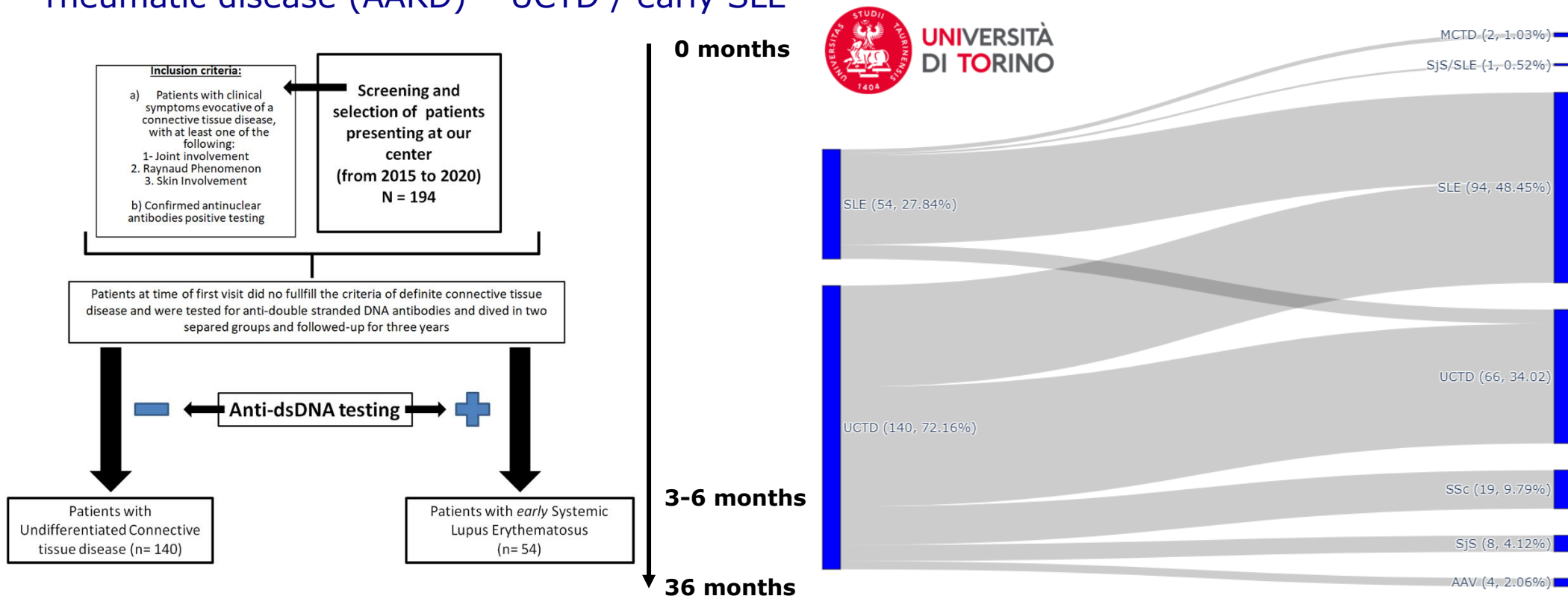
Sciascia, S., Roccatello, D., Radin, M. et al. Differentiating between UCTD and early-stage SLE: from definitions to clinical approach. *Nat Rev Rheumatol*. 2022;18,9–21.



The future is here

Autoantibody profiling – Prediction and early diagnosis

- Autoantibody profiling (>30) has the potential to improve early diagnosis of ANA associated rheumatic disease (AARD) – UCTD / early SLE



Radin M, et al. **Identifying subsets of patients with undifferentiated connective tissue disease: Results from a prospective, real-world experience using particle-based multi-analyte technology.** *Autoimmun Rev* 2023, **22**:103298.

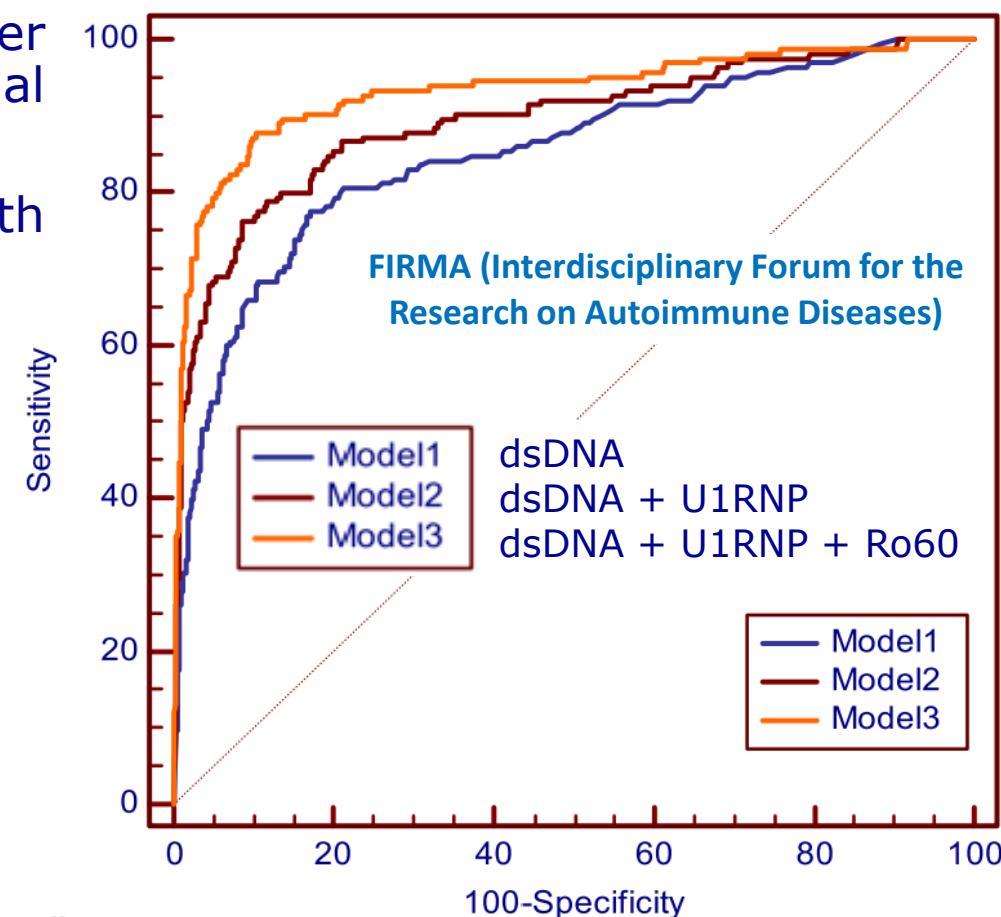
The future is here

Autoantibody profiling – Prediction and early diagnosis

- Enlarged antibody profiles have a higher diagnostic efficiency than that of individual antibodies
- The probability of disease increases with multiple positive autoantibodies

Disease probability according to multiple antibody presence

	Autoantibody combination	Probability (%)
SLE	dsDNA alone	42.3
	dsDNA+Sm	52.1
	dsDNA+Sm+ U ₁ RNP	96.9
	dsDNA+Sm+ U ₁ RNP+Ro60	99.6
	dsDNA+Sm+ U ₁ RNP+Ro60+Rib P	99.8
	dsDNA+Sm+ U ₁ RNP+Ro60+Rib P+Ro52	100

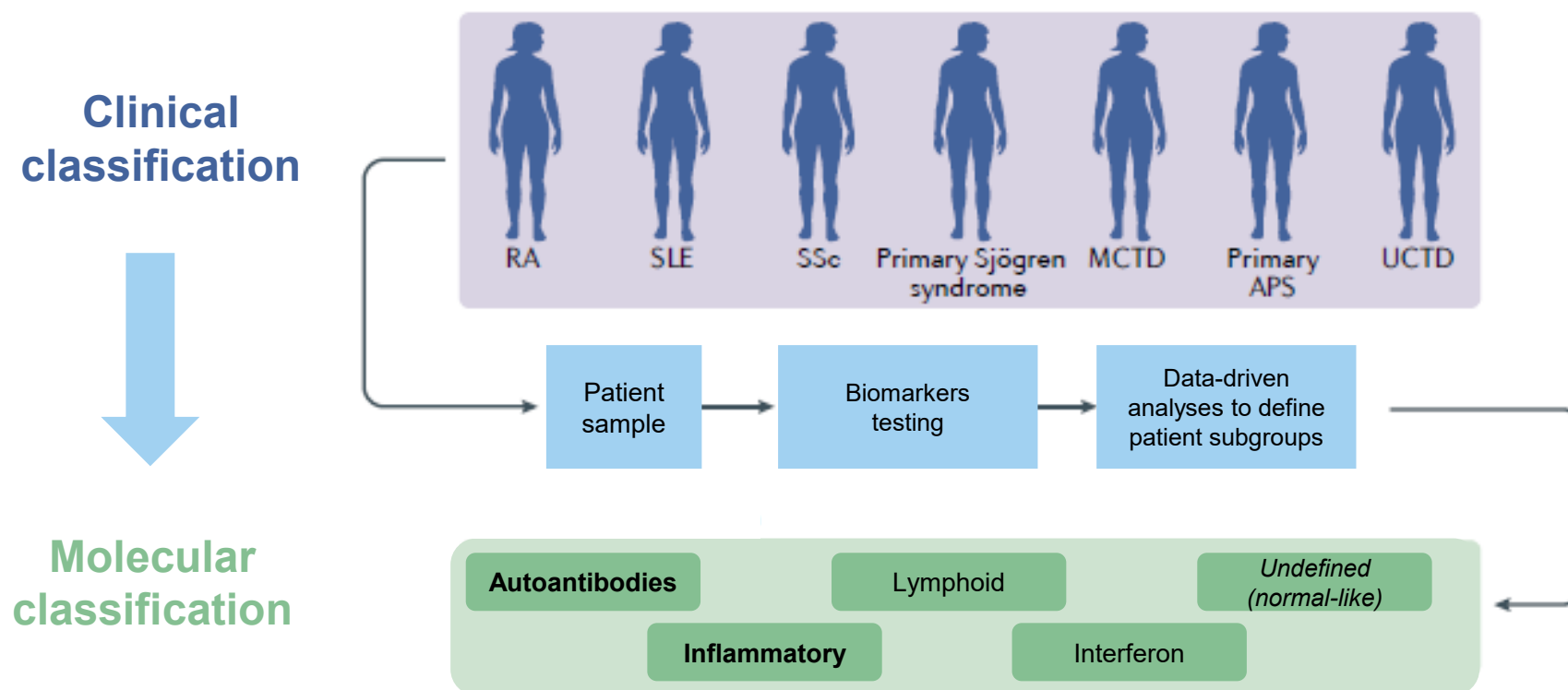


Bizzaro, N., Villalta, D., Bini, V. *et al.* **Multiparametric autoantibody analysis: a new paradigm for the diagnosis of connective tissue diseases.** *Arthritis Res Ther* 2022;**24**, 278.

The future is here

Autoantibody profiling – Patient stratification

- The field of rheumatology is poised to categorize systemic autoimmune diseases based on measurable and quantifiable molecular signatures

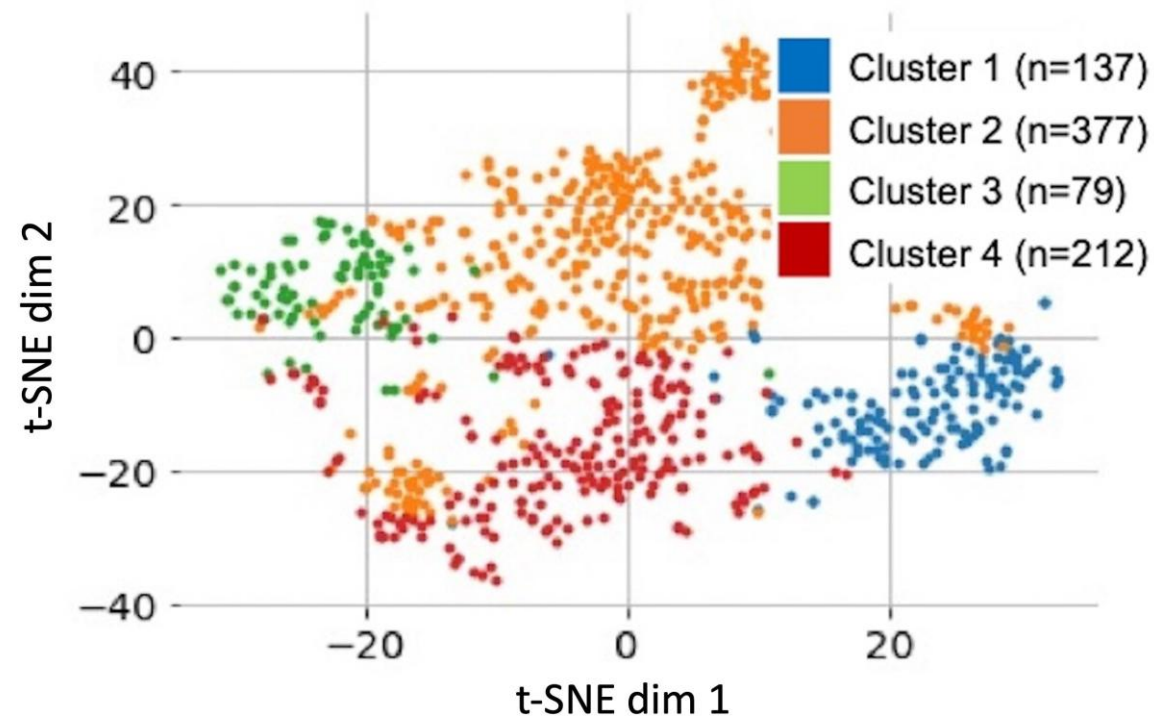


Modified from Whitfield, M.L. *Nat Rev Rheumatol.* 2021;**17**:193–194.

The future is here

Autoantibody profiling – Patient stratification

- Large, well-characterized cohort of SLE patients with a longitudinal and ML approach
- Comprehensive panel of autoantibodies (20 autoantibodies and 29 ANA pattern interpretations)
 - HEp-2; aCL and β 2GP1 IgG and IgM; anti-PS/PT IgG and IgM; anti-dsDNA IgG, anti- β 2GP1-domain 1 IgG, anti-DFS70 IgG; RiboP, Ro52, SSA/Ro60, SSB/La, Sm, U1RNP, Jo-1, centromere B, PCNA and histones
- Four distinct serological clusters (endotypes) in the first 5 years of disease
 - Associated with demographic and clinical features (age of onset, race/ethnicity, BMI)
 - **Predictive** of disease activity, organ involvement and **treatment course** at 10 years of follow-up, and mortality



The future is here

Autoantibody profiling – Prognosis (ILD)

DISEASE	MCTD	SSc 	IIM 	SjS 	AAV 	RA 	SLE 
ILD prevalence	56%	47%	41%	17%	13%	11%	6%
ANTIBODIES 	RNP U1RNP	Sc170 Centromere RNA pol III	tRNA synthetases (Jo-1, PL-7, PL-12, EJ, OJ, Ha, Zo, KS...) MDA5 Mi2, NXP2, TIF1-g, SRP, HMPCR, SAE	Ro52 (SSA) Ro60 (SSA) La (SSB)	PR3-ANCA MPO-ANCA	RF CCP	dsDNA Ro52 (SSA) Ro60 (SSA) La (SSB) Sm RNP
		Ro52 (SSA) La (SSB) PM/Scl U1RNP Th/To Fibrillarin Ku					

Joy GM, et al. Eur Respir Rev. 2023;32:220210.
 Doliner B, et al, Rheumatology. 2023;62:716–725.

The future is here

Autoantibody profiling – Prognosis (ILD)

ACR 2023 ILD Screening Guidelines

“There is a need for an improved understanding of risk factors, including **expanded autoantibody profiling**, to inform ILD screening and monitoring.

Together, radiographic patterns, **autoantibody profiles**, and/or other features may allow for the development of specific screening and monitoring recommendations for subsets of patients with SARD-ILD.”

The future is here

AI in autoimmunity

AVISE Lupus (Exagen, LDT)

- 10-marker diagnostic test designed to aid healthcare providers in a timely diagnosis of patients suspected of SLE

AVISE Lupus
Powered by CB-CAPs Technology

Sample Test Report



AVISE® Lupus is the only lupus test that incorporates Cell-Bound Complement Activation Products (CB-CAPs) assays which have been shown to have higher sensitivity for diagnosing SLE than C3/C4 levels.

- 22% greater sensitivity than C3/C4
- 33% greater sensitivity than anti-dsDNA
- 52% greater sensitivity than anti-Smith

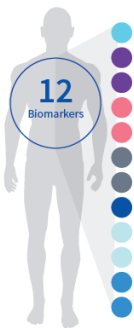
This proprietary test also allows for the efficient measurement of essential markers simultaneously and has the opportunity to reduce inconsistencies in diagnostic workups and standardize test results.

AVISE Lupus has the potential to improve the diagnostic landscape for SLE by:

- Improving accuracy by using assays with greater sensitivity and specificity
- Standardizing diagnostic approach through conducting tests simultaneously and combining results into a single index score
- Allowing for earlier diagnosis and thus mitigating downstream organ involvement

Vectra – RA (Labcorp, LDT)

- Personalized score by measuring 12 biomarkers and incorporating information on age, gender and adiposity to measure inflammation and predict risk of radiographic progression



Vectra® by labcorp

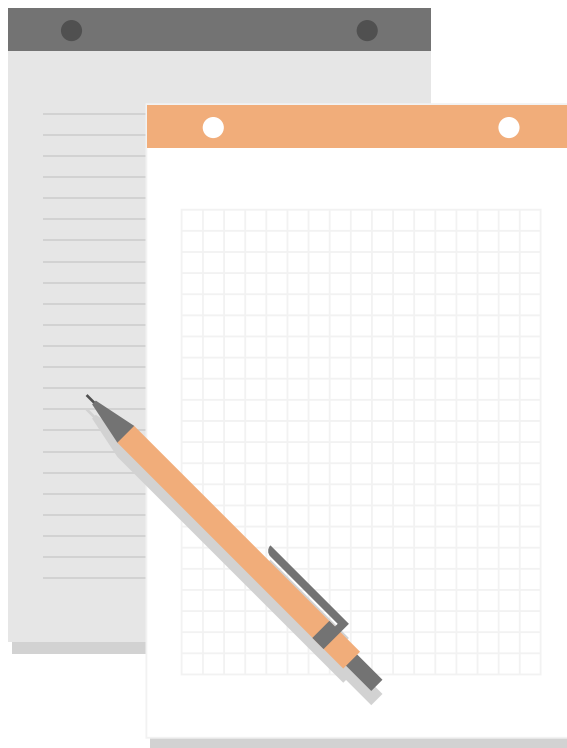
- Vectra measures 12 biomarkers and combines them into a single score thus allowing providers to incorporate molecular insight from various inflammatory pathways driving RA disease activity
- Vectra incorporates information on age, gender and adiposity to provide a score that reflects a patient's personalized disease activity and inflammation level
- Vectra is an unsurpassed predictor of radiographic progression compared to CDAI, SDAI, DAS28-CRP and CRP

Vectra is a molecular measurement of disease activity and RA inflammation							
Adhesion Molecules	Growth Factors	Cytokines/ Receptors	Matrix Metalloproteinases	Skeletal-Related Proteins	Hormones	Acute-Phase Proteins	
VCAM-1	EGF	IL-6	MMP-1	YKL-40	Leptin	SAA	
	VEGF-A	TNF-RI	MMP-3		Resistin	CRP	

The Vectra Score is reported on a scale of 1-100. Patients in the high and moderate categories are considered to have uncontrolled inflammation, and may require treatment modification.

Level of Disease Activity	LOW	MODERATE	HIGH
Vectra Score	1 to 29	30 to 44	45 to 100

Take-home messages



- ✓ Significant progress over the last decades in the development and validation of new technologies and platforms
- ✓ A wide range of research tools and laboratory technologies and tests are available for antibody testing today
- ✓ Serological biomarkers represent useful tools for patient care in autoimmune diseases
- ✓ Benefit of **autoantibody profiling** leveraging **multi-analyte testing** for prediction, diagnosis, patient stratification, prognosis...
- ✓ Opportunities with AI

