# seranova Bio

## Discovering drug targets from clinical trials of nature

Our goal is to discover novel drug targets and develop therapeutic antibodies by screening patients for “protective” autoantibodies that correlate with favorable responses.

We combine high-quality, comprehensive protein sampling with yeast display with next-generation DNA sequencing to profile patient plasma/serum samples with much greater throughput and fidelity than existing technologies.

We will screen 1,000s of patient samples from autoimmune disease, neurodegeneration and cancer (post-treatment with immunotherapy) to identify novel disease targets and potentially therapeutic antibodies cloned directly from patient B cells.

seranova

# Seranova team overview

**Aaron Ring, M.D., Ph.D.**

Assistant Professor of Immunobiology, Yale School of Medicine
NIH Director's Early Independence Award Recipient
Pew-Stewart Award for Cancer Research
Track-record of inventing and translating academic compounds to the clinic

- ALX148 (High affinity SIRPα): Ph2 at the Smilow Cancer Hospital at Yale
- MDNA109 (First described CD122 biased IL-2): IND Q4 2020
- ST-067 (Decoy-resistant IL-18): IND Q1 2021

Co-founder of Ab Initio Biotherapeutics, Forty Seven Inc., ALX Oncology
Founder of Simcha Therapeutics ($25m Series A 6/2020)

**Colin Ng, M.S., PMP**

Yale Blavatnik Fellow 2020-21

VP at IsoPlexis, led team of 30+ people to manufacture and launch IsoCode consumable kit in over 30 labs across the globe

- Established and led a contract research team that produced more than $1M annually servicing academic and industry leaders in immuno-oncology (2016-18)
- Led team that developed and patented new single-cell assays and consumables in single-cell proteomics, metabolomics and transcriptomics (2016-19)

seranova

# Patient autoantibodies can both cause and ameliorate disease

Autoantibodies(AAbs) are extremely valuable not only as diagnostic biomarkers but can identify targets for therapeutic antibodies

**Autoimmune Disease**

Anti-IL-1a AAbs in RA[1]

Anti-IFN AAbs in SLE[2]

**Cancer**

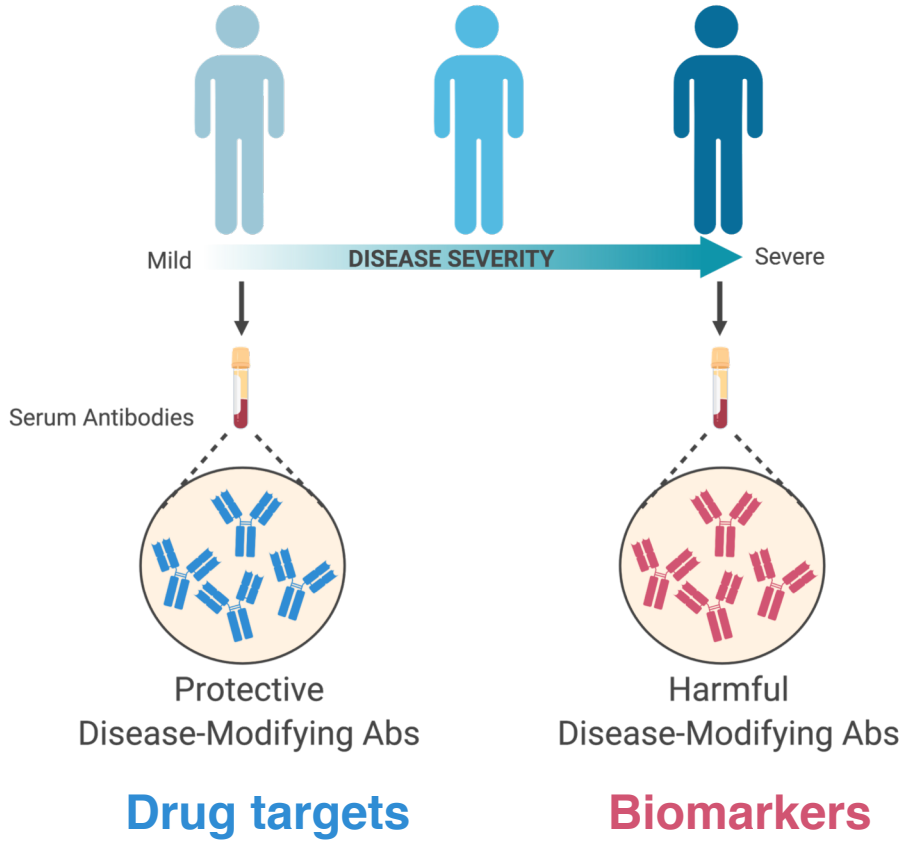
Anti-HER2 AAbs in Breast Cancer[3]

Anti-MUC1 AAbs in Carcinoma[4]

**Neurodegeneration**

Anti-amyloid AAbs in AD[5]

Anti-prion Aabs[6]



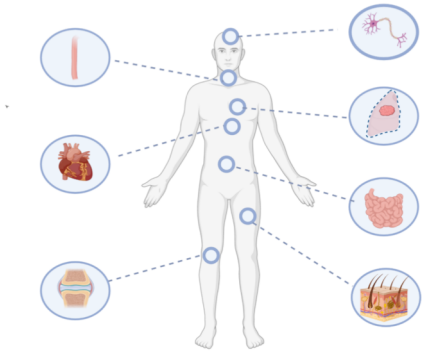

See Appendix for references

seranova

# Market opportunity for autoantibody target discovery

Mining autoantibodies for therapeutic targets has huge commercial potential

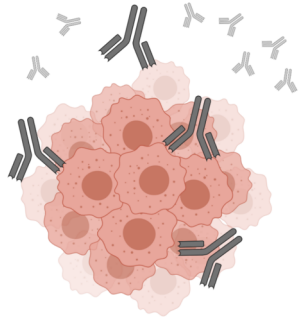
## Autoimmune Disease Market[7]
**$149.4B** by 2025, CAGR of **4.34%**



**10 million** Americans **(>2.5% )** suffer from autoimmune disease[10], which is often inadequately treated

Autoantibodies **ameliorate**[13] and **induce**[14] autoimmune diseases

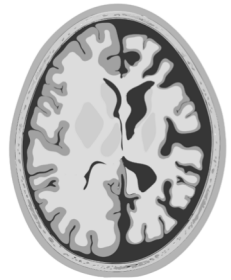
## Cancer Immunotherapy market[8]
**$126.9B** by 2026, CAGR of **9.6%**



Of patients treated with checkpoint inhibitors (ICI), only **12% respond**[11] and **>15% suffer**[12] severe adverse events

Autoantibodies are associated with both **toxicity** and **efficacy** of **ICIs**[15]

## Neurodegeneration market[9]
**$62.7B** by 2026, CAGR of **7.2%**



Few effective therapies exist for neurodegeneration. New **disease insights/drug targets** are needed.

Protective autoantibodies are being developed as **novel therapies**.

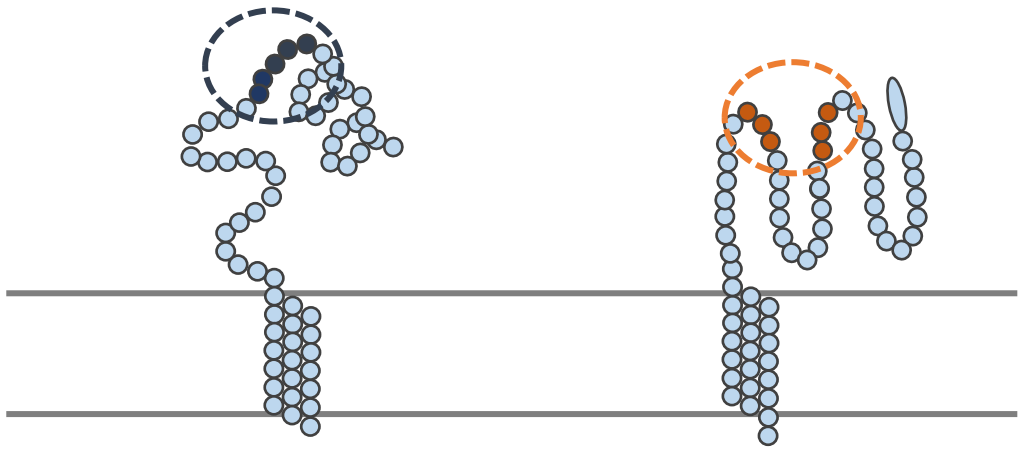
See Appendix for references

seranova

# Conformational epitopes are the key to discover functional AAb targets

Our technology is capable of profiling conformational epitopes by utilizing yeast display

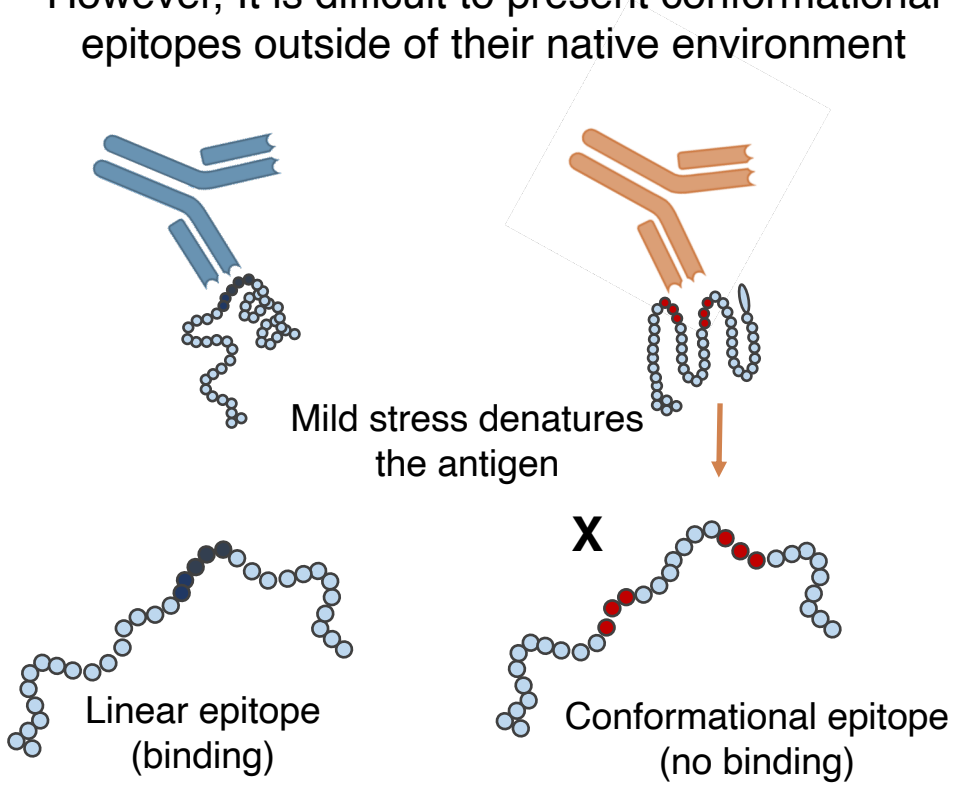
90% of autoantibodies recognize conformational epitopes[16]



**Linear** epitope
Continuous amino acid residues

**Conformational** epitope
Discontinuous amino acid residues

However, It is difficult to present conformational epitopes outside of their native environment




See Appendix for references

seranova

# Existing autoantigen discovery technologies are limited

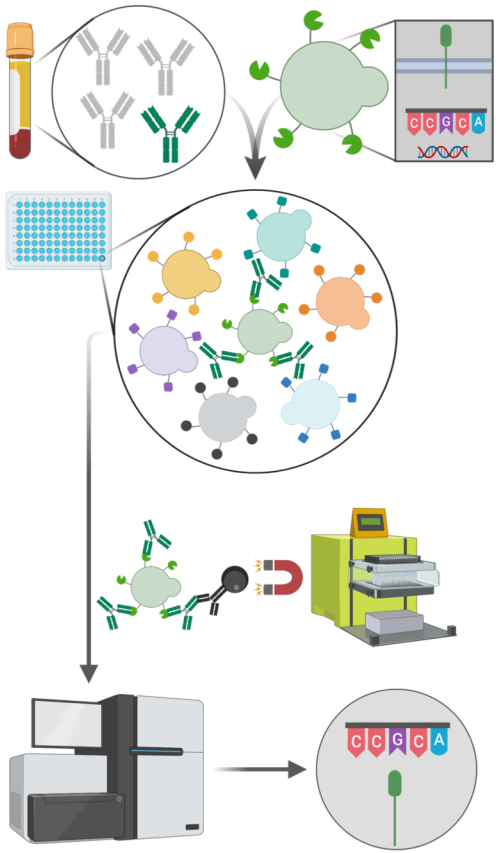
State-of-the-art methods are poorly suited to identify functional AAbs due to low throughput or fidelity for conformational antigens

| | Serimmune | CDI | Oncimmune | CDI | Ordinatrix Precision Translational Proteomics | sengenics |
|---|---|---|---|---|---|---|
| **Technology** | bacteria display | phage display | bead display | microarray | microarray | microarray |
| **Sample Throughput** | High | High | Medium | low | low | Low |
| **Conformational Epitopes** | No | No | Variable | Variable | Variable | Yes |

seranova

# Our Technology: Rapid Exoproteome Antigen Profiling (REAP):

A high-throughput, sensitive, and quantifiable platform for AAb discovery




Comprehensive, genetically barcoded library of ~3,000 extracellular /secreted proteins displayed on yeast

Patient samples applied to yeast library in microtiter plates

IgG bound clones isolated by high-throughput magnetic selection

Quantitative readout by next-generation sequencing of antigen barcodes

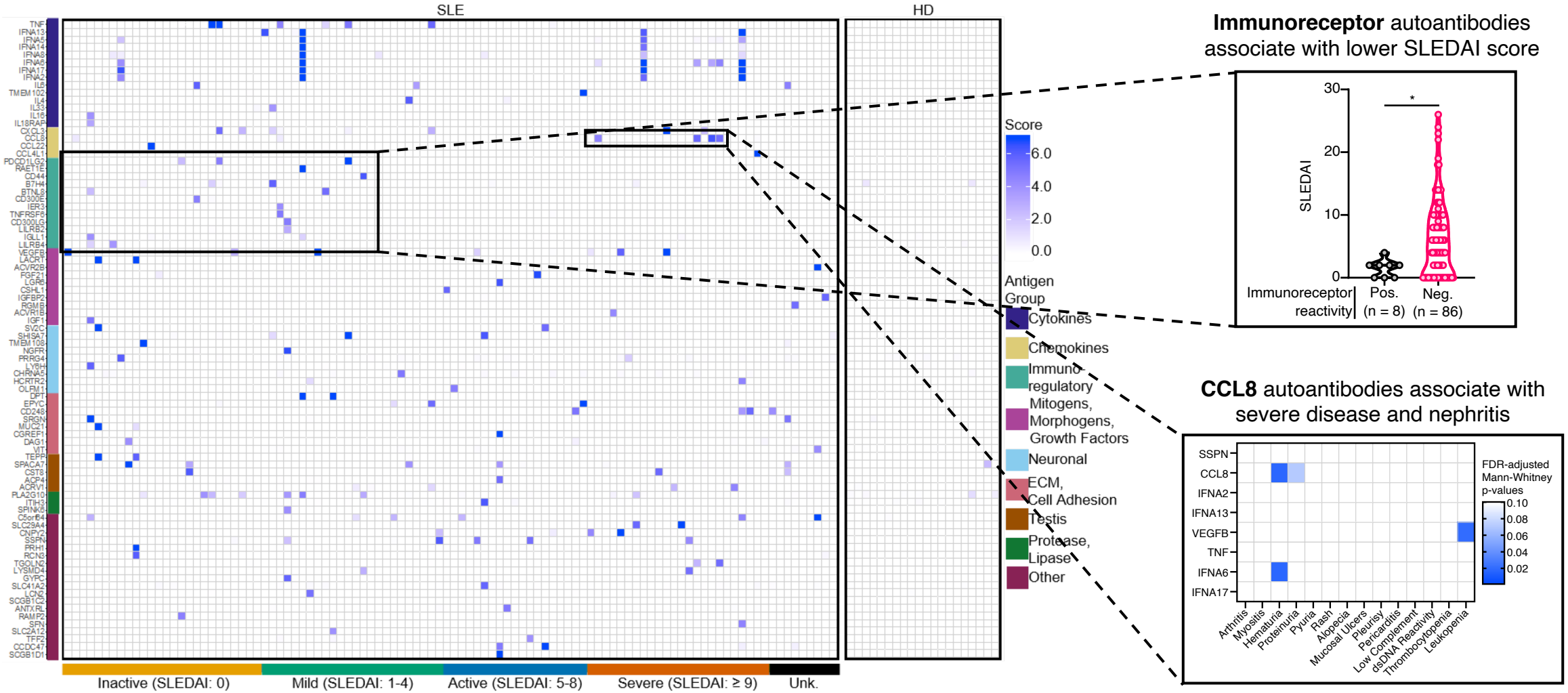
## REAP Capabilities

- Detection of autoantibody responses to ~3,000 human extracellular antigens with **conformational epitopes**
- Low sample requirements: 10 µg of patient IgG or 50-100 µL of serum/plasma
- High throughput (**10-100x faster)** than existing technologies
- Utilizes molecular barcoding and next-generation sequencing (run on 96-well format)

seranova

# Serological profiling in systemic lupus erythematosus (SLE)

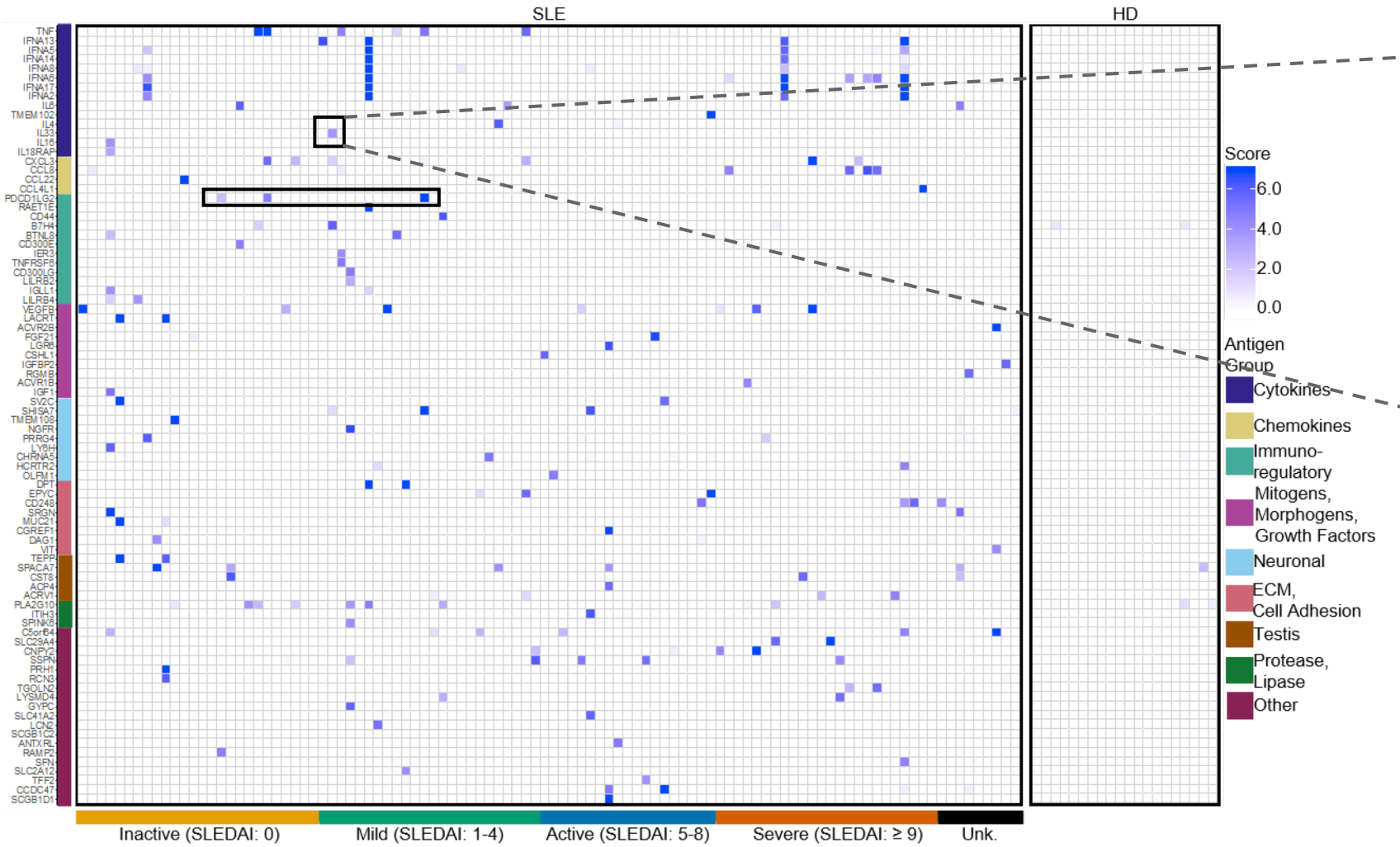
REAP identifies novel, private autoreactive responses in SLE



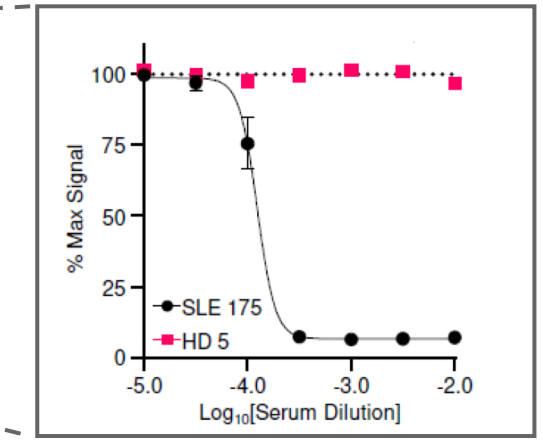

seranova

# Serological profiling in systemic lupus erythematosus (SLE)

REAP identifies novel, private autoreactive responses in SLE




**Anti-IL-33** autoantibodies neutralize IL-33 signaling




## IL-33 in SLE

**IL-33 levels are elevated in serum of SLE patients**[17]

**IL-33 Promotes BAFF-dependent autoantibody production**[18]

**IL-33 neutralization suppresses disease in lupus-prone mice**[19]

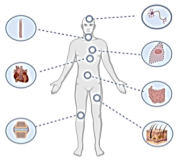
See Appendix for references

seranova

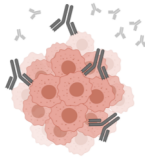
# Our Plan: Develop unprecedented database of patient AAb responses

Our database will provide key insights into new drug targets (e.g., protective autoantibody responses) and potentially new drugs themselves. Other successful platform companies have been successful with this model (e.g. Adaptive Biotech, MC $6.72B)

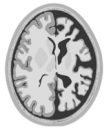
### 1. Sample Acquisition
Acquire well annotated serum/ plasma from commercial biobanks.



Autoimmune disease

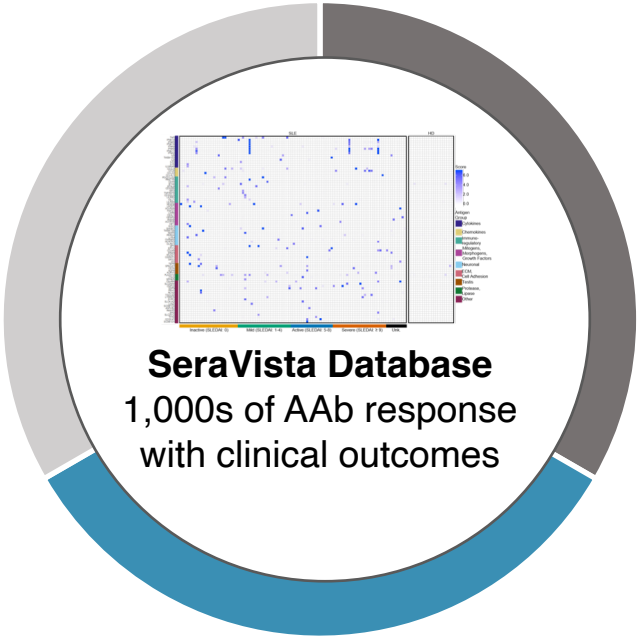


Cancer immunotherapy



Neurobiology

### 2. Build Database (SeraVista)
Results of ultra-high throughput REAP profiling added to database. Identify targets.



**SeraVista Database**
1,000s of AAb response with clinical outcomes

### 3. Therapeutic Discovery / Dev
Clone patients' natural antibodies or develop via traditional approaches

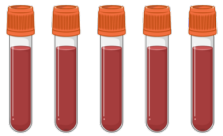
- Program 1: SLE antibody
- Program 2: RA antibody
- Program 3: Scleroderma antibody
- Program 4: I/O antibody
- Program 5: I/O antibody
- Program 6: AD antibody
- Program 7: PD antibody

seranova

# Overview of Seranova's Proposal to the Blavatnik Fund for Innovation

Seranova's REAP platform is ready to commercialize therefore we will apply for Blavatnik Development Funding ($**300k**)

**Activity 1:** Build ≥1,000 lupus patient autoantibody focus in SeraVista database **($230k**)



1. Acquire ≥1,000 lupus serum/plasma samples with associated high-quality clinical annotations with matched PBMCs, ~$200/serum sample ($200k)
2. Reagents and sequencing costs to run REAP process ($30k)

**Activity 2**: Initiate a lead antibody program **($70k**)

1. Antibody discovery (e.g., Alloy mouse immunization, IPI yeast display, cloning from patients' B cells; choice depends on the specific AAb target) ($45k)
2. Conduct *in vitro* validation of antibody candidates (e.g., signaling assays, ADCC/ADCP, receptor/ligand blocking, etc.) ($25k)

seranova

# Appendix: References


1. Graudal, N A et al. “Autoantibodies against interleukin 1alpha in rheumatoid arthritis: association with long term radiographic outcome.” Annals of the rheumatic diseases vol. 61,7 (2002): 598-602. doi:10.1136/ard.61.7.598
2. Morimoto, Alyssa M et al. “Association of endogenous anti-interferon-α autoantibodies with decreased interferon-pathway and disease activity in patients with systemic lupus erythematosus.” Arthritis and rheumatism vol. 63,8 (2011): 2407-15. doi:10.1002/art.30399
3. Tabuchi, Yukiko et al. “Protective effect of naturally occurring anti-HER2 autoantibodies on breast cancer.” Breast cancer research and treatment vol. 157,1 (2016): 55-63. doi:10.1007/s10549-016-3801-4
4. Hirasawa, Y et al. “Natural autoantibody to MUC1 is a prognostic indicator for non-small cell lung cancer.” American journal of respiratory and critical care medicine vol. 161,2 Pt 1 (2000): 589-94. doi:10.1164/ajrccm.161.2.9905028
5. aducanumab
6. Senatore, A et al. “Protective anti-prion antibodies in human immunoglobulin repertoires.” EMBO Mol Med (2020) 12: e12739. doi: 10.15252/emmm.202012739
7. KBV Research. “Autoimmune Disease Therapeutics Market Size.” 2019. https://www.kbvresearch.com/autoimmune-disease-therapeutics-market/
8. Grand View Research. “Cancer Immunotherapy Market Size Worth $126.9 Billion By 2026.” 2019. https://www.grandviewresearch.com/press-release/global-cancer-immunotherapy-market
9. Medgaget. “Neurodegenerative Diseases Drugs Market to Worth USD 62.7 Billion by 2026.” 2019. https://www.medgadget.com/2019/09/neurodegenerative-diseases-drugs-market-to-worth-usd-62-7-billion-by-2026-global-industry-share-and-growth-analysis-by-top-10-players.html
10. Ludwig, Ralf J et al. “Mechanisms of Autoantibody-Induced Pathology.” Frontiers in immunology vol. 8 603. 31 May. 2017, doi:10.3389/fimmu.2017.00603[5] (Haslam et al. 2019)
11. Xu Cheng, Chen Yu-Pei, Du Xiao-Jing, Liu Jin-Qi, Huang Cheng-Long, Chen Lei et al. Comparative safety of immune checkpoint inhibitors in cancer: systematic review and network meta-analysis BMJ 2018; 363 :k4226. doi: 10.1136/bmj.k4226.
12. König D, Läubli H: Mechanisms of Immune-Related Complications in Cancer Patients Treated with Immune Checkpoint Inhibitors. Pharmacology 2020. doi: 10.1159/000509081
13. Meyer, SteffenMeloni, Antonella et al. “AIRE-Deficient Patients Harbor Unique High-Affinity Disease-Ameliorating Autoantibodies.” Cell, Volume 166, Issue 3, 582 - 595
14. Ludwig, Ralf J et al. “Mechanisms of Autoantibody-Induced Pathology.” Frontiers in immunology vol. 8 603. 31 May. 2017, doi:10.3389/fimmu.2017.00603
15. de Moel, Emma C et al. “Autoantibody Development under Treatment with Immune-Checkpoint Inhibitors.” Cancer immunology research vol. 7,1 (2019): 6-11. doi:10.1158/2326-6066.CIR-18-0245
16. Sanchez-Trincado, Jose L et al. “Fundamentals and Methods for T- and B-Cell Epitope Prediction.” Journal of immunology research vol. 2017 (2017): 2680160. doi:10.1155/2017/268016
17. Toama et al. Serum Level of Interleukin 33 and its Relation with Disease Activity and Clinical Presentation in Systemic Lupus Erythematosus. J Clin Exp Dermatol Res 2017, 8:3 DOI: 10.4172/2155-9554.1000390
18. Rose, William A 2nd et al. “Interleukin-33 Contributes Toward Loss of Tolerance by Promoting B-Cell-Activating Factor of the Tumor-Necrosis-Factor Family (BAFF)-Dependent Autoantibody Production.” Frontiers in immunology vol. 9 2871. 6 Dec. 2018, doi:10.3389/fimmu.2018.02871
19. Li, Pin et al. “IL-33 neutralization suppresses lupus disease in lupus-prone mice.” Inflammation vol. 37,3 (2014): 824-32. doi:10.1007/s10753-013-9802-0


seranova