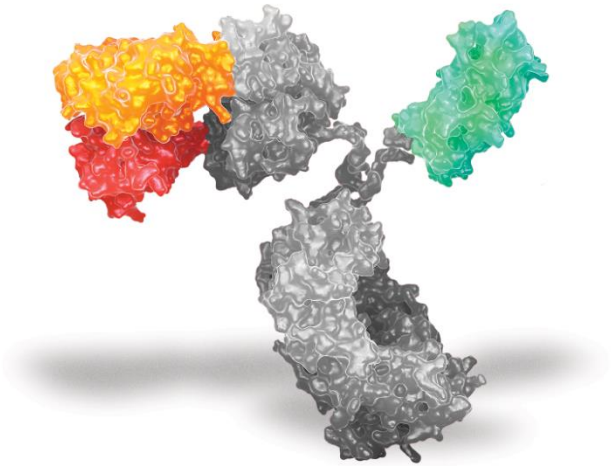
Teneobio

Multi-specific therapeutic antibodies



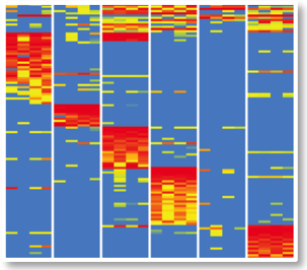
Slide Presentation is Available on Teneobio's Website

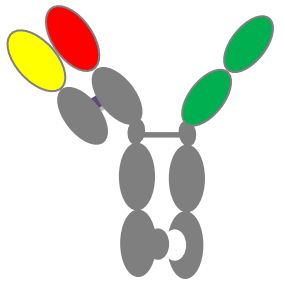
Teneobio Overview

- **Proprietary transgenic rats for human antibody discovery**
  - UniRat and Omniflic
- **High throughput sequence-based human antibody discovery engine**
  - Next-gen sequencing + custom bioinformatics
  - High throughput recombinant expression and functional screening
- **Multi-valent therapeutics with superior efficacy**
  - Anti-CD3 T-cell redirection platform
    - Anti-BCMAxCD3 lead program, Phase 1 complete 2021
    - Anti-PSMAxCD3, Anti-CD19xCD3 INDs 2020
  - IL2Rβ/γ agonists
  - T-cell co-stimulation platform
  - Anti-CD38 enzyme inhibitor for Autoimmunity/Inflammation
- **Product development partnerships**
  - UniAbs for CAR-Ts, ADC's, nanoparticles, viral delivery, etc.
  - Multi-target discovery through IND-enabling capabilities

UniRat
naturally optimized human antibodies™

OmniFlic
naturally optimized human antibodies™





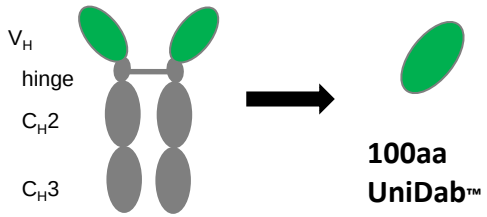
Human Ig Transgenic Rats for Antibody Discovery

UniRat
naturally optimized human antibodies™

KO of rat Ig loci
Fully human VH,
Heavy chain antibody (UniAb)
or domain antibody (UniDab)

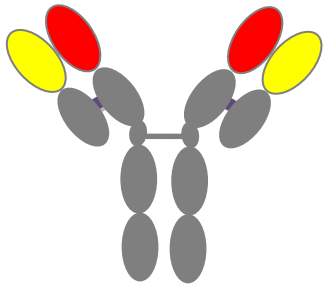
OmniFlic
naturally optimized human antibodies™

KO of rat Ig loci
Fully human VH,
fixed light chain IgG



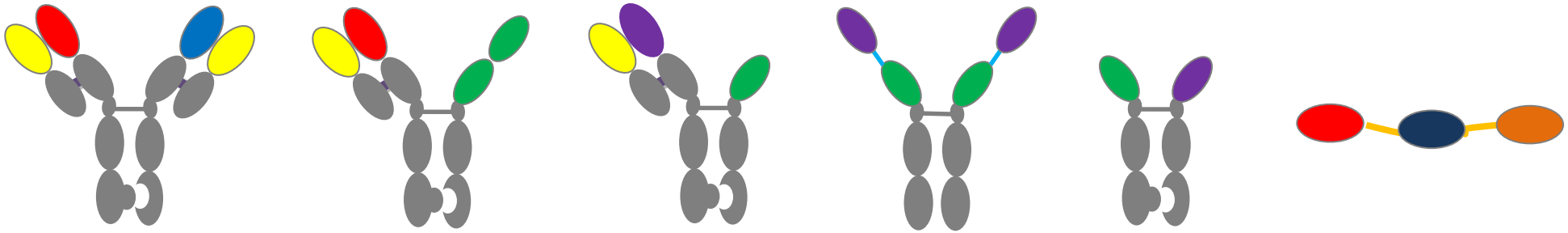
UniAb™

100aa
UniDab™



FlicAb™

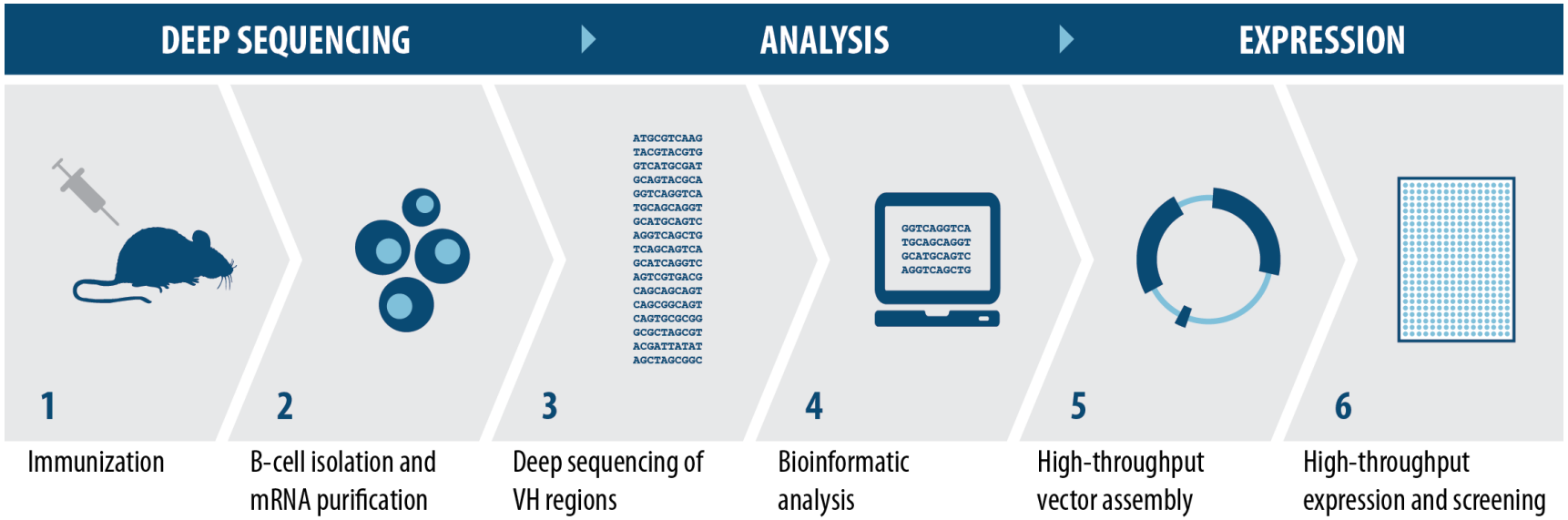
Flexible and robust human multi-specific antibodies



Sequence-based Antibody Discovery

Our platform is a unique combination of:

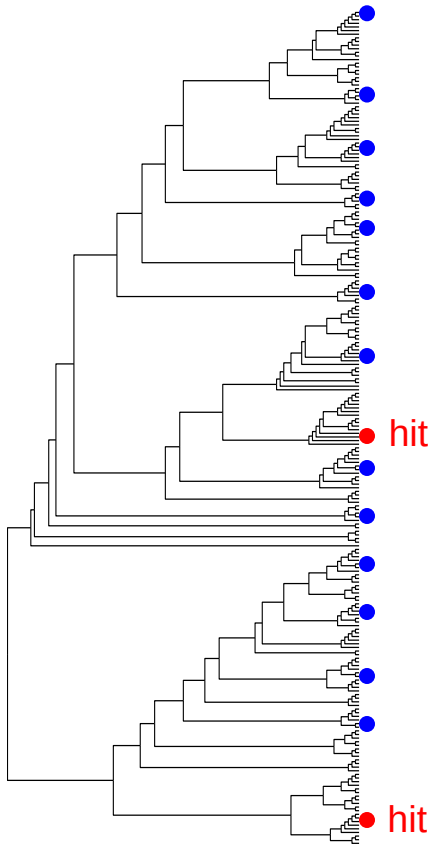
- Antibody repertoire deep sequencing
- Custom bioinformatics analysis
- High-throughput vector assembly
- Recombinant expression and screening



frontiers in Immunology **Harris *et al*. Front. Immunol. 24 April 2018**

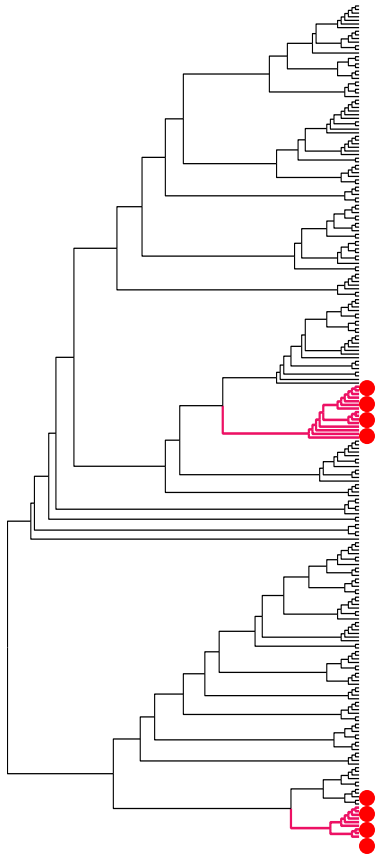
Screening design and strategy

- **Primary screen:** diverse CDR3 sequence families, **broad epitope coverage**
- **Secondary screen:** family members of primary hits, **optimize function**



Primary Screen: 300-400 diverse CDR3 sequences

Maximize epitope coverage



Secondary Screen: 50-100 unique sequences per lineage

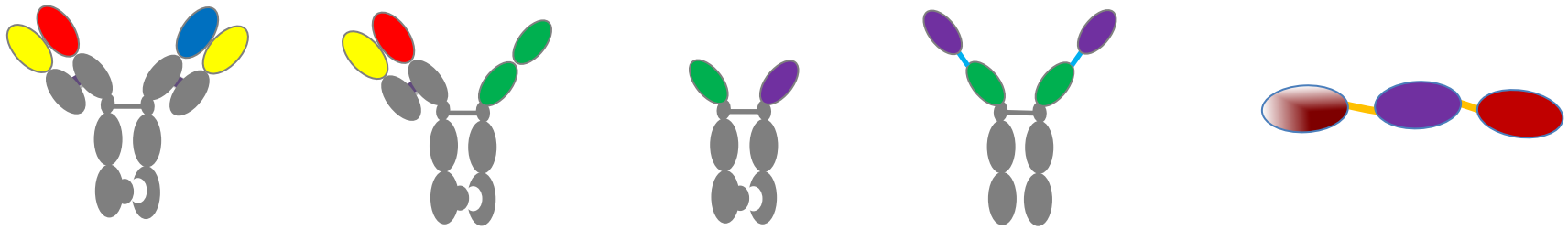
Includes rare sequences in lineages of interest

Sequence-based Antibody Discovery

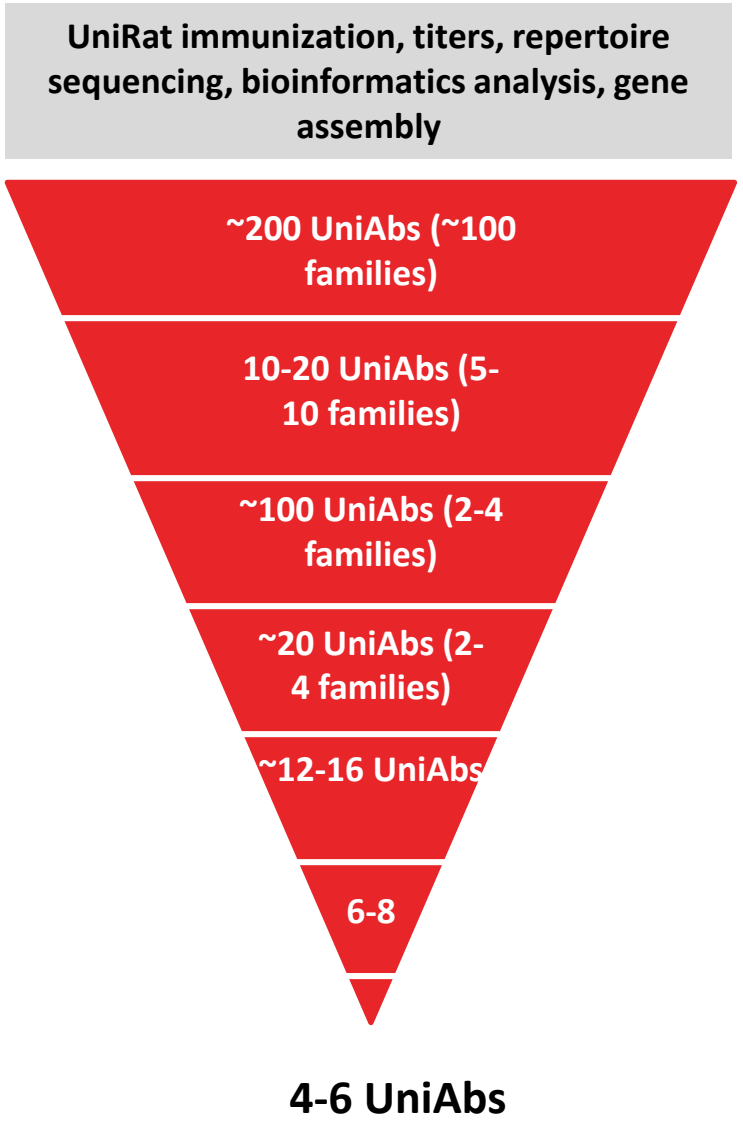
We discover 100X more antibodies 3X faster than traditional approaches

	Total
Total number of discovery projects	100
Total number of targets	39
Total number of animals	1,346
Total number of NGS sequence reads generated	1,817,332,666
Total number of unique antibodies screened	39,260
Total number of antigen-specific antibodies	11,778

100% Success rate



High Throughput Screening Allows Early Selection for Manufacturability



Early testing for developability

Stage	Goal
Primary screen (96well supernatants)	ID ag+ CDR3 families (poly-reactivity)
Family characterization (24well purified)	ID ag+ families with other desired functions (%HMW, Tm, Tagg)
Diversity screen (96well supernatant)	Expand range of fxn activity (screen add'l family members)
Secondary screen (24well purified)	In-depth comparison of family members (%HMW, Tm, Tagg)
Secondary screen (5-20mg purified)	Additional functional assessment, protein analytics (Thermal Stability after stress)
Final lead evaluation	

Corporate Strategy Drives Teneobio's Non-Dilutive Strategy

- **Diversification is Important**
  - Oncology: T-Cell Engagement, T-Cell Co-Stimulation
  - Autoimmunity: CD38 Enzyme Inhibition
  - Infectious Disease: Polyomavirus, Hepatitis B Virus

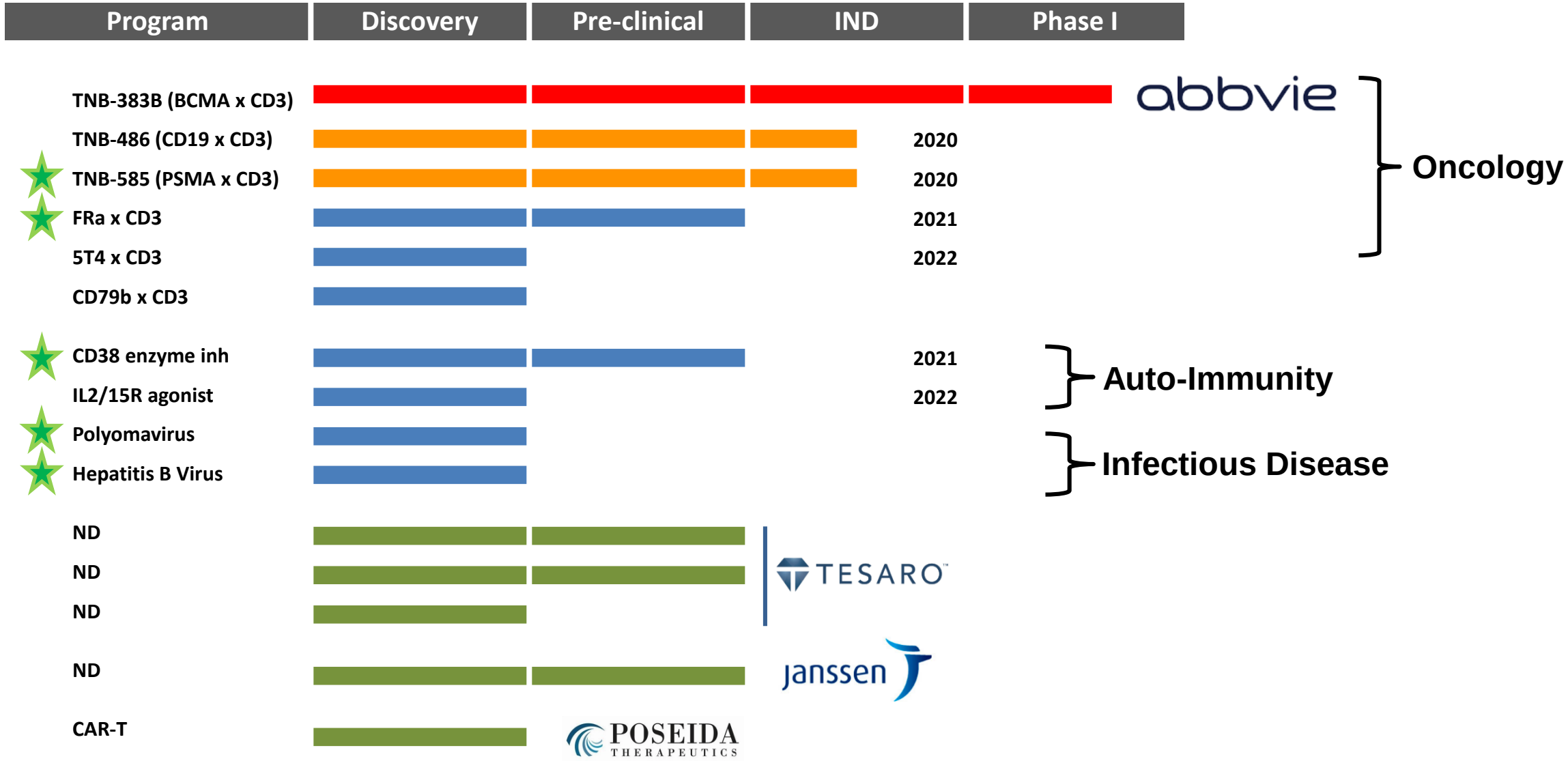
- **Focus on problems that demand a multi-specific or HCA approach: Teneo's T-Cell Engagers**

- **Be Collaborative: CD38 Enzyme Inhibition**
  - Academic Researchers
  - Service Providers
  - Biotech
  - Physicians

- **Pursue High-Risk, High-Reward Programs: Anti-Polyoma Domain Antibody Strings**

- **Grant Writing/Execution as a Crucible**

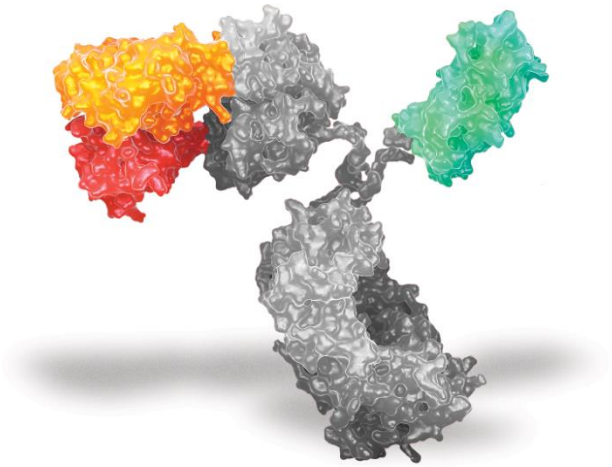
Teneobio's Pipeline: Diversification through Non-Dilutive Funding



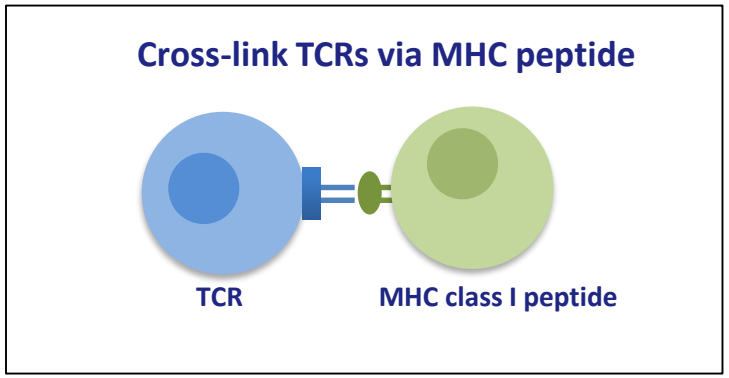
(ND= Not disclosed)

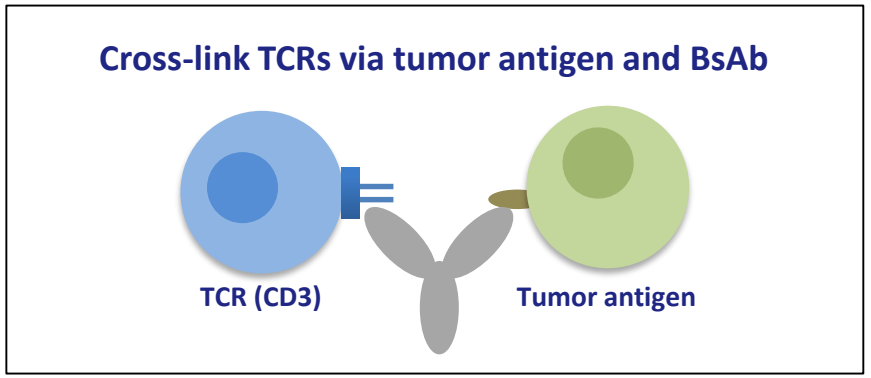
Teneobio's T-Cell Engagement Platform

Better Bispecific T-Cell Engagers Using UniAbs



Teneobio's Next-gen CD3 Bispecific Platform for T-cell Redirection





- MHC display of foreign antigens triggers T-cell activation through TCR
- Bispecific antibody binds tumor-associated antigen and activates T-cells independent of pMHC

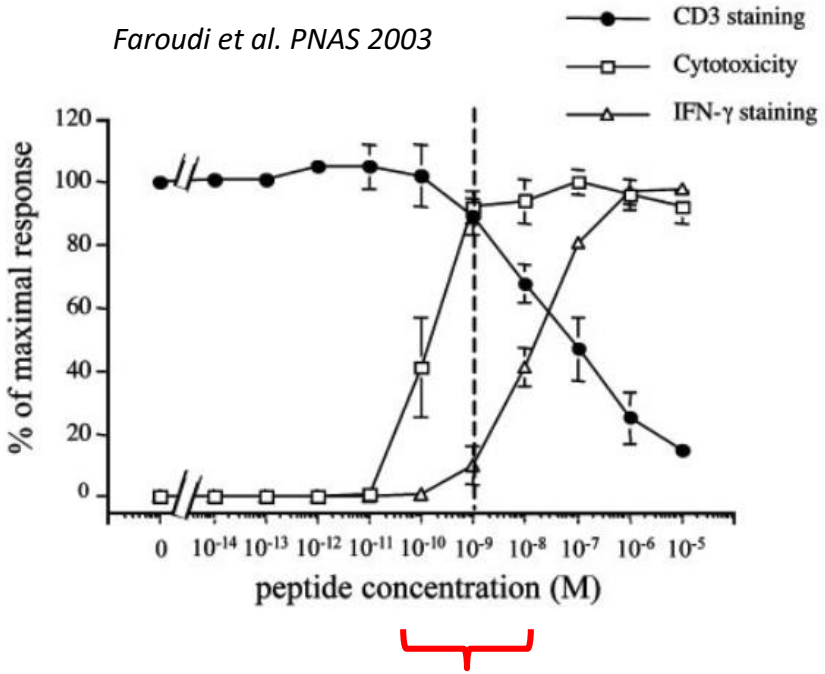
- **~75% of BsAbs in development use an anti-CD3 derived from SP34, OKT3, or UCHT1 (Wu et al. Pharm. and Ther. 2017)**
- **Our goal: discover new anti-CD3 antibodies that in bispecific format are well tolerated and efficacious**
  - Efficient tumor cell lysis
  - Minimal CRS, T-cell exhaustion and AICD
  - Low immunogenicity
  - Long Half-Life

Dual thresholds for TCR Signaling and Activation Enable Selective Killing Without Cytokine Storm

T cell activation occurs in discrete stages based on TCR-pMHC complex formation

- *Faroudi et al. PNAS 2003*
- *Purbhoo et al. Nature Imm. 2004*

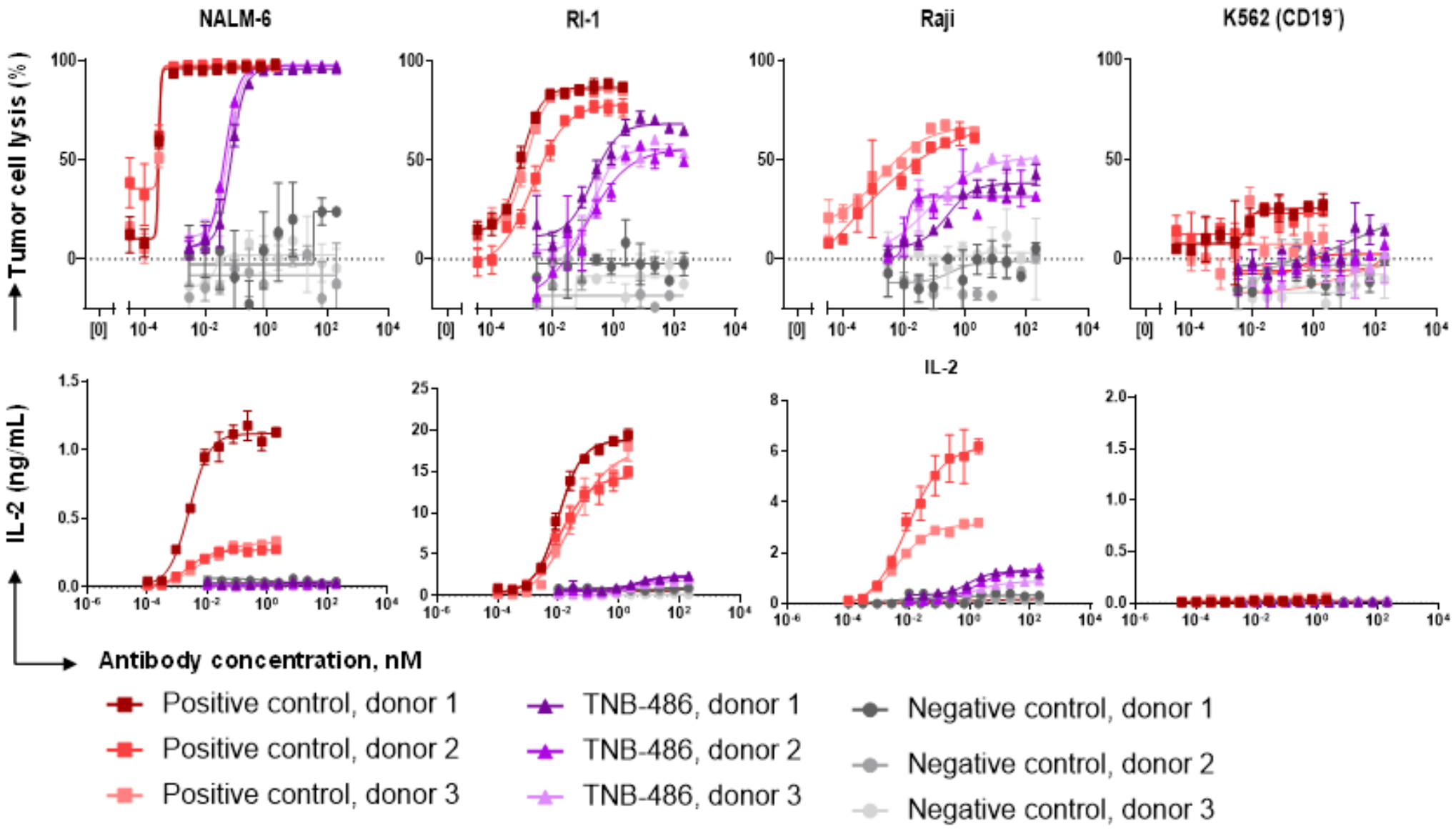
Faroudi et al. PNAS 2003



- **Mature immune synapse is not necessary for cytolytic activity**
- **2 TCR-pMHC complexes sufficient for inducing cytotoxicity = *threshold 1***
- **>10 necessary for full synapse formation and cytokine release = *threshold 2***
- **Can new CD3 antibodies be developed that stimulate threshold 1 but not threshold 2?**

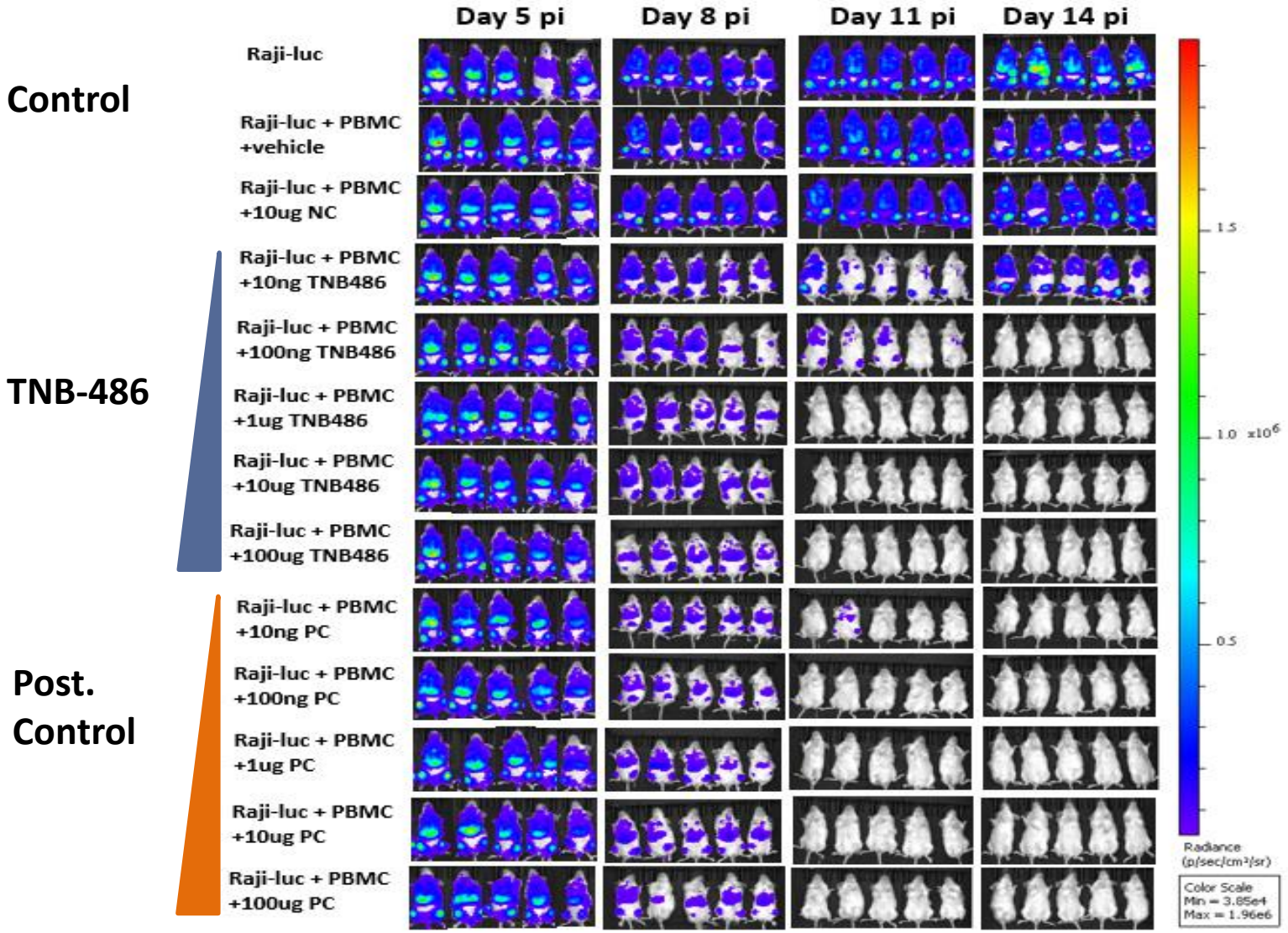
Window of engagement to stimulate tumor cell lysis without cytokine release

TNB-486 (anti-CD19/CD3) is Efficacious With Low Cytokine Release



TNB-496 Is Efficacious In Vivo

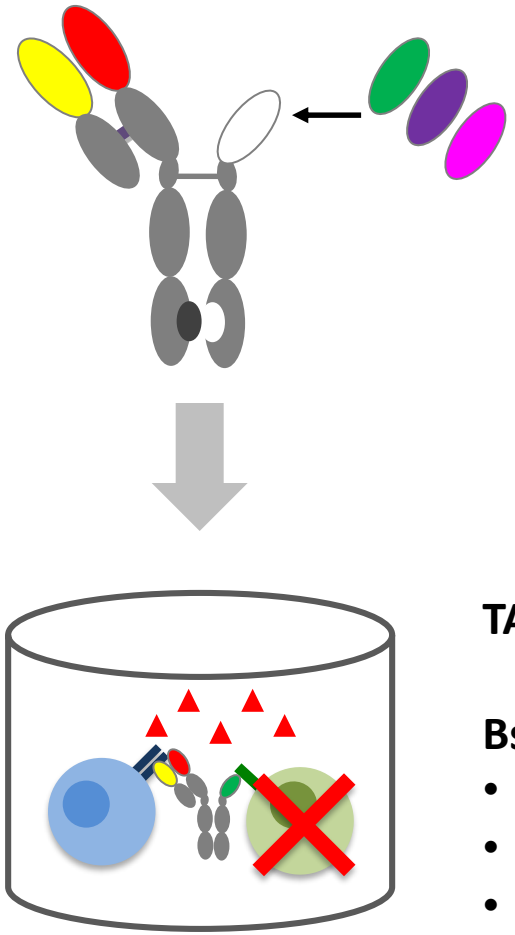
In Vivo Efficacy of TNB-486 in Disseminated Murine Model of Burkitt Lymphoma



TNB-486 results in tumor regression in Burkitt Lymphoma disseminated model

Modular Bispecific Antibody Development

Anti-CD3 T-cell activator



High affinity
anti-Tumor antigen

TAA+ Tumor cells + T-cells

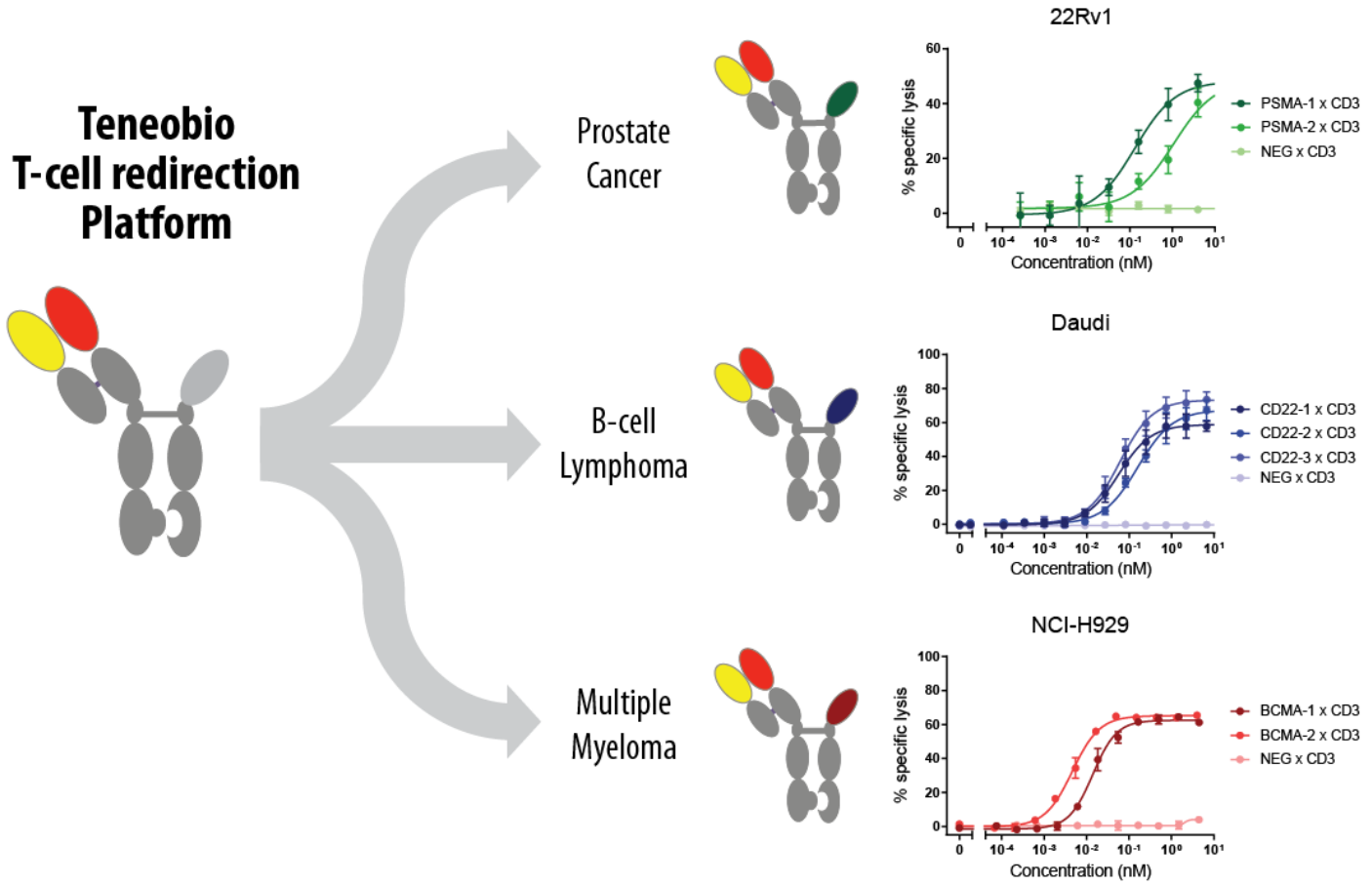
BsAb-mediated

- T-cell activation,
- Cytokine release
- Tumor cell lysis

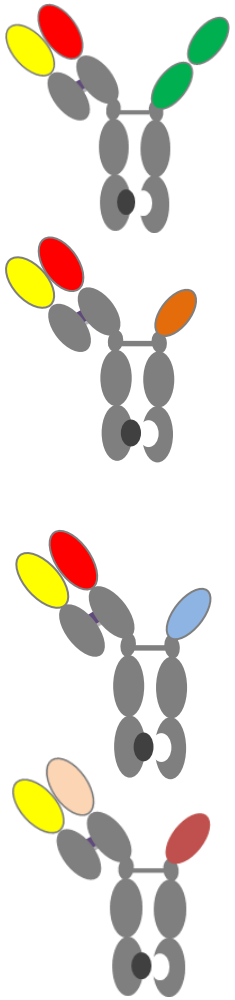
mAbs Trinklein *et al.* mAbs 20 Feb 2019

Teneobio's Platform has been Validated Both Solid and Liquid Tumors

- BsAb-mediated tumor lysis for multiple different tumor associated antigens



TNB-Bispecific Molecules on Track for IND Throught 2021



TNB-383B Phase 1 initiated Q2 2019, Multiple Myeloma
Stable Cell Line Yield: 4.7 g/L

TNB-486, IND in July 2020, Lymphoma
Stable Cell Line Yield: 4.5 g/L

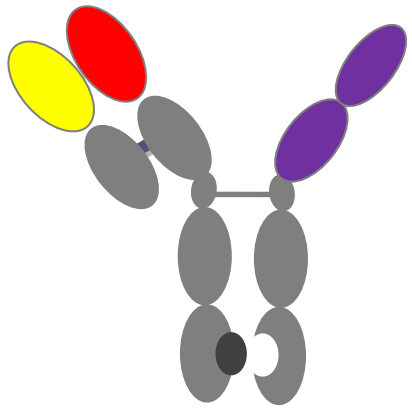
TNB-585, IND in November 2020, Prostate cancer
Stable Cell Line Yield: 7.6 g/L

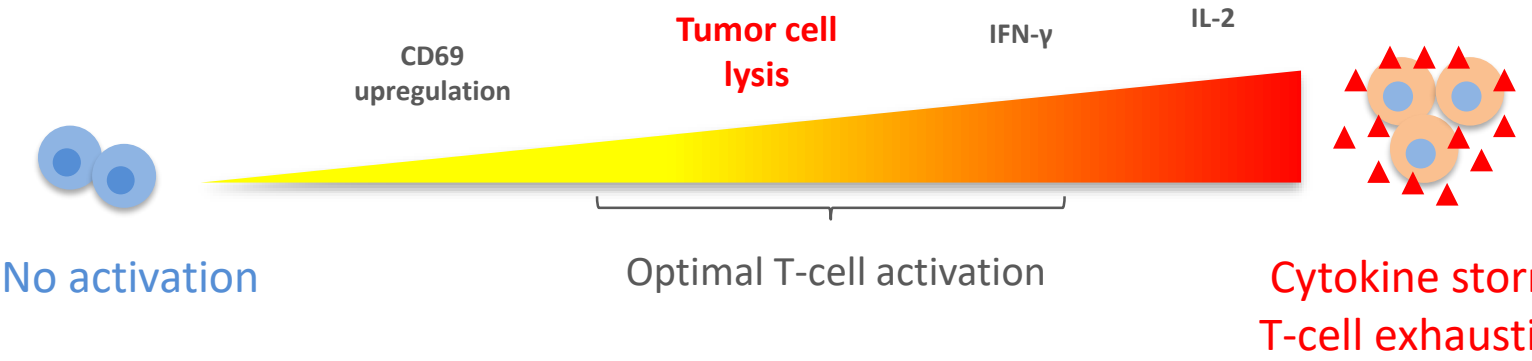
TNB-###, IND in Q3 2021, Ovarian cancer

Grant Supported

Teneobio T-cell Engager Platform

- **Novel proprietary fully human anti-CD3 antibodies**
  - Novel epitope, large range of affinities
- **One-of-a-Kind, Plug-and-Play, Stable Protein Chemistry**
- **Unique MOA**
  - Retained Anti-Tumor Efficacy
  - Improved Safety: Dramatically Reduced Cytokine Secretion
  - Reduced Treg stimulation, Reduced Exhaustion
- **Low immunogenicity**
- **Long half-life**
- **High affinity/avidity TAA binding**





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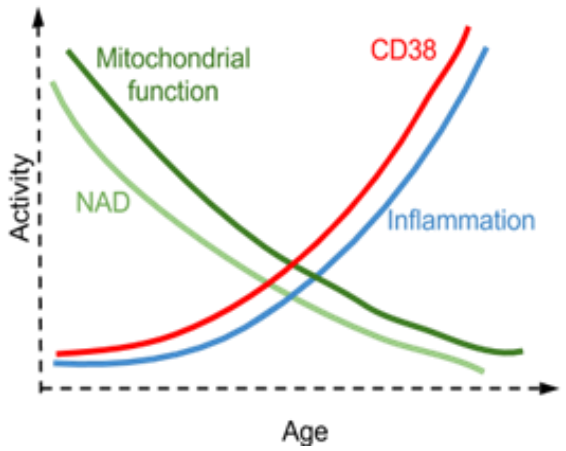
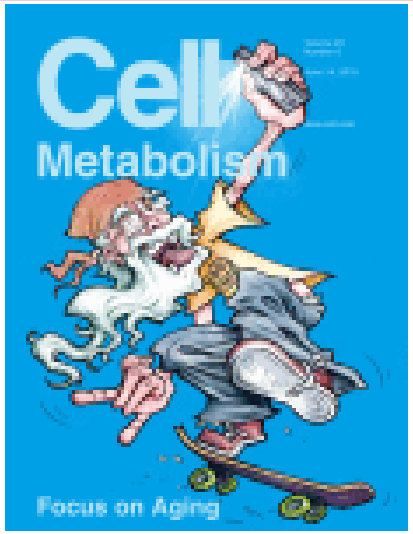
Teneobio's CD38 Enzyme Inhibitor

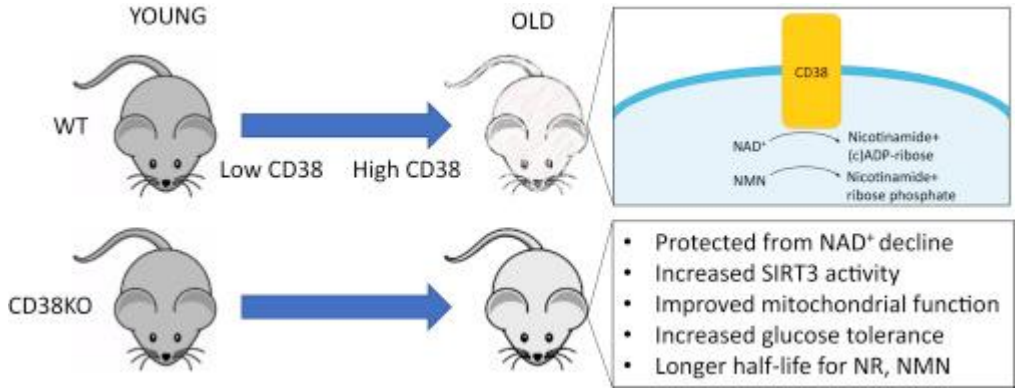
Cutting Edge Autoimmunity Therapy via Metabolic Regulation

CD38 Dictates Age-Related NAD Decline





[CD38 Dictates Age-Related NAD Decline and Mitochondrial Dysfunction through an SIRT3-Dependent Mechanism.](#) Camacho-Pereira J, Tarragó MG, Chini CC, Nin V, Escande C, Warner GM, Puranik AS, Schoon RA, Reid JM, Galina A, Chini EN. Cell Metab. 2016 Jun 14;23(6):1127-39.



Why NAD(+) Declines during Aging: It's Destroyed.
[Schultz MB](#), [Sinclair DA](#). [Cell Metab.](#) 2016 Jun 4;23(6):965-6.

21

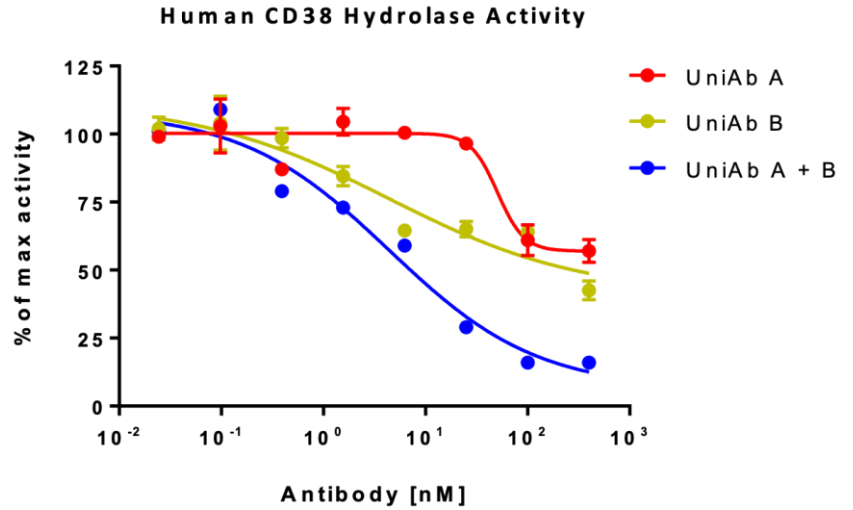
Potent Inhibition of hCD38 by Biepitopic UniAbs

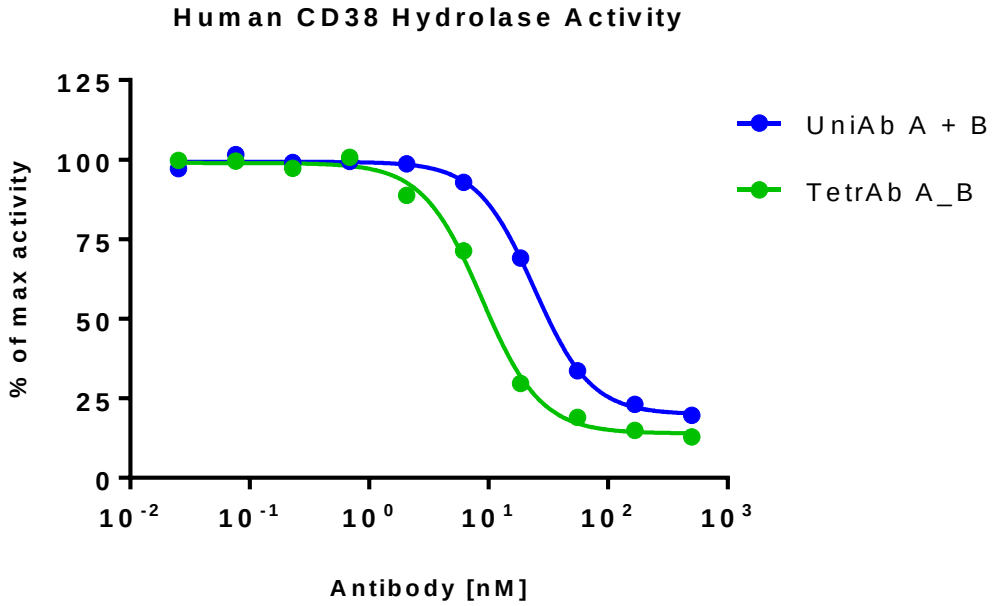
CD38_A
Competition group 3

CD38_B Competition group 1

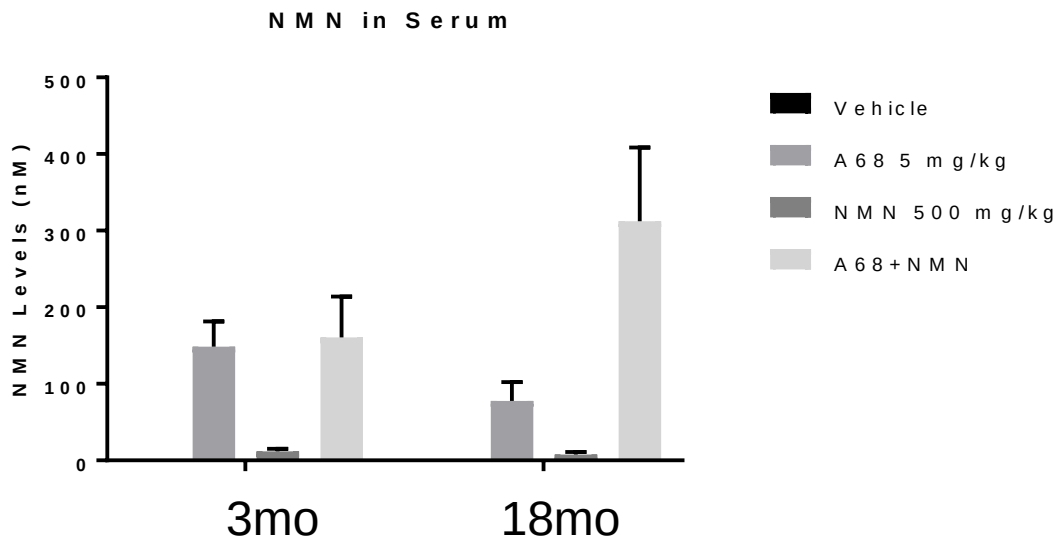
Synergy

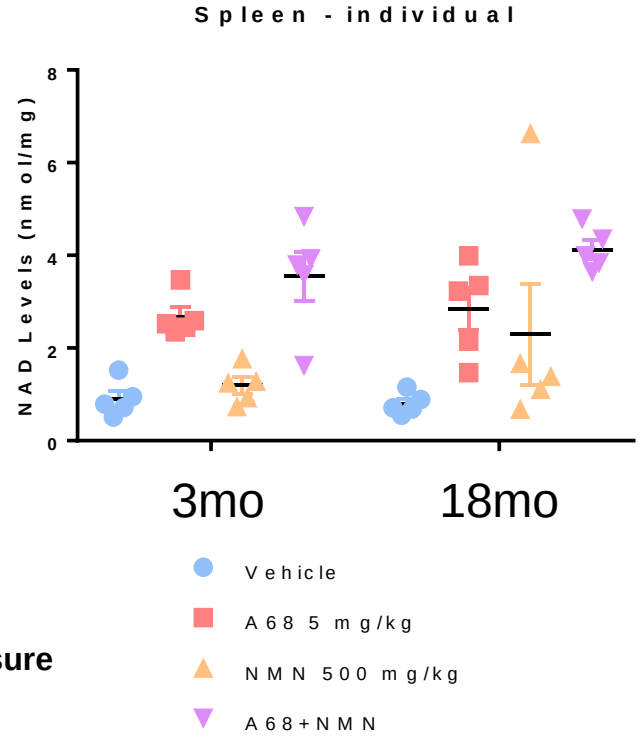
Tetravalent
CD38_A_B





CD38 Regulates NMN/NAD+ in Young and Old Mice





Day one
A68 injection
Ip, 5 mg/kg

Day three

- ✓ 0h - NMN Injection 500 mg/kg
- ✓ 6h – Euthanasia and tissue collection

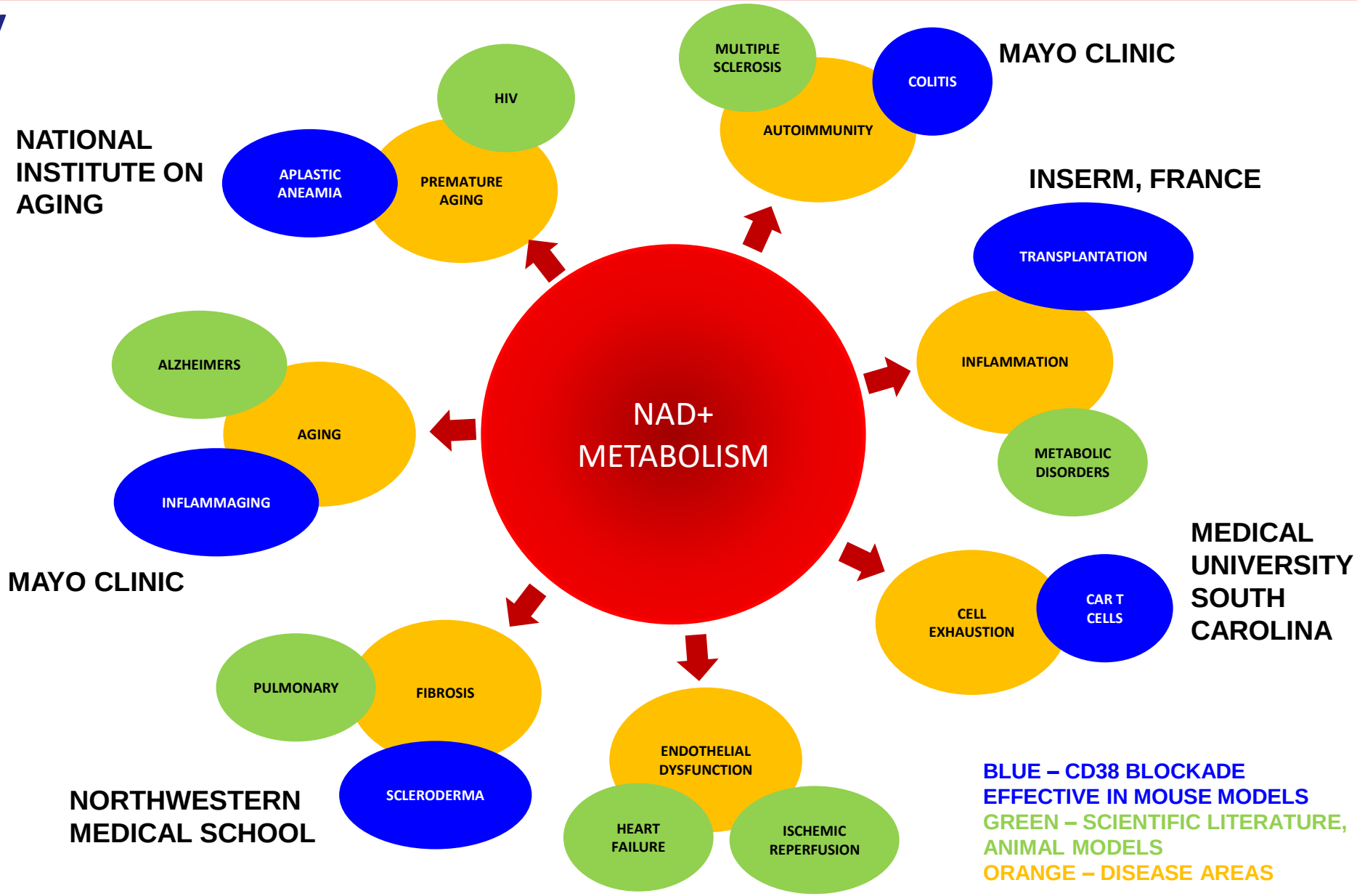
Groups
Young and Old
Control, A68, NMN, NMN+A68

Measure
NAD, NMN, NA

Tissues:

- Spleen
- Liver
- Mesenteric Fat
- Muscle (Gast)
- Inguinal Fat
- Jejuno
- Blood/Plasma

Teneobio's CD38 Inhibitor: Collaboration to Solve Complex Biology



Teneobio's CD38 Inhibitor: A Unique Modulator of NAD+

- **TNB-738 Solves Critical Problems with Existing CD38i Therapies**
  - Existing Inhibitory Antibodies are Cytotoxic
  - Small Molecule Inhibitors Enter the CNS
  - NMN Supplementation Does Not Increase Tissue NAD+, and Increases NAD Degradation Products

- **TNB-738 is a Potent CD38 Inhibitor with Long Half-Life and Good Manufacturability**
  - Sustained Increases in Tissue NAD+
  - Stable Protein Chemistry
  - Robust Process for Manufacturing/Purification

- **Broad Collaboration with Metabolic Experts Enables Bench-to-Bedside Transition**
  - CD38 Inhibition Improves Diverse Disease States
  - Independent Validation of MOA
  - Provides Foundation for Clinical Development with IND in 2021.

Teneobio's Anti-Polyoma Virus Therapy

Novel Domain Antibody Strings to Reach Immune-Priviledged Sites

Antibodies to Treat BK/JC Viral Diseases

Polyomaviruses Threaten Immune Compromised Patients

- **BK Nephropathy:** 5-10% of Kidney Transplants, incl. graft loss

  Peak Sales Projection = ~$200M/Year
- **Progressive Multifocal Leukoencephalopathy (PML):** up to 5% of HIV pts, 30-50% mortality

  Peak Sales Projection = $550M/Year
- **Hemorrhagic Cystitis:** Rare complication of marrow transplant, 2-4% mortality
- **Interstitial Cystitis:** Correlative association with BK. US prevalence ~1,000,000. significant morbidity.

  Peak Sales Projection = $250M+/Year

No effective treatment for any BK/JC viral disease!

Antibodies are a Promising Therapeutic Approach

- **Novartis:** huMAb (MAU 868) against BK virus to treat BK nephropathy; entered Phase 1.
- **Neurimmune:** huMAb against JC virus to treat PML
- High dose IVIg has shown limited efficacy
- ***Conventional antibodies cannot enter the urinary space where polyomaviruses replicate.***

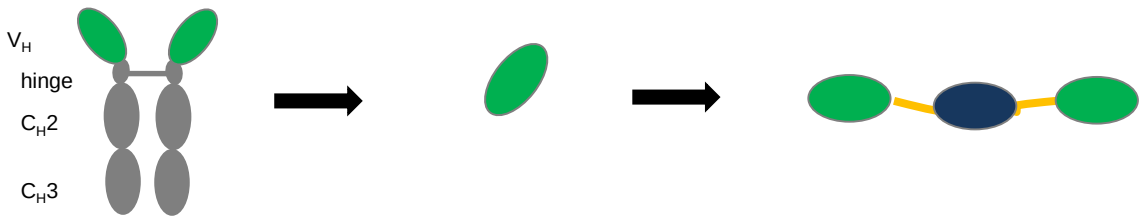
Antibodies to Treat BK/JC Viral Diseases

Slowly Mutating Viruses

- Limited Escape from Antibody Therapy

Replicate in the Urinary Space

- Inaccessible to Conventional Antibodies
- Domain Antibodies (UniDAbs) and 2-4 UniDAb ‘strings’ are freely filtered into the Urine

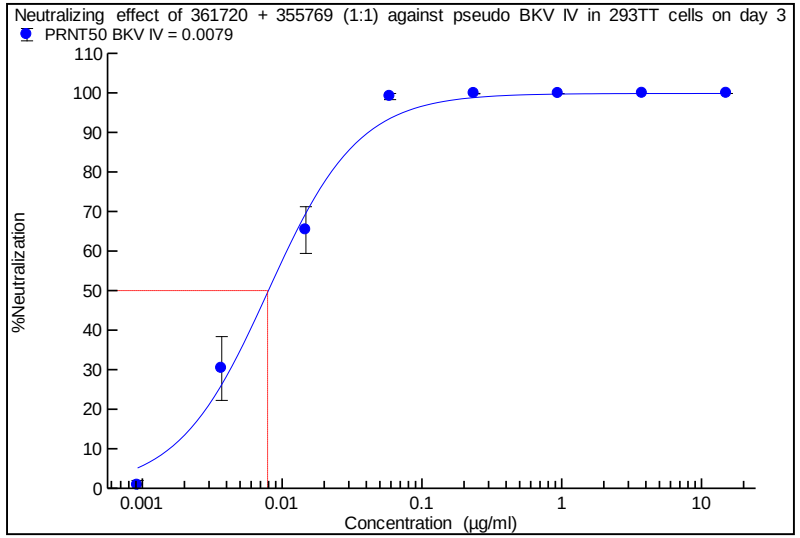


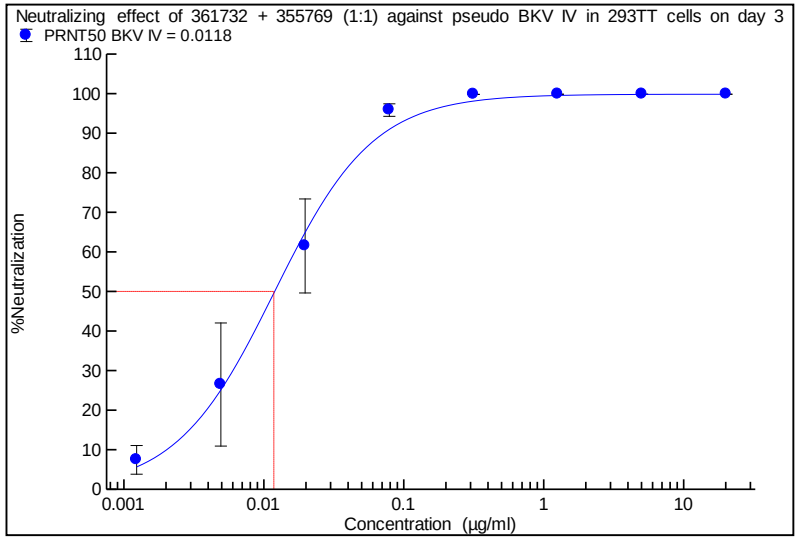
Multiple Serotypes Necessitate a Broadly Neutralizing Approach

- Teneoseek Enables Identification of Broadly Neutralizing Antibodies
- *UniDAb Strings can Combine Multiple Specificities in a Single Molecule*

Teneobio's Anti-Polyoma UniAbs

- **2 Broadly Neutralizing UniAb families**
- **<100 pM IC50 against ALL tested PYV strains**
  - BK I
  - BK IV
  - JCV WT
  - JCV S293F (PML-inducing mutant)
- **Good Developability**
  - Well expressed
  - Tm/Tagg
  - Stable at 37ºC for 1 mo.
- **Domain UniAb strings in development**





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Anti-BK/JC UniAbs and Domain UniAb Strings: Summary

- **Validated Scientific Rationale**
  - Multiple huMAbs in development to treat Polyomaviral diseases

- **UniAbs are Uniquely Suited to Combat BK/JC-Mediated Diseases**
  - Broad Neutralization: <100 pM IC50 for all tested BK/JC strains
  - Multivalency: Expect tetravalent IC50 ~10-100X stronger than bivalent (~5pM-500fM IC50)
  - Small Size: UniDAb strings can enter the urine
  - Excellent Manufacturability: Grams/L yields anticipated
  - Customizable Half-Life: HSA- or Ig-binding
  - Absence of framework regions: No STRATIFY cross-reactivity

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The Crucible: Grant Writing as a Means towards Better Science

- **Grant Proposal ≈ Detailed TCP**
  - Feasibility
  - Timelines
  - Cost/FTE
  - Gap Analysis: Where do You Need Help?

- **Grants as a Catalyst for Collaboration**
  - Funding to Support Collaborators
  - Scientific Credibility

- **Review Process Validates Approach**

Lessons From Teneobio's Non-Dilutive Funding Strategy

- **Diversification is Important → Use Grants to Expand Your Pipeline (Especially Early Pipeline)**
  - Oncology: T-Cell Engagement, T-Cell Co-Stimulation
  - Autoimmunity: CD38 Enzyme Inhibition
  - Infectious Disease: Polyomavirus, Hepatitis B Virus

- **Teneo's T-Cell Engagers → Play to Your Strengths, Find Problems Suited to Your Innovations**

- **CD38 Enzyme Inhibition → Grants Enable, and Thrive on, Collaboration**
  - Academic Researchers
  - Service Providers
  - Biotech
  - Physicians

- **Anti-Polyoma Domain Antibody Strings → Use Grants to Try the Crazy Stuff You've Always Wanted to Try!**
  - Grant Writing/Execution as a Crucible