

Benchmarking discovery-stage antibodies from OmniChicken[®] against clinical-stage antibodies from other sources

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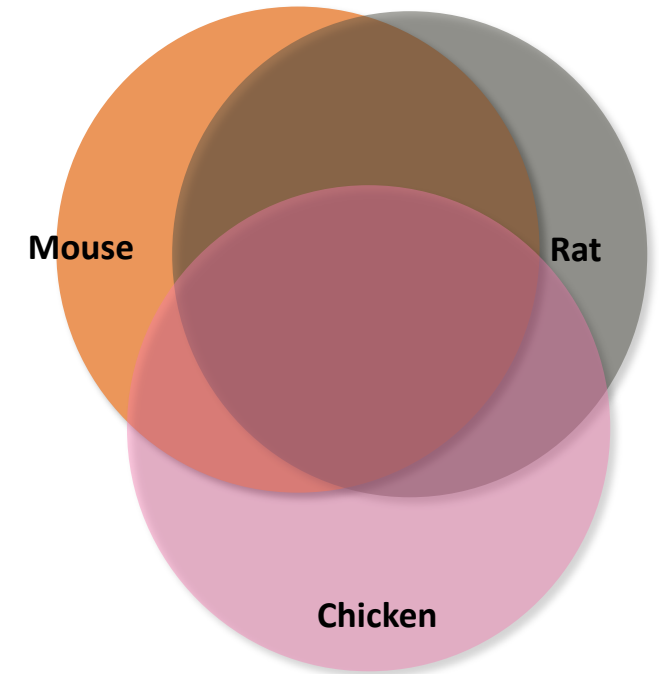
Sept. 2019

Ligand[®]

Best-In-Class Antibody Discovery Technology

- Human Ig-transgenic animals leveraged across 3 species
 - OmniRat®, OmniMouse®, OmniChicken®
 - OmniFlic® (rat) and OmniClic™ (chicken) for bispecific applications
- Each platform with optimized human V genes
 - 100% VH and >70% VL human germline diversity for rodents
 - Selected single framework for chicken
- Each platform with diverse genetic background
 - Mixed genetic backgrounds for rodents
 - Outbred chickens (diverse MHC)
- *In vivo* platforms that deliver excellent specificity, affinity, and developability
- Well validated technology
 - >150 active projects with >40 partners (large pharma and small biotech)
 - **10 programs in clinical trials (Phase 1 to Phase 3)**

Epitope coverage



Different species generate different epitope coverage

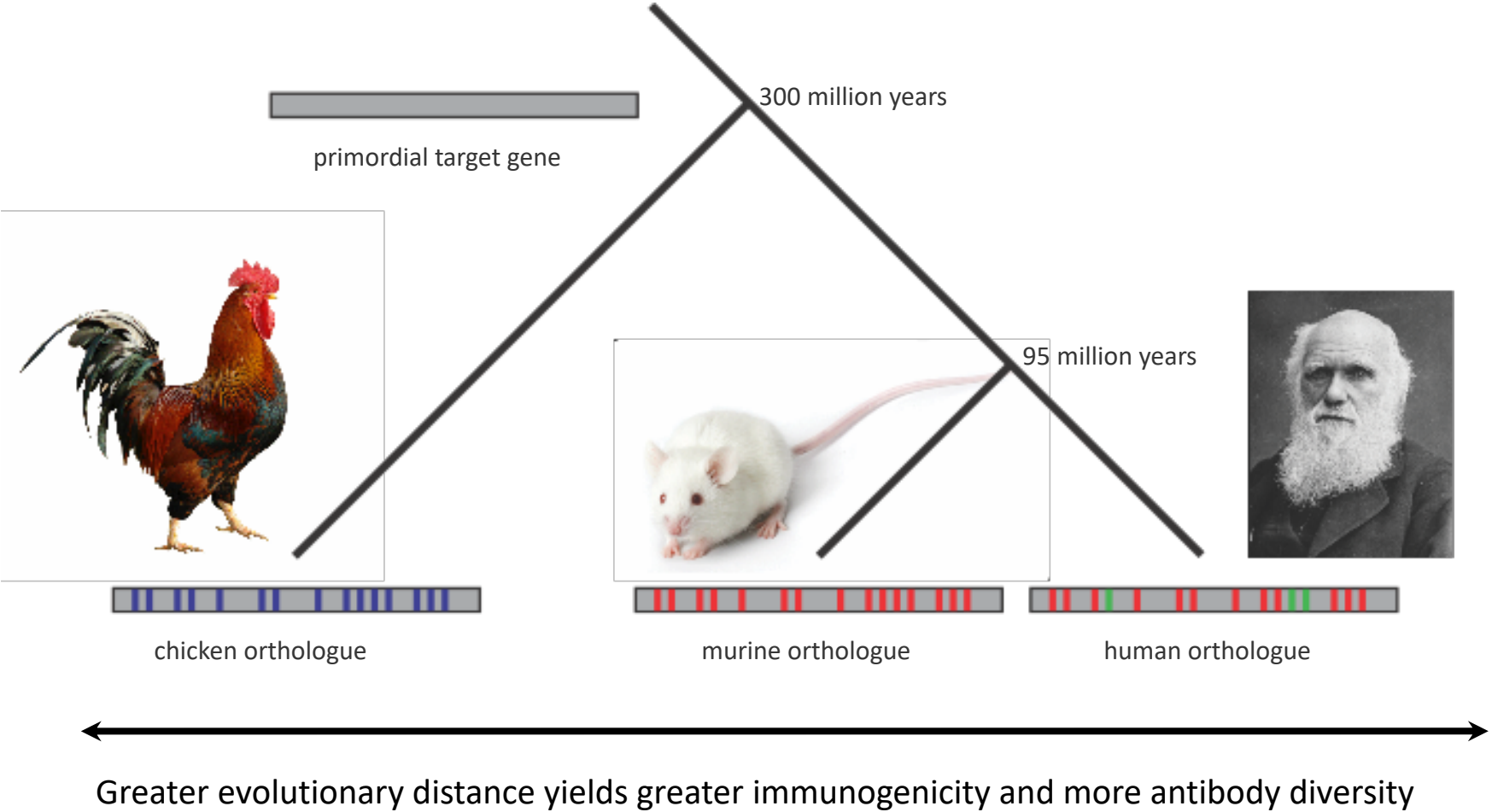
Five Platforms

Three Species

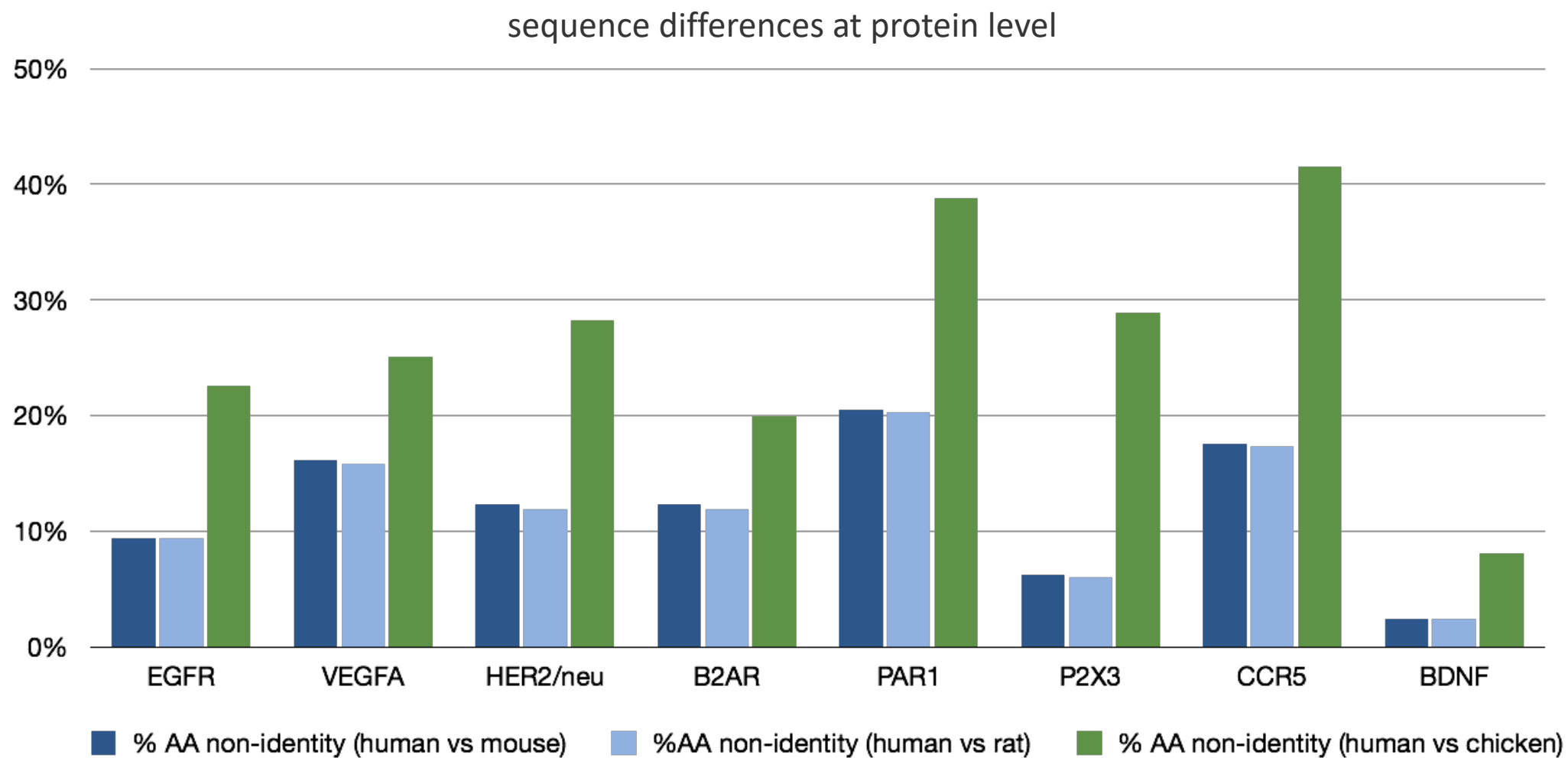


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Orthologue Comparison



Chicken orthologues are always more divergent from human than those from mammalian species

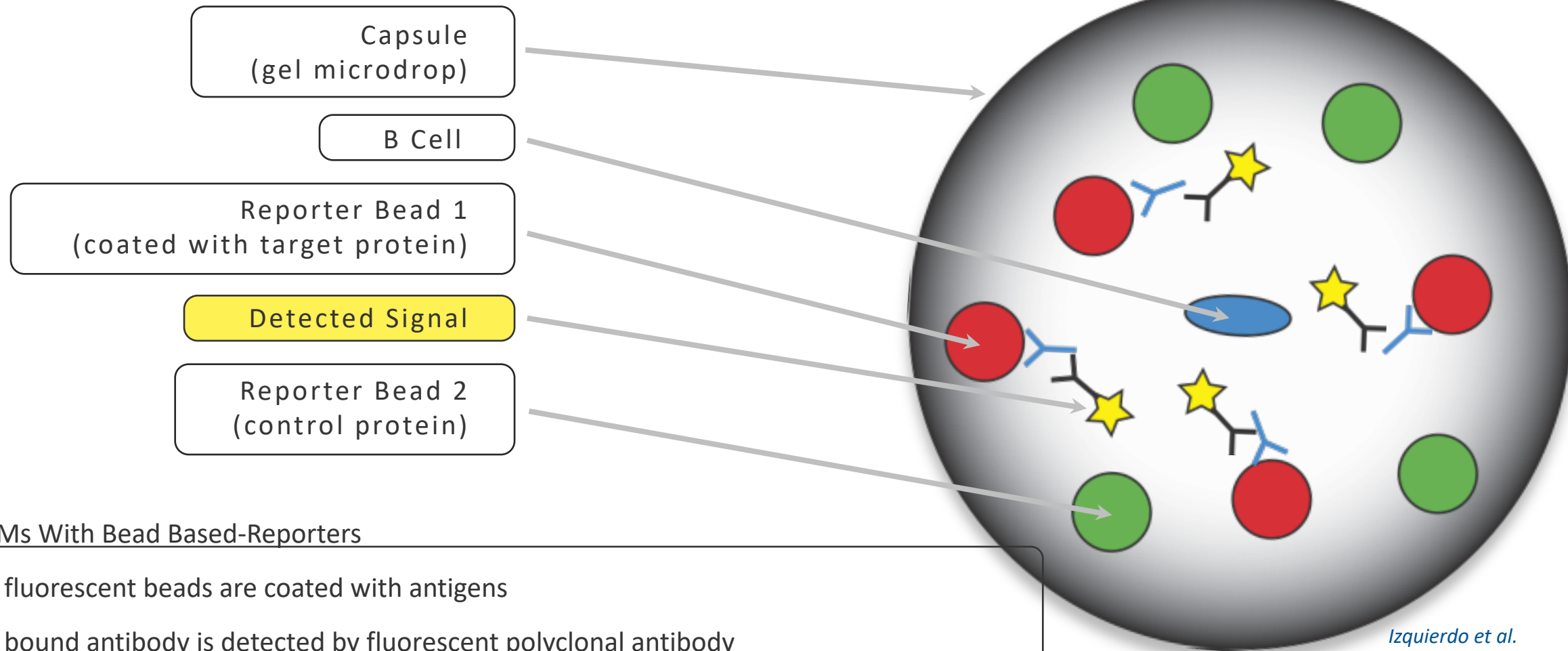
Recognition of Highly Conserved Targets by Chickens

Chickens have been used historically to generate antibodies to mammalian conserved targets – but only as polyclonals, not monoclonals

Antigen	Reference
RNA polymerase II - bovine	(Carroll and Stollar 1983)
β 2-microglobulin - human	(Horton, Holden et al. 1985)
Kallikrein - human	(Burger, Ramus et al. 1985)
IGF1-R & Insulin-R - human	(Stuart, Pietrzyk et al. 1988)
PCNA - bovine	(Gassmann, Thommes et al. 1990)
Activin A - human	(Murata, Saito et al. 1996)
Prion protein (PrP) peptide - bovine	(Matsushita, Horiuchi et al. 1998)
Mannose-6-P/IGFII-R - human	(Lemamy, Roger et al. 1999)
Hypoxia Inducible Factor-1 α - human	(Camenisch, Tini et al. 1999)
Melatonin receptor - human	(Williams, Drew et al. 2001)
Cystatin C - human	(Hansson, Flodin et al. 2008)

Screening for mAbs Using GEMs

Gel Encapsulated Microenvironments

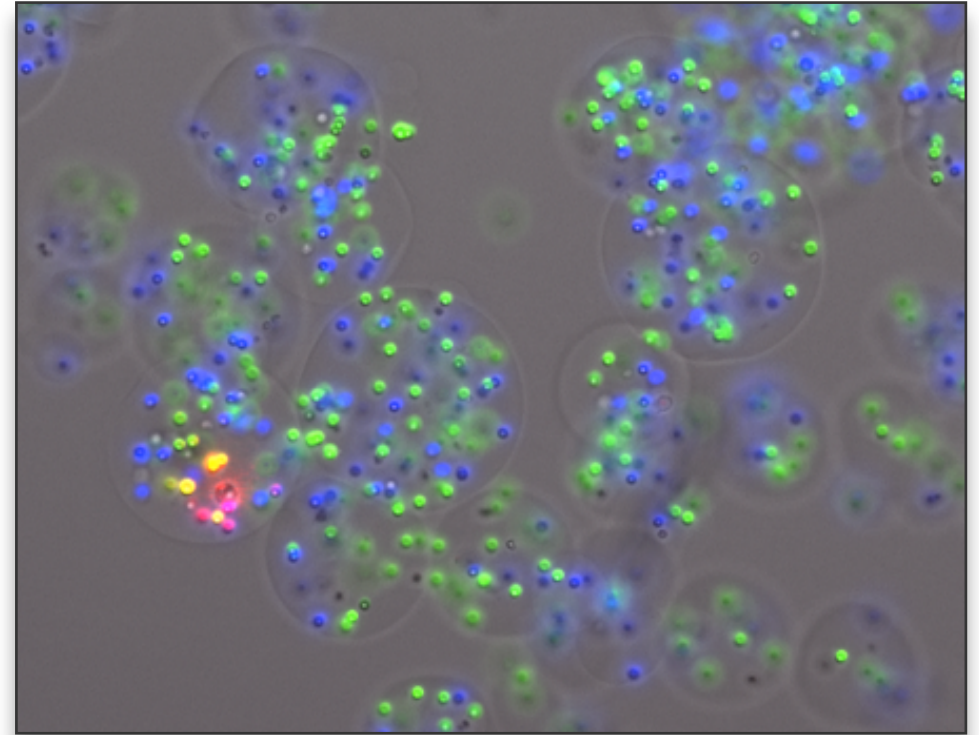
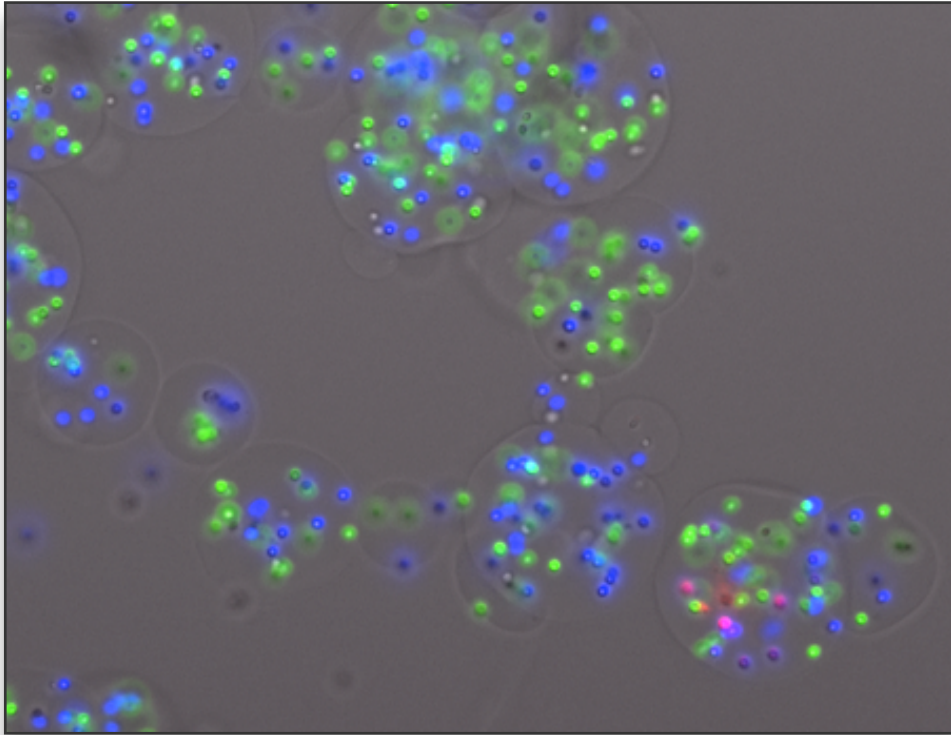


GEMs With Bead Based-Reporters

- fluorescent beads are coated with antigens
- bound antibody is detected by fluorescent polyclonal antibody
- antigen specificity is determined by colocalization of signal with alternative bead types

*Izquierdo et al.
Microscopy, 2016, 1-12*

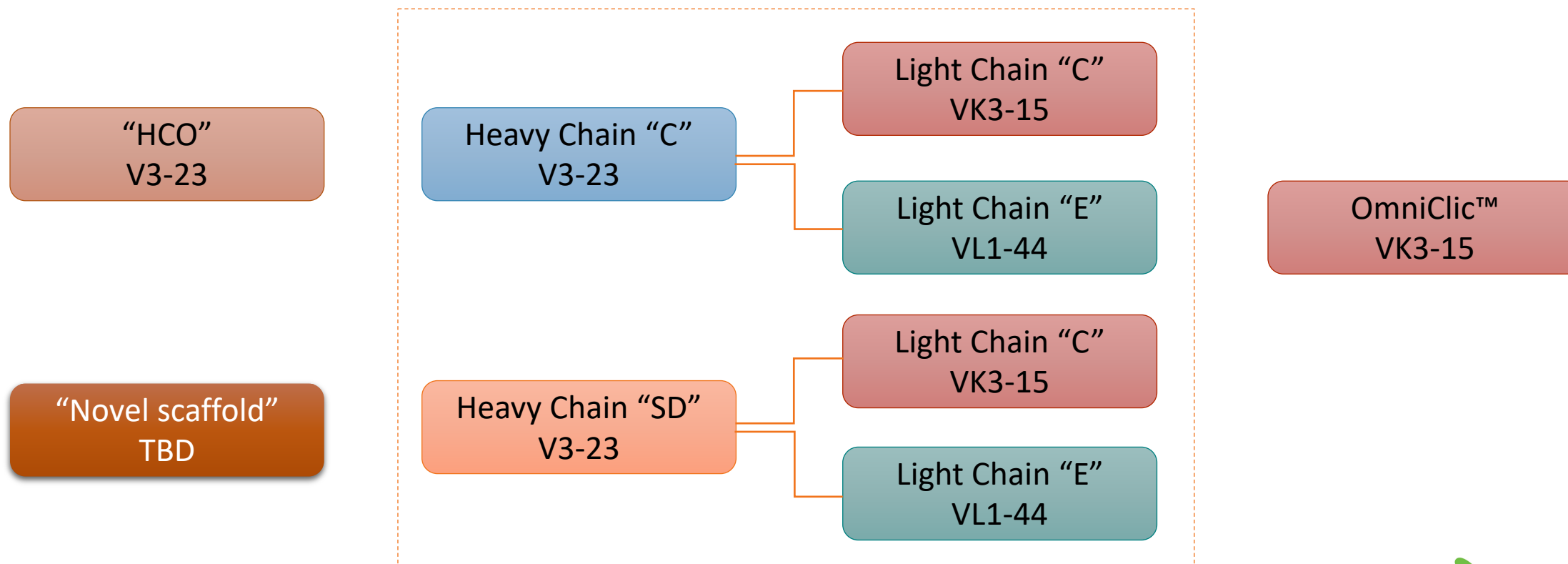
Dual Bead GEM Assay



GEMs can be used to determine specificity and cross-reactivity

- Red secondary antibody is applied
- If antigen on blue bead is bound, signal appears purple
- If antigen on green bead is bound, signal appears yellow

Current and Upcoming Tg chicken Platforms



In development:

Heavy Chain Only scaffold

Novel scaffold HC



Conventional HxL antibodies

Choice of heavy and light chain combinations



Common LC antibodies

For bispecific applications

Selected Targets – Clinical Activity

Target	% homology with human		Molecule in development (Sponsor)	Phase	Indications
	Mouse	Chicken			
B7-H3	93	64	Enoblituzumab (MGA271) (MacroGenics)	I	Melanoma, prostate, solid tumors, HNSCC, NSCLC, others
			MGD009 (B7H3xCD3 DART) (MacroGenics)	I	Melanoma, NSCLC, mesothelioma, urothelial cancer
			8H9 (Y-mAbs Therapeutics)	I	Neuroblastoma, solid tumors, gliomas, CNS malignancies
ICOS	69	29	JTX-2011 (Jounce Therapeutics) - Agonist	I/II	Solid tumors
			GSK3359609 (GSK) - Agonist	I	Solid tumors
			MEDI-570 (NCI) - Antagonist	I	NHL
TIGIT	56	0	OMP-31M32 (OncoMed)	I	Advanced cancers, metastatic cancers
			Atezolizumab/MTIG7192A (Roche/Genentech)	II	Locally advanced or metastatic tumors NSCLC
			BMS-986207 (BMS)	I/II	Advanced solid cancers
			MK-7684 (Merck &Co)	I	Advanced solid tumors
			AB154 (ARCUS)	I	Advanced solid tumors
TIM-3	55	0	MBG453 (Novartis)	I/II	Advanced malignancies
			SYM023 (Symphogen/Baxalta/Shire)	I	Advanced solid tumors or lymphomas
			LY3321367 (Lilly)	I	Advanced relapsed/refractory solid tumors
			TSR-022 (Tesar)	I	Advanced cancer/NSCLC,
			BGB-A425 (BeiGene)	I/II	Locally advanced or metastatic tumors
CD38	58	47	Darzalex (Genmab)	Approved	MM
			MORO3087 (Morphosys)	I/II	Relapsed/refractory MM
			Isatuximab (Sanofi)	III	MM, plasma cell myeloma, prostate cancer and NSCLC
			CAR2 Anti-CD38 A2 CAR-T Cells (Sorrento Therapeutics)	I	Relapsed/refractory MM
			CD38/BCMA CAR-T cells (Chinese PLA General Hospital)	I/II	MM
			GBR 1342 (CD38/CD3 bispecific) (Glenmark)	I	MM
			Multi specific gene-engineered T cells (Universities in China)	I/II	Relapsed/refractory AML

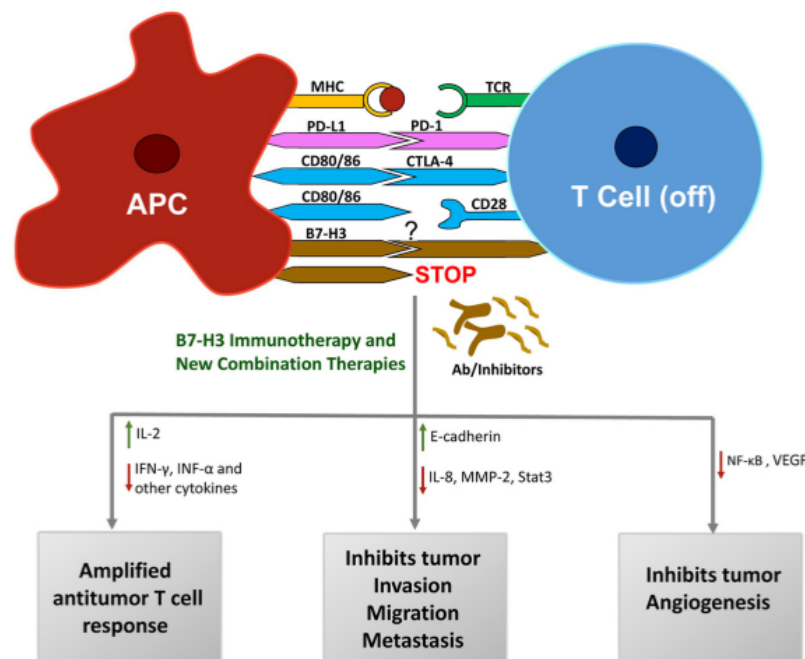


B7-H3

B7-H3

Inhibitor of T Cell Activation, Proliferation and Cytokine Production, Promoter of Cancer Cell Invasion

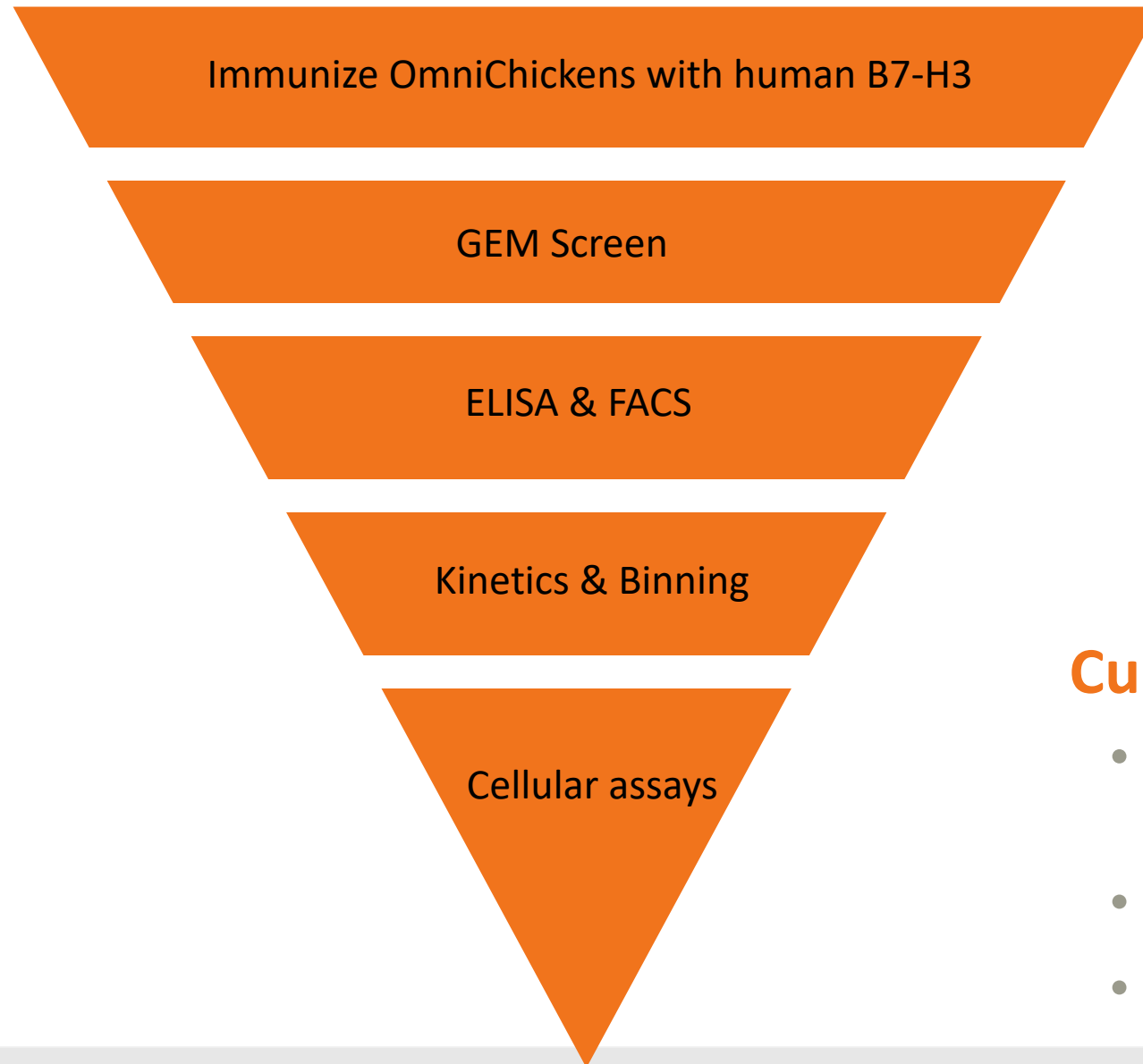
- Immune checkpoint member of B7 family, expressed on Antigen Presenting Cells
- Aberrantly expressed in wide variety of cancers (bladder, pancreatic, prostate, osteosarcoma, breast, cervical colorectal, ovarian, glioma, melanoma, gastric cancers etc.)
- Unknown receptor



Target Profile: Functional blocker

- Initial mAb panel obtained
- Murine & cyno cross-reactivity
- Advanced characterization in progress

B7-H3 Screening Cascade

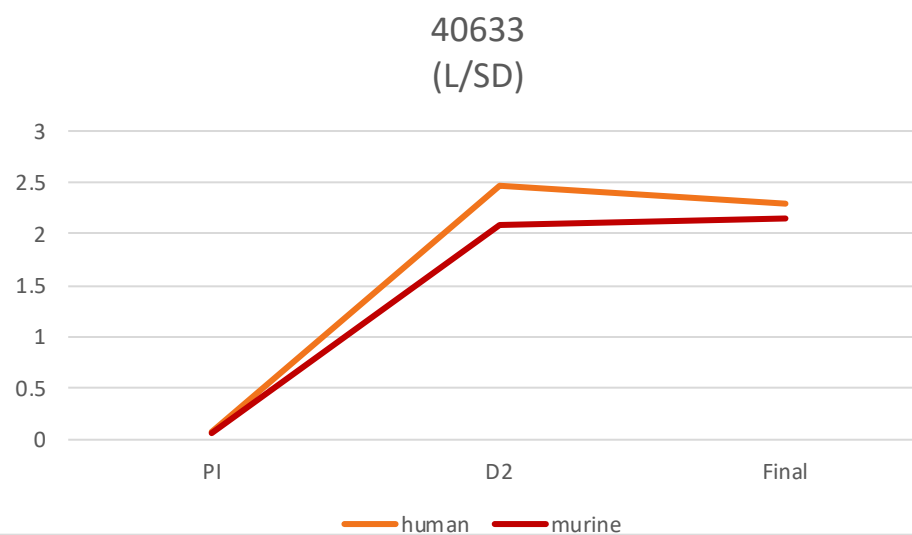
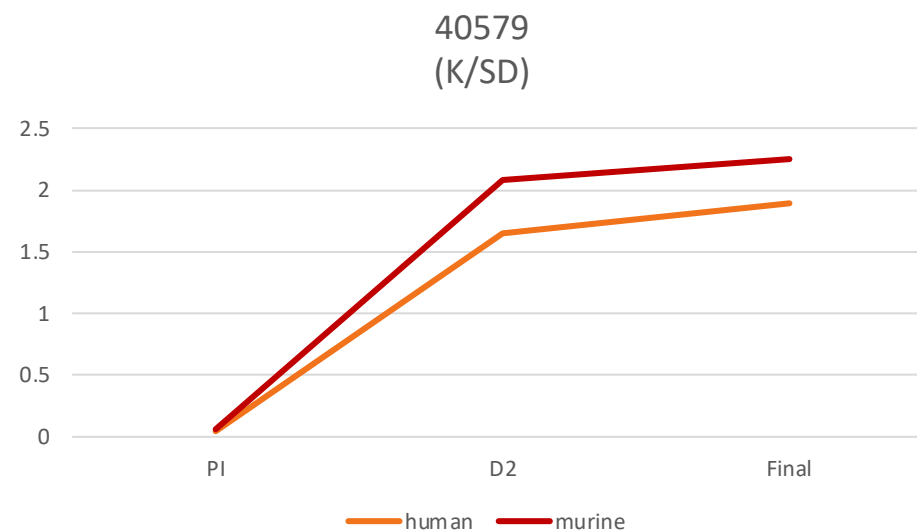
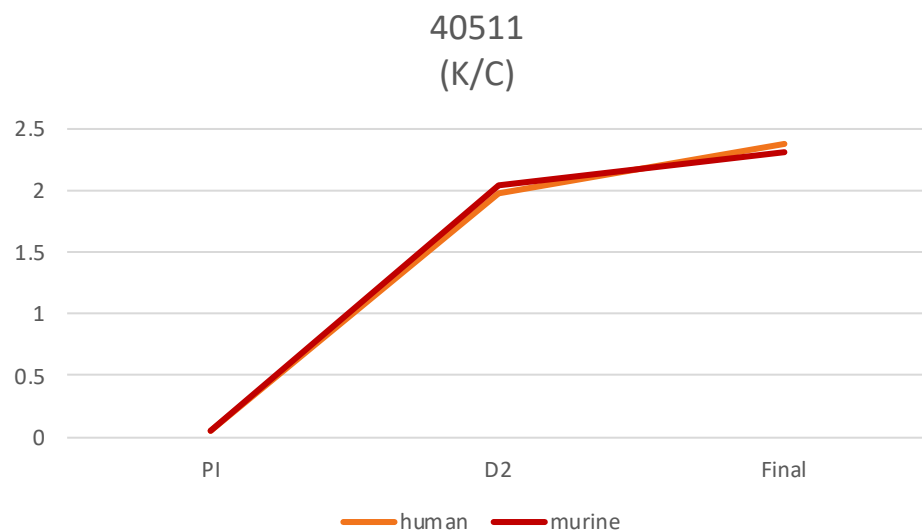


Current Panel

- 54 antibodies that bind B7-H3 expressed on cells
- 53 cross-react to cyno
- 52 cross-react to murine

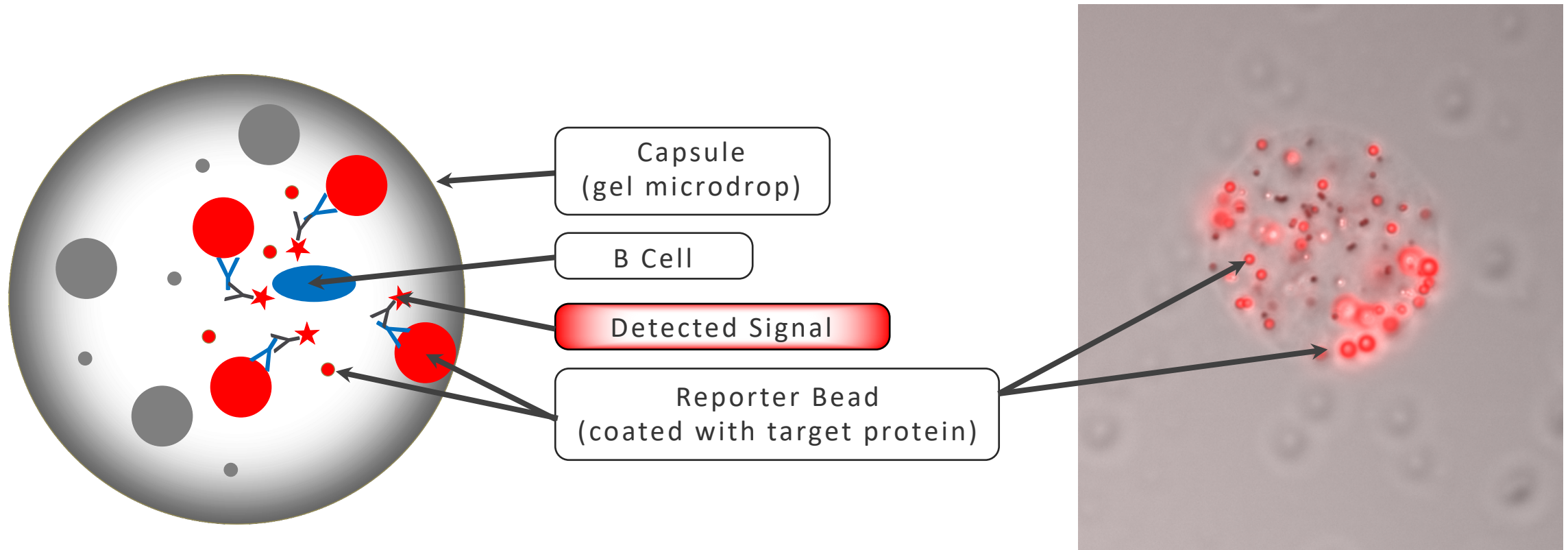
B7-H3 Serum Titers

Immunized with human B7-H3 only



GEM Screen for Species Cross-reactivity

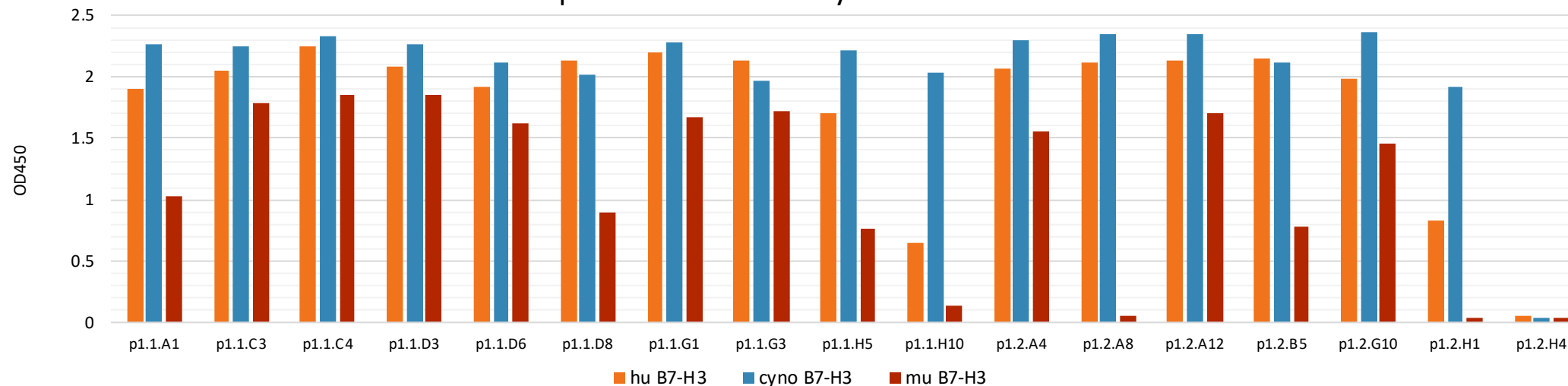
- GEM screens contained 2 beads
 - Large bead coated with human
 - Small bead coated with murine



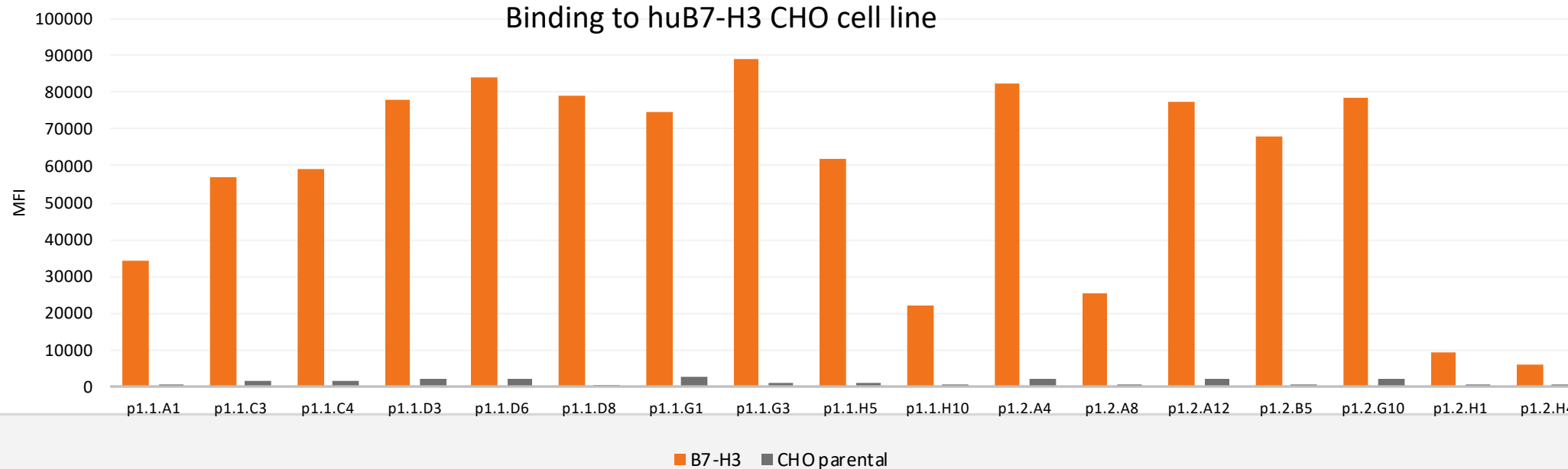
OmniChicken 40511

B7-H3 Elisa and cell binding

Species cross-reactivity ELISA

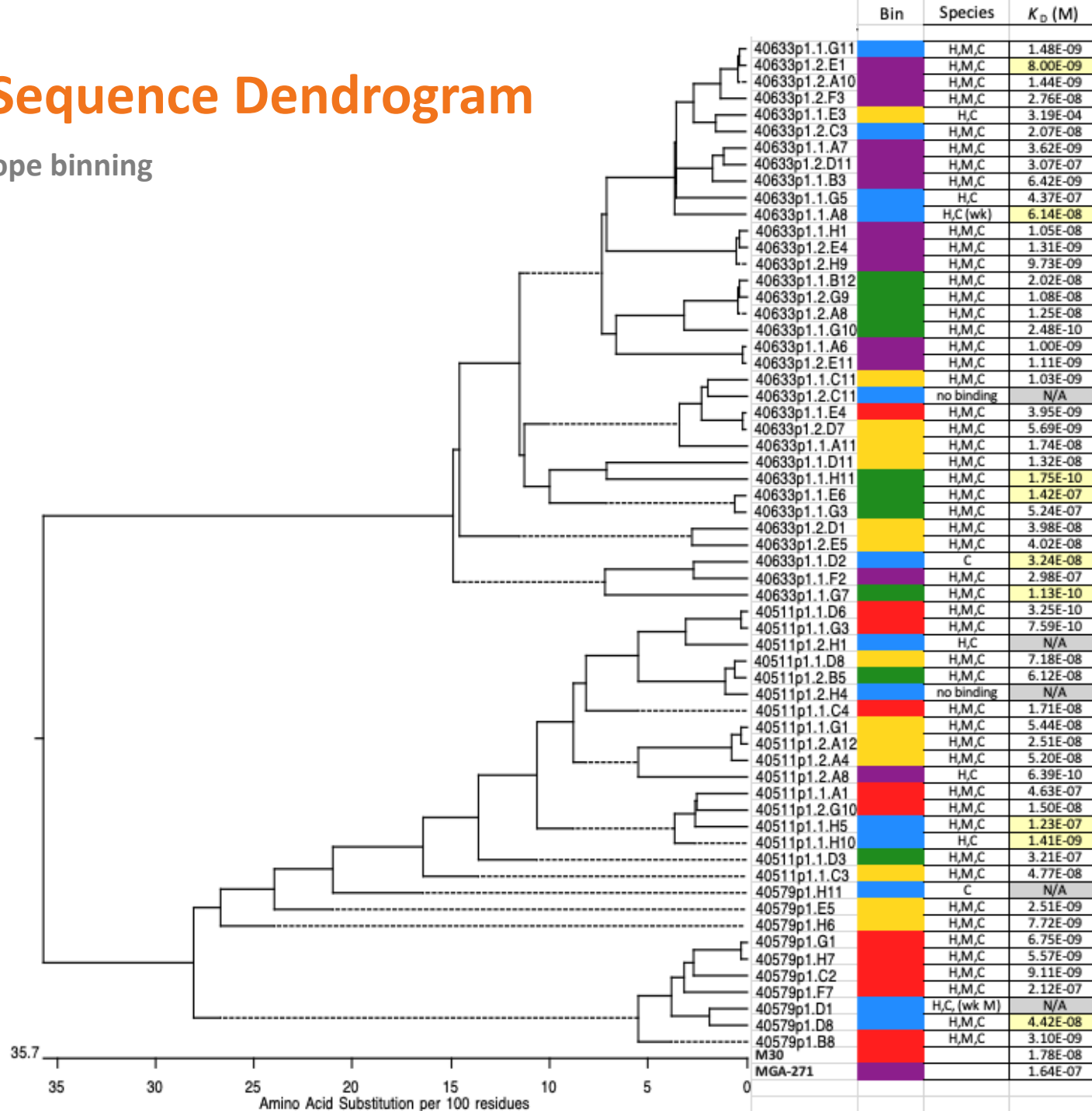


Binding to huB7-H3 CHO cell line



B7-H3 Ab Sequence Dendrogram

Kinetics and epitope binning

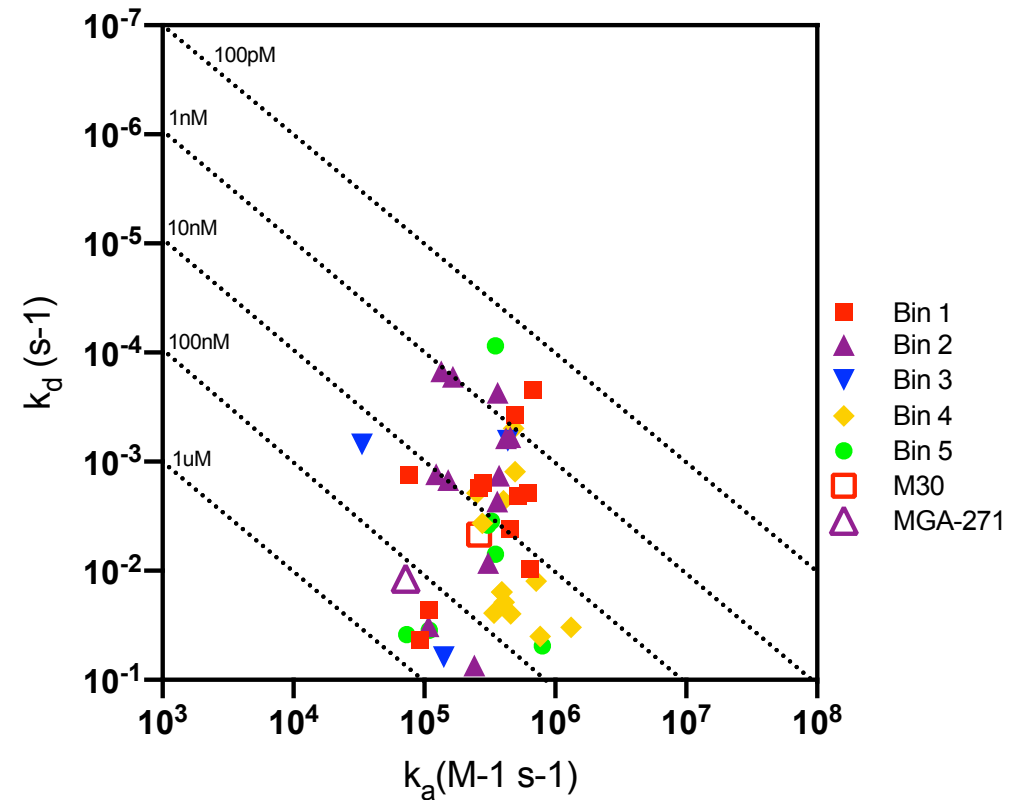


B7-H3

Epitope binning and kinetics results

OmniChicken derived mAbs cover epitopes represented by clinical grade antibodies

OmniChicken mAb cohorts contain clones with superior affinities



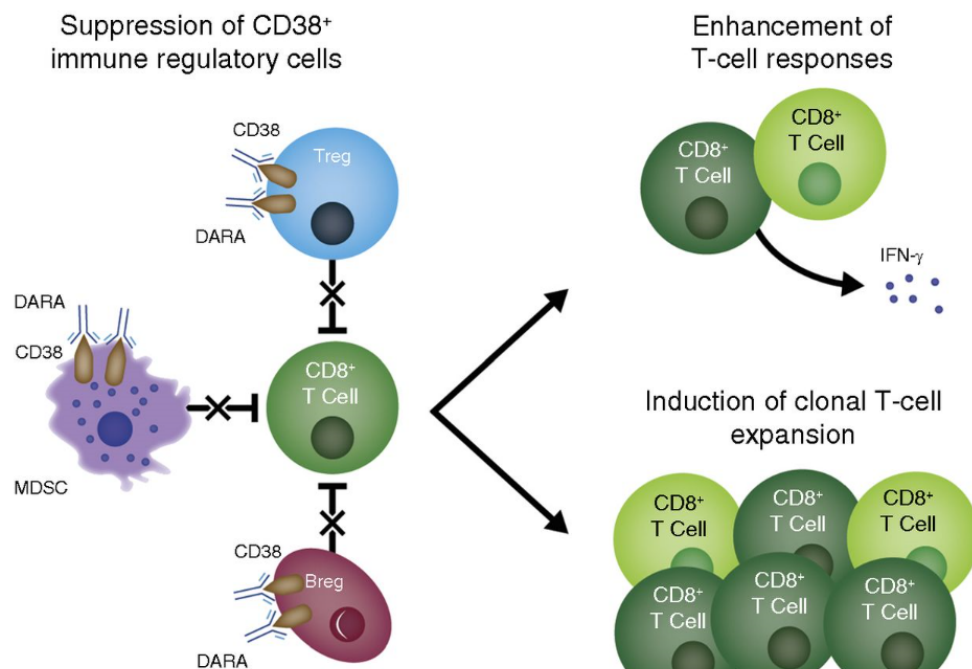


CD38

CD38

Inhibitor of Cytotoxic T Cell Activation and Proliferation, Inducer of Immature B Cell Differentiation

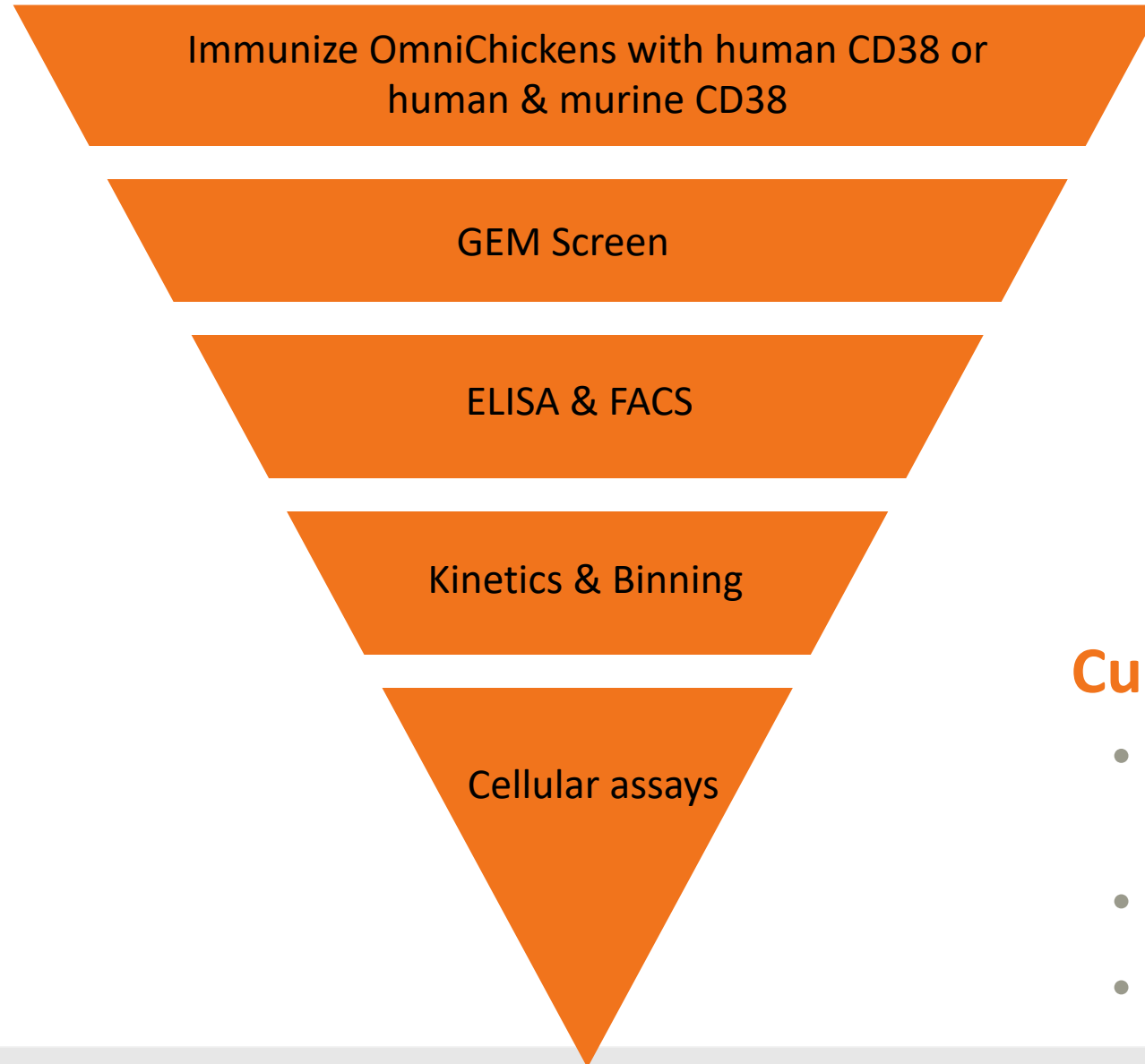
- Expressed on CD4+ and CD8+ T cells, B cells, NK cells
- Upregulated following PD1/PD-L1 blockade (resistance mechanism)
- Ectoenzyme that catalyzes the synthesis and hydrolysis of cADP-ribose from NAD⁺ to ADP-ribose



Target Profile: Antagonist

- Initial mAb panel obtained
- Murine & cyno cross-reactivity
- Advanced characterization in progress

CD38 Screening Cascade

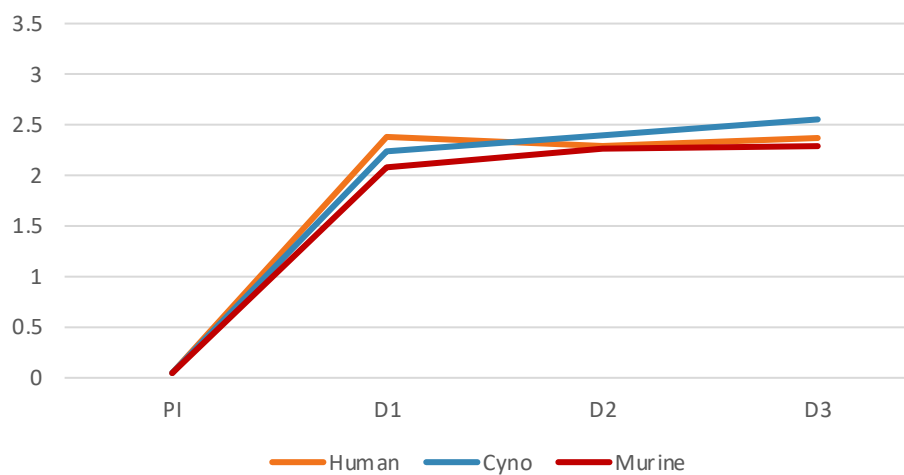
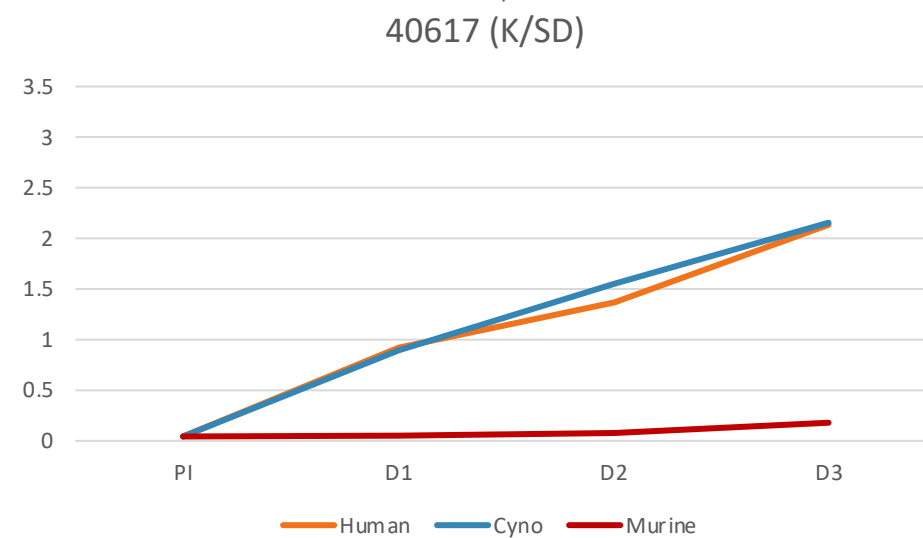
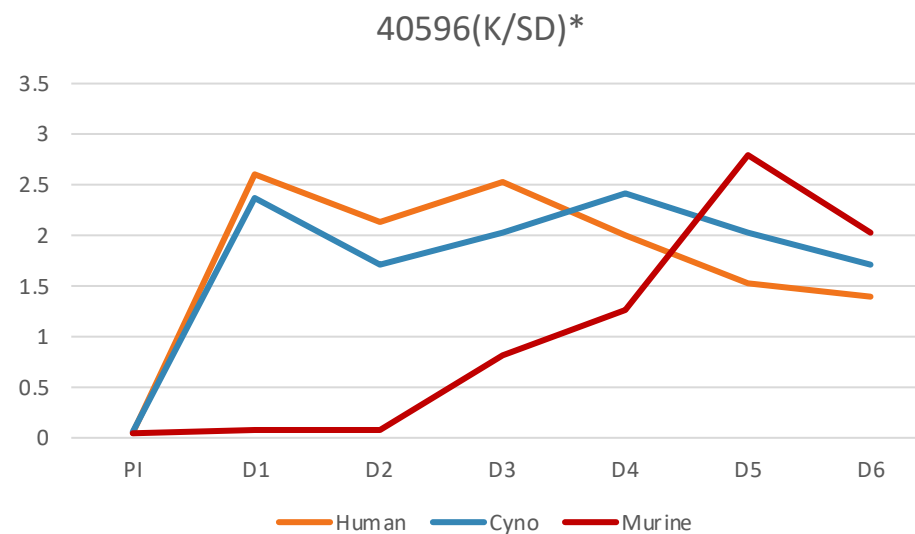
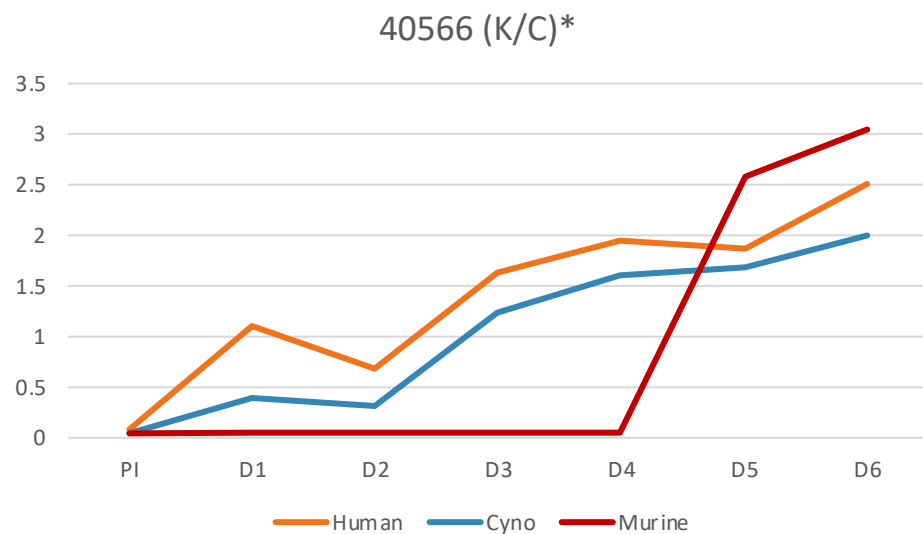


Current Panel

- 53 antibodies that bind CD38 expressed on cells
- 53 cross-react to cyno
- 35 cross-react to murine

CD38 Serum Titers

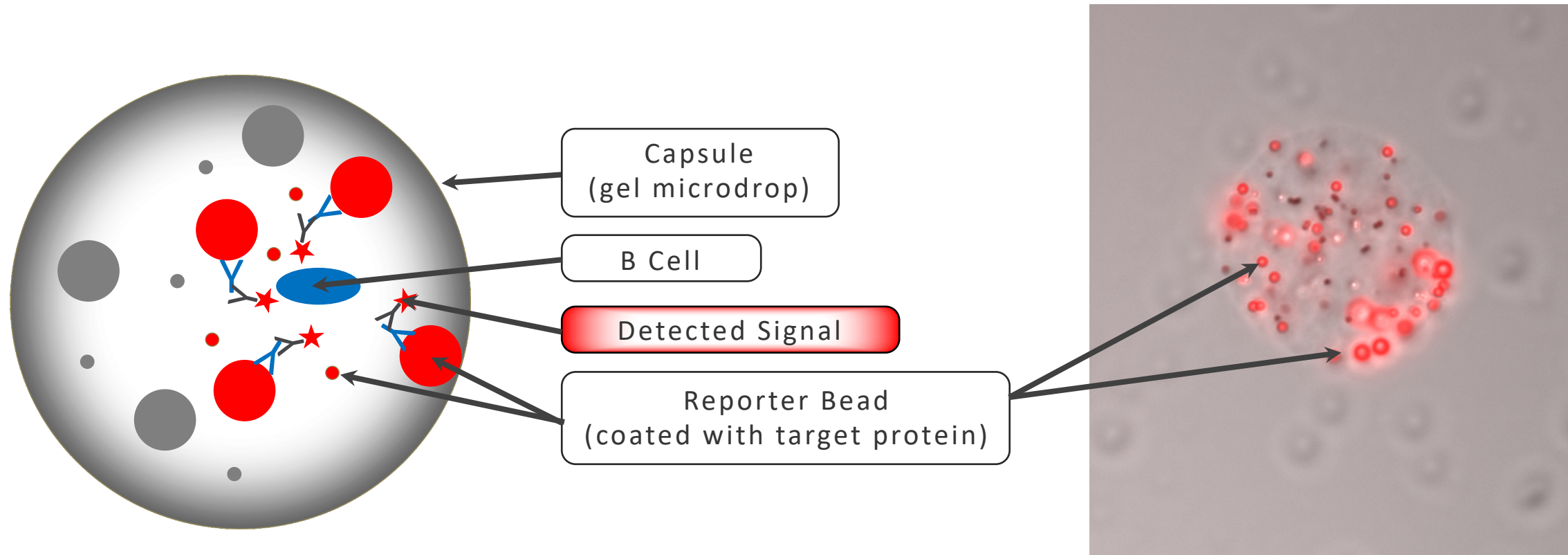
Human only and Human / Murine immunizations



* Human/Murine Immunization

GEM Screen for Species Cross-reactivity

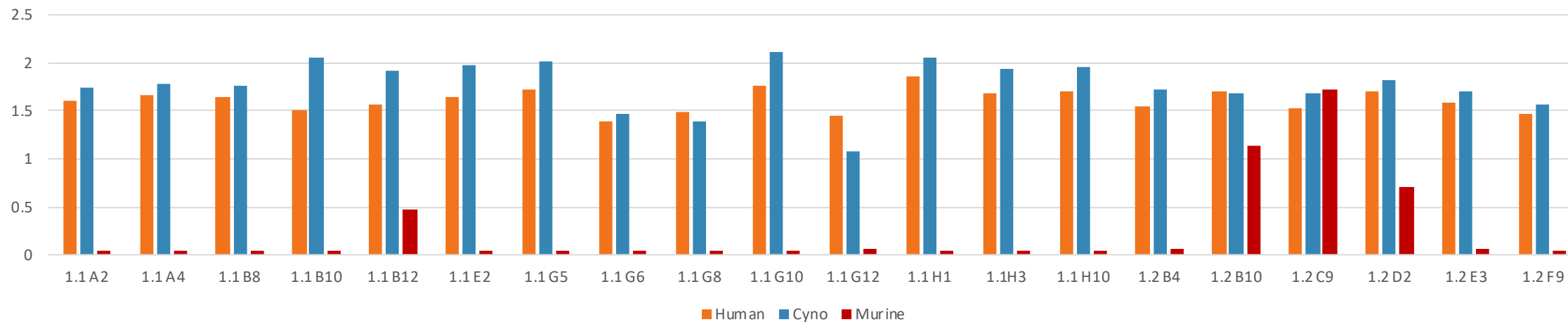
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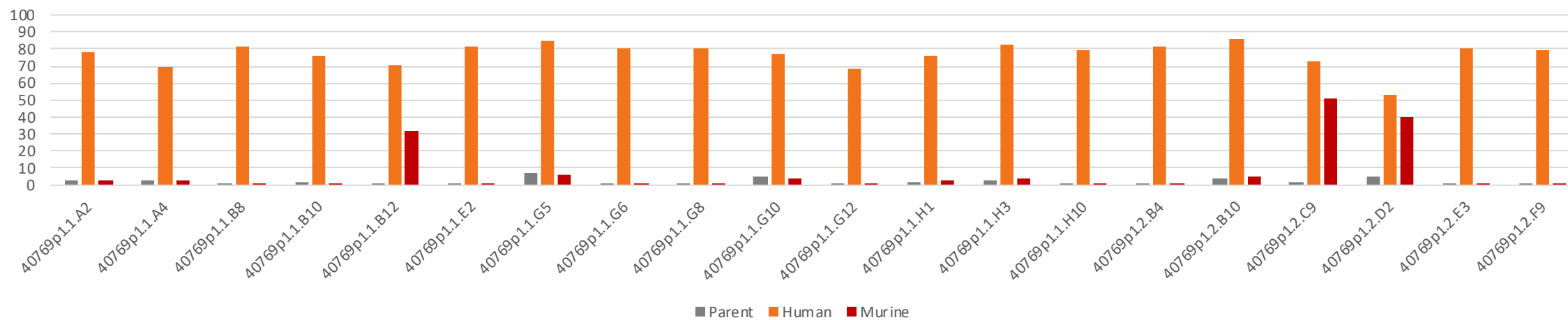
OmniChicken 40769

CD38 ELISA and cell binding

Species Cross-reactive ELISA



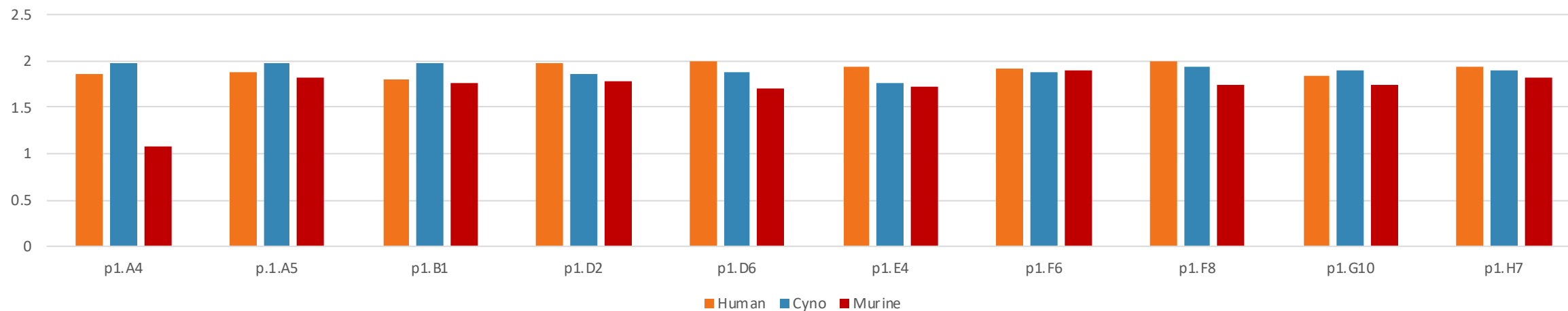
Binding to transiently transfected 293



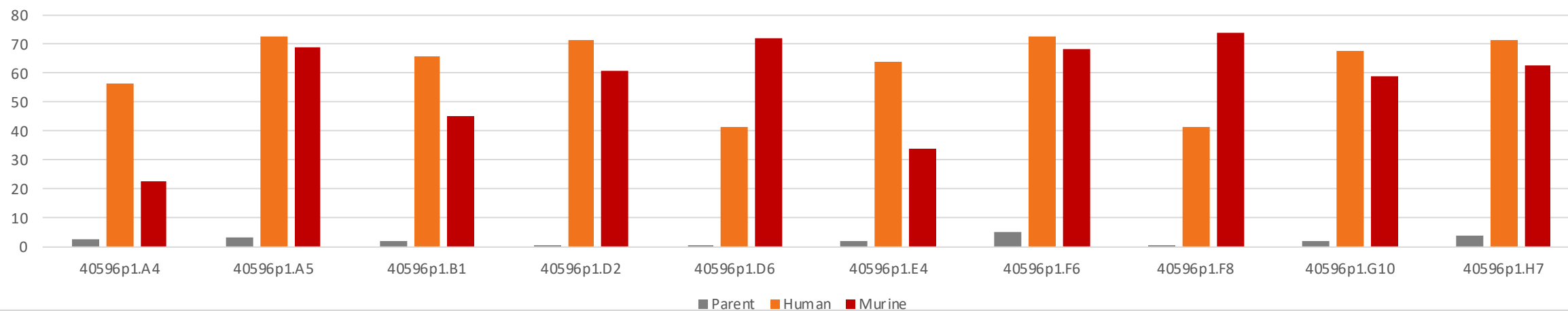
OmniChicken 40596*

CD38 ELISA and cell binding

Species Cross-reactive ELISA

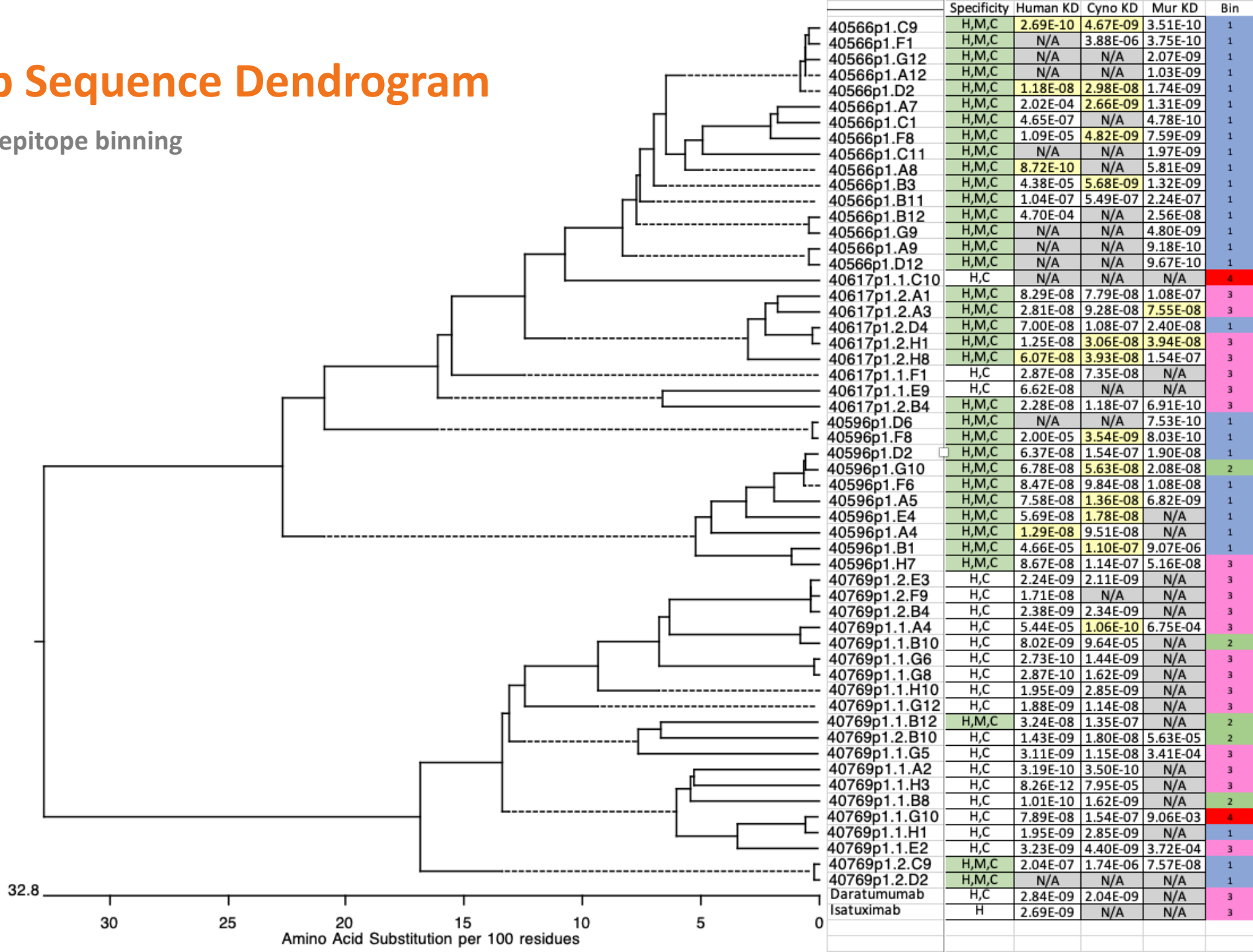


Binding to transiently transfected 293



CD38 Ab Sequence Dendrogram

Kinetics and epitope binning

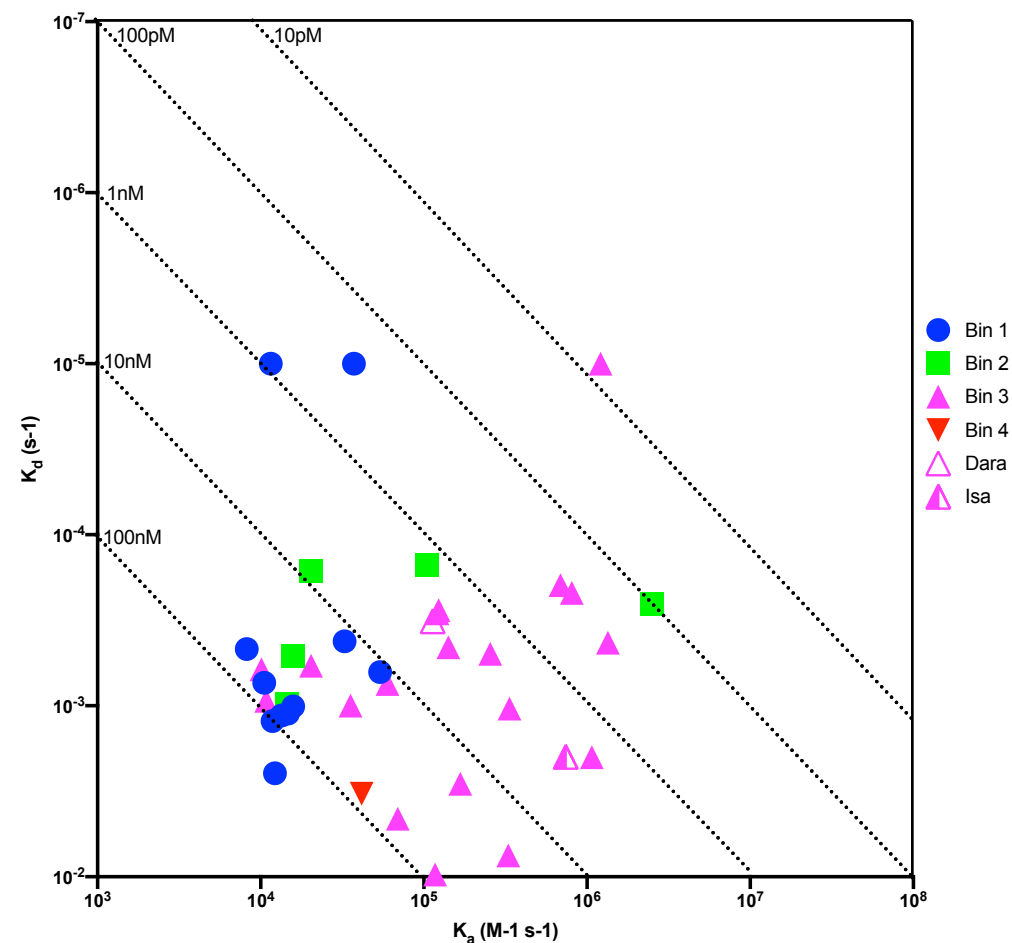


CD38

Epitope binning and kinetics results

OmniChicken derived mAbs cover epitopes represented by clinical grade antibodies

OmniChicken mAb cohorts contain clones with superior affinities



Summary of B7-H3 and CD38

- OmniChicken has demonstrated the ability to generate diverse antibody panels with broad epitope coverage and multi-species cross-reactivity.
- OmniChicken derived mAbs cover epitopes covered by clinical grade antibodies for both programs.
- OmniChicken derived mAbs contained clones with superior affinity when compared to clinical grade antibodies.
- Serval OmniChicken genotypes expand the OmniAb portfolio of antibody discovery platforms that are available to partners.



Discovery Package Content

Confidential data set for potential partners

- Antigen prep
- Genotypes used
- Immunization strategy
- Titer data
- GEM strategy
- Clone selection and initial characterization
 - ELISA
 - FACS
- Secondary characterization (Carterra)
- Benchmark antibody comparison
- Sequence dendrograms overlay with functional data
- Cellular assay data
- IP filing info

Acknowledgements

- Kristen Chan
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