Sep 20th, 12:00 PM

Pilot Project Funding Opportunities

Nathaniel Hafer
University of Massachusetts Medical School

Et al.

Pilot Project Funding Opportunities

September 20, 2012

Nate Hafer, PhD
Director of Operations
UMCCTS

Pilot & Collaborative Translational & Clinical Studies

Programs

- Pilot Project Program (PPP)
- Life Science Moment Fund (LSMF)
- Pfizer CTI Program
- Next Hundred Million Pilot Projects (NHMPP)

UMCCTS Pilot Grant Programs 2009-2012

1. **Life Sciences Moment Fund $1.9M**
2. **Pilot Project Program $2.4 M**
3. **WPI/UMMS Collaborative Pilot Project Program $600K**

Pilot Project Program

Specific Aims:

1. Stimulate the development of new clinical and translational inter- and multi-disciplinary teams
2. Provide novel support mechanisms for junior investigators
3. Increase the emphasis on pilot funding for community-based research
4. Develop new methodologies to leverage institutional strengths and new initiatives
5. Pursue high-risk, high reward studies
6. Support projects utilizing the unique core facilities at the medical school and throughout the University
7. Encourage collaboration across the five UMass campuses

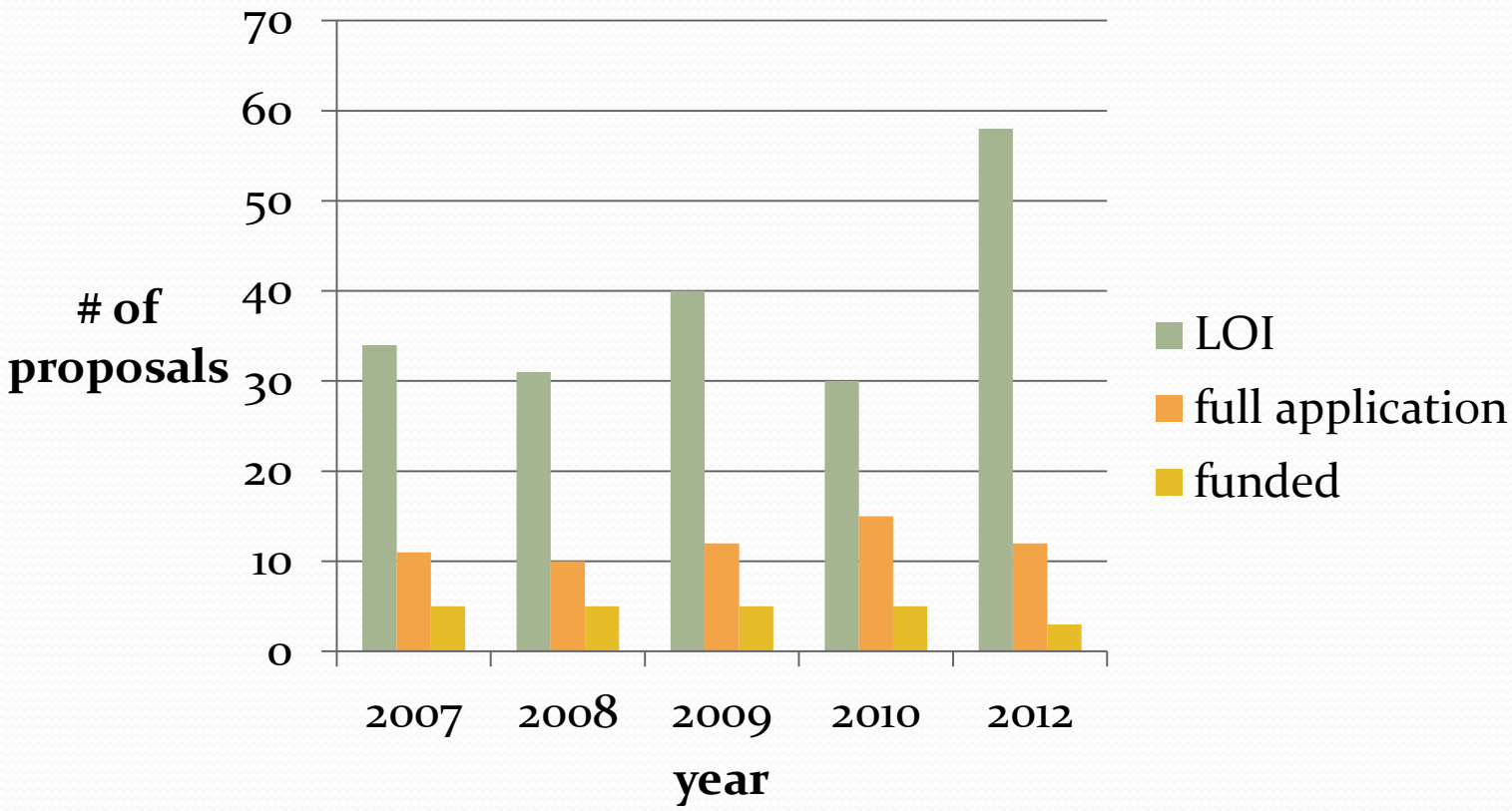
Pilot Project Program

Individual Proposals $100,000 max for 1year
$150,000 max for 2 years

Projects span the translational spectrum, T1 – T4+

<u>2 Stages</u>
Letter of Intent (2 pages)
Full Proposal (Abbreviated NIH-style 10 pages)

Pilot Project Program – success rate



2012 Pilot Program Project Recipients

UMMS Collaborator(s)/Dept	UMass Collaborator/Dept	Project Title
Hua (Julia) Fang, PhD Department of Quantitative Health Sciences	**DiFranza, Moormann, Ma, Kim, Houston, Barton, Allison, Ash**	A New Tool for Studying Heterogeneity of Treatment Effects in Longitudinal Translational Research
Brian Lewis, PhD Program in Gene Function and Expression	**Venu Bathini, MD** Department of Medicine	Combined Inhibition of MEK and IGF1Ras an Effective Therapeutic Strategy for Pancreatic Ductal Adenocarcinoma
Zuoshang Xu, PhD Biochemistry and Molecular Pharmacology	**Guangping Gao, PhD** MaPS **Robert Brown, MD, PhD** Department of Neurology	Deliver RNAi for Treatment of ALS using AAV

Pilot Project Program (PPP)

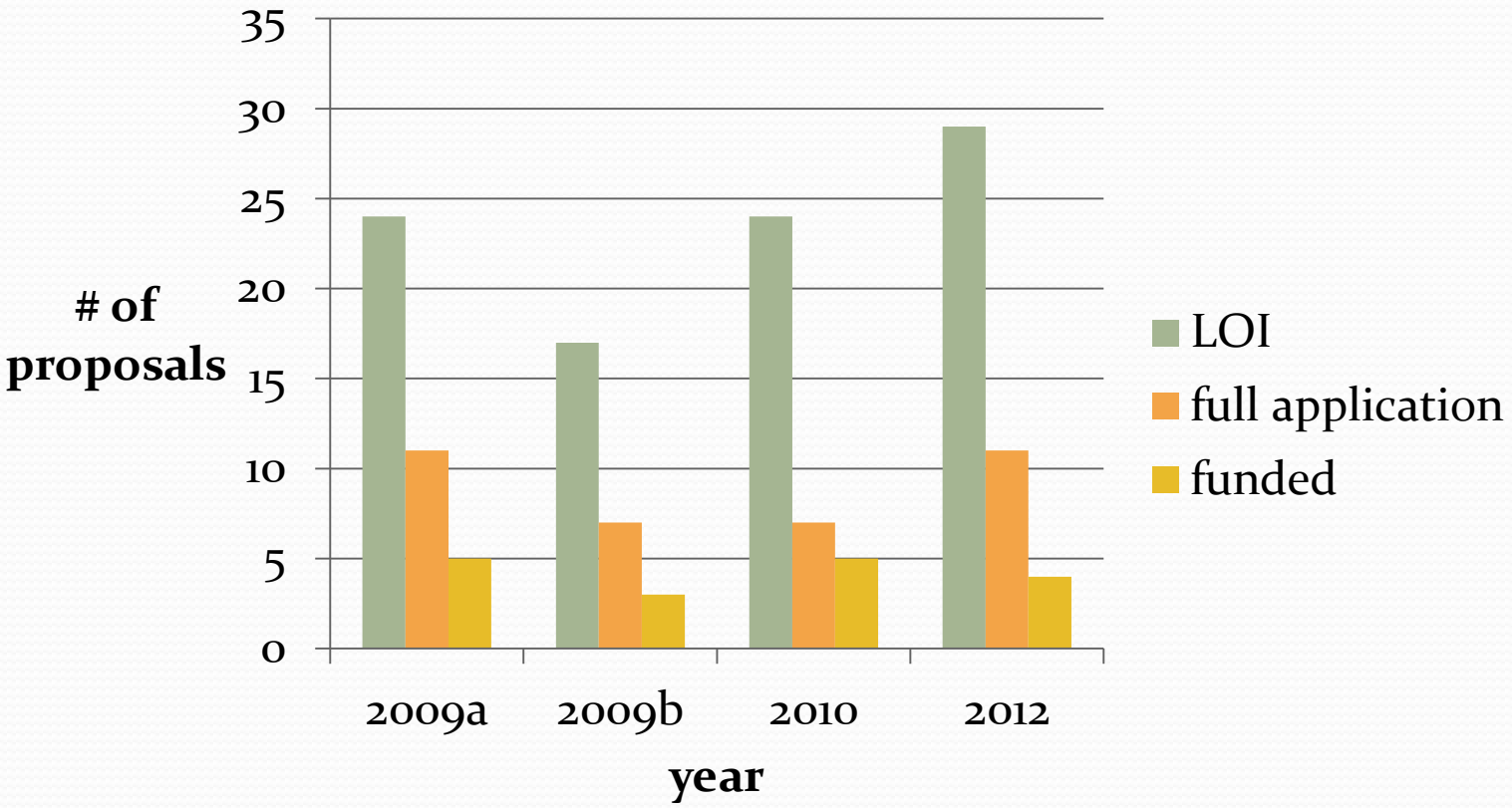
Tentative Timeline:	
Request for Letters of Intent	Monday, November 19, 2012
Letters of Intent Due	Thursday, December 20, 2012
LOI Finalists Notified	Friday, January 11, 2013
Full Proposals Due	Friday, February 8, 2013
Full Proposal Finalists Notified	Friday, March 1, 2013
Project Start Date	Monday, April 1, 2013

UMass Life Sciences Moment Fund

Funds dedicated to multi-investigator pilot projects identified as key strategy to incentivize collaborative partnerships across campuses.

- Inter-campus collaborative projects, involving at least one faculty member from the Worcester campus & one faculty member from another UMass campus.
- Collaborative projects must be oriented towards clinical and translational research.
- Funding levels and application review process same as PPP.

LSMF – success rate



2012 Life Sciences Moment Fund Recipients

UMMS Collaborator(s)/Dept	UMass Collaborator/Dept	Project Title
Wenjun Li, PhD Department of Medicine	**Scott Crouter, PhD, FACSM** Department of Exercise and Health Sciences, Boston Campus	Residential Environment and Coronary Heart Disease Risk Factors (REACH) Pilot Study
William Theurkauf, PhD Program in Molecular Medicine **Zhiping Weng, PhD** Biochemistry and Molecular Pharmacology	**Lawrence Schwartz, PhD** Department of Biology Amherst campus **Priscilla Clarkson, PhD** Department of Kinesiology Amherst campus	microRNA Control of Muscle Atrophy and Death
Tiffany Moore Simas, MD, MPH, MEd OB/GYN and Pediatrics	**Ling Shi, PhD** College of Nursing and Health Sciences, Boston campus **Laura Hayman, PhD, RN, FAAN** College of Nursing and Health Sciences, Boston campus	Effects of soy protein and isoflavone supplementation for improved glucose metabolism and lipid profiles in pregnant women at high risk for gestational diabetes mellitus
Karl Simin, PhD Cancer Biology	**Joseph Jerry, PhD** Veterinary and Animal Sciences Amherst campus	Gene expression signatures defining high risk premalignant breast lesions

Life Sciences Moment Fund (LSMF)

Tentative Timeline:	
Request for Letters of Intent	Monday, February 11, 2013
Letters of Intent Due	Friday, March 8, 2013
LOI Finalists Notified	Friday, March 29, 2013
Full Proposals Due	Friday, April 26, 2013
Full Proposal Finalists Notified	Tuesday, May 28, 2013
Project Start Date	Monday, July 1, 2013

Centers for Therapeutic Innovation (CTI)

CTI VISION

Accelerate the translation of innovative discoveries from bench to the clinic

CTI STRATEGY

OPEN INNOVATION model that deploys Pfizer R&D resources where breakthrough science is happening

CTI APPROACH

A new entrepreneurial partnership at Academic Medical Centers focused on translational medicine

Inflammation (systemic Lupus Erythematosus/Lupus Nephritis)

Proposals are sought for novel large molecule applications with a path to a clinical proof of mechanism study

Clinical Concept	New and more effective treatments that can induce and maintain remission
Mechanisms of interest	- Prevention of underlying dysregulation of B- and T- cells - Modulation of innate immunity - Targeting or interruption inducers of persistent immune activation/inflammation - Inhibition or modulation of inflammatory processes involved in flares (renal, synovial or cutaneous) - Regulation of handling and clearance of apoptotic bodies - Promotion of immune homeostasis and immunoregulation (i.e., functional tolerance).
Precision Medicine	It is preferred if submissions incorporate a hypothesis-driven strategy for patient selection, i.e. rationale for patient subset where drug would be most efficacious

Renal Disease

(Kidney Injury/Lupus nephritis, IgA Nephropathy)

Proposals are sought for novel large molecule applications with a path to a clinical proof of mechanism study†

Clinical Concept

- Novel approaches (targets, pathways or interventions) that would alter the course of a disease which directly or indirectly results in kidney injury and failure

Mechanisms of Interest

- - Block intrarenal inflammation
- - Regulation of leukocyte-endothelial cell interactions
- - Prevention of tubular atrophy and interstitial injury
- - Inhibition of specific components of the immune response related to renal damage (i.e., aberrant mesangial Ab:IC deposition or handling).
- - Approaches aimed at promoting responses leading to improved renal function, such as repair and/or restoration of renal epithelium and nephron integrity

Precision Medicine

It is preferred if submissions incorporate a hypothesis-driven strategy for patient selection, i.e. rationale for patient subset where drug would be most efficacious

Cardiovascular

(Congestive Heart Failure, Post-Myocardial Infarction and Acute Coronary Syndrome)

Proposals are sought for novel large molecule applications with a path to a clinical proof of mechanism study

Clinical Concept

Cardiac remodeling events post-MI and in CHF leads to progressive deterioration of health with few options for patients and physicians.

- Reduced mortality, CV events, and/or improved cardiac function is the ultimate goal

Mechanisms of Interest

- - Those that impact extracellular matrix turnover, fibrosis, restore cardiac tissue & function, apoptosis & proliferation, cardioprotection and neovascularization.
- - Novel mechanisms that impact endothelial repair (beyond standard of care) such as plaque stabilization and dissolution, mast cell & macrophage regulation

Precision Medicine

Defined patient populations at highest risk of CV events that would benefit most from this therapeutic approach **is required**

CTI – Next Steps

- If interested in submitting a proposal, please contact the UMass Center for Clinical and Translational Science to inquire about meeting with CTI staff prior to submitting a proposal
  - Nathaniel Hafer, nathaniel.hafer@umassmed.edu, 508-856-2511

- Pre-proposals due to the UMass Center for Clinical and Translational Science by October 19th

To learn more and obtain the pre-proposal template, please visit https://ctipartners.ideareach.com and create a user profile

New UMCCTS-MassBiologics Collaboration

The Next Hundred Million Pilot Projects

- Inter-campus collaborative projects, involving at least one faculty member from MassBiologics & one faculty member from the Worcester campus.
- Collaborative projects must be oriented towards clinical and translational research.

Individual Proposals	$100,000 maximum for 1 year
	$150,000 maximum for 2 years

<u>2 Stages</u>

Letter of Intent (2 pages)

Full Proposal (Abbreviated NIH-style 10 pages with presentation)

The Next Hundred Million Pilot Projects

Tentative Timeline:	
Request for Letters of Intent	Monday, August 27, 2012
Letters of Intent Due	Friday, October 5, 2012
LOI Finalists Notified	Monday, October 22, 2012
Full Proposals Due	Wednesday, November 21, 2012
Full Proposal Review/Presentations	December 2012-January 2013
Project Start Date	February 2013

Questions?

Research, Process Development, GMP Manufacturing, Education and Training at

MassBiologics of UMMS

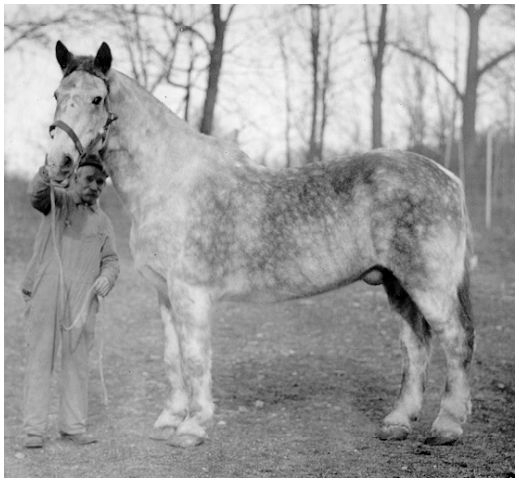
UMASS MEDICAL SCHOOL MassBiologics Medicine for Better Lives

An Abridged History of MassBiologics of the UMMS

Dates	Name	Affiliation
1894	The State Labs-One lab at the Statehouse and one at the Bussey Institute at Jamaica Plain	Massachusetts Department of Health
1895		Theobald Smith, MD arrives as Director of the State Labs and Professor of Comparative Pathology at the Harvard Veterinary School
1903	The Antitoxin and Vaccine laboratories are launched at the Bussey Institute	MA State Department of Health
1917	License #64 to manufacture "Diphtheria antitoxin, vaccine virus and bacterial vaccine made from the typhoid bacillus"	MA State Department of Health

Theobald Smith, MD

Captain



Captain produced enough antitoxin in less than a year to protect 86,000 people from diphtheria

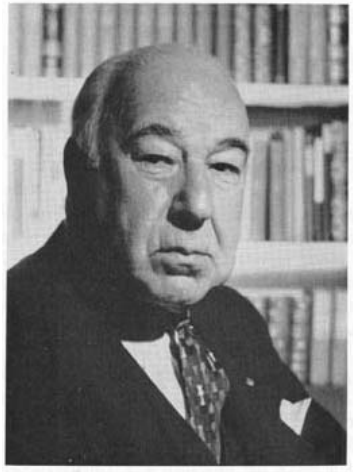
UMASS MEDICAL SCHOOL MassBiologics Medicine for Better Lives

An Abridged History of MassBiologics of the UMMS

Dates	Name	Affiliation
1894	The State Labs-One lab at the Statehouse and one at the Bussey Institute at Jamaica Plain	Massachusetts Department of Health
1895		Theobald Smith, MD arrives as Director of the State Labs and Professor of Comparative Pathology at the Harvard Veterinary School
1903	The Antitoxin and Vaccine laboratories are launched at the Bussey Institute	MA State Department of Health
1917	License #64 to manufacture "Diphtheria antitoxin, vaccine virus and bacterial vaccine made from the typhoid bacillus"	MA State Department of Health
1946	The State Laboratories for Plasma Fractionation	Edwin J Cohn, PhD, Harvard Medical School
Between 1946 and 1968	Massachusetts Public Health Biologic Laboratories, Institute of Laboratories, Massachusetts Health Research Institute	Massachusetts Department of Public Health, Harvard
1969	State Laboratory Institute	Department of Public Health

UMASS MEDICAL SCHOOL MassBiologics Medicine for Better Lives

Edwin J. Cohn, PhD



Dr. Edwin J. Cohn, at Harvard, demonstrating the feasibility of collecting blood and separating it into component parts -- note donors above and fractionation machines below. (Taken at HMS Amphitheater,1940s.)

UMASS MEDICAL SCHOOL MassBiologics Medicine for Better Lives

An Abridged History of MassBiologics of the UMMS

Dates	Name	Affiliation
1894	The State Labs-One lab at the Statehouse and one at the Bussey Institute at Jamaica Plain	Massachusetts Department of Health
1895		Theobald Smith, MD arrives as Director of the State Labs and Professor of Comparative Pathology at the Harvard Veterinary School
1903	The Antitoxin and Vaccine laboratories are launched at the Bussey Institute	MA State Department of Health
1917	License #64 to manufacture "Diphtheria antitoxin, vaccine virus and bacterial vaccine made from the typhoid bacillus"	MA State Department of Health
1946	The State Laboratories for Plasma Fractionation	Edwin J Cohn, PhD, Harvard Medical School
Between 1946 and 1968	Massachusetts Public Health Biologic Laboratories, Institute of Laboratories, Massachusetts Health Research Institute	Massachusetts Department of Public Health, Harvard
1969	State Laboratory Institute	Department of Public Health
1997-1998		
2007	MassBiologics Per FDA License #1779 to produce Td vaccine	UMMS
2012	MassBiologics of the UMMS	UMMS

UMASS MEDICAL SCHOOL MassBiologics Medicine for Better Lives

MassBiologics Mabs
2002- 2010

Monoclonal Antibody	Indication	Stage of Development	Business Model	
1 SARS1	Prevention of SARS	Completed through manufacturing	50/50 collaboration with Medarax to Phase 1	NIH Funded
2 MBL-CDA1 and 3 MBL-CDB1	Treatment of *C. difficile* infection	Phase 3	50/50 collaboration with Medarex through Phase 2	Merck April 2009 License, Development and Commercialization Agreement
4 MBL-RAB1	Rabies post-exposure prophylaxis in conjunction with rabies vaccine	Phase 2/3 (India)	MBL through discovery	Serum Institute of India September 2006 License and Collaboration Agreement
5 MBL-HCV1	Prevention and treatment of HCV infection	Phase 2	MBL (collaboration with UMMS)	N/A
6 ALS	Treatment of Amyotrophic Lateral Sclerosis	Preclinical	MBL (collaboration with UMMS)	N/A

UMASS MEDICAL SCHOOL MassBiologics Medicine for Better Lives

Millions of Life Saving Doses of “Medicine for Better Lives” from MassBiologics of UMMS

Diphtheria Antitoxin-Equine	
Botulism Antitoxin-Equine	
Tetanus Antitoxin-Equine	
Rabies Immunoglobulin-Equine	
Human Serum Albumin	
Human Immune Globulin	
Human Hyper-Immune Globulin to	**Scarlet Fever, Pneumococcus, Meningococcus, Tetanus, Measles, CMV, RSV, Varicella-zoster, Rabies, Hepatitis A**
Tetanus Toxoid Vaccine	
Diphtheria Toxoid Vaccine	
Td Vaccine	
Human Monoclonal Antibodies against	**SARS, C diff Toxins A and B, Rabies, Hepatitis C, Tetanus and Diphtheria Toxins, SOD1 for ALS, sFlt-1 for Pre-Eclampsia**

UMASS MEDICAL SCHOOL MassBiologics Medicine for Better Lives

Going Forward

- Research on Human Monoclonal Antibody Development
- Research and Development of New Therapeutic MAbs-
- Research and Development of New Prophylactic MAbs
- Innovation in Process Development, Manufacturing
- Innovation in Quality Assessment tools
- Innovation in Business Development
- Emphasis on Training/Mentoring
- Custom Contract Manufacturing

UMASS MEDICAL SCHOOL MassBiologics Medicine for Better Lives

“The Next Hundred Million” Pilot Projects

DATE: September 4, 2012

TO: All UMass Faculty with an Interest in Clinical & Translational Science

FROM: Katherine Luzuriaga, MD, Director, UMass Center for Clinical & Translational Science; Mark Klempner, MD, Executive Vice Chancellor for MassBiologics of the University of Massachusetts Medical School

RE: NEW FUNDING OPPORTUNITY: The “Next Hundred Million” Pilot Projects (NHMPP)

Introduction

The University of Massachusetts Center for Clinical and Translational Science (UMCCTS) and MassBiologics of the University of Massachusetts Medical School are pleased to announce a funding call for “The Next Hundred Million” Pilot Projects (NHMPP). The NHMPP will serve as a dedicated pool of funding to spur innovative collaborations between UMMS, MassBiologics of UMMS and investigators across the UMass System with the goal of enhancing the translation of discoveries for clinical use.

Purposes

In 2013, MassBiologics of the University of Massachusetts Medical School (www.umassmed.edu/massbiologics) will celebrate discovery, manufacture and delivery to the American people of 100 Million doses of vaccines and immunotherapeutics during its 118 year history. **We are looking for pilot projects that will contribute to the discovery, preclinical and clinical research, manufacture and delivery of the “next hundred million doses” of products to improve public health**. The NHMPP will serve as a dedicated pool of funding to spur inter-campus collaboration and strengthen the University’s research portfolio in clinical and translational research. To support this mission, projects must include at least one investigator from MassBiologics of UMMS (see below and www.umassmed.edu/massbiologics) and a faculty investigator from at least one UMass campus. Inclusion of collaborators from UMMS is highly encouraged but not required. The following Division Leaders (all are UMMS faculty) should serve as initial points of contact for expertise at MassBiologics:

- For discovery research, Greg Babcock, greg.babcock@umassmed.edu
- For clinical research, Deb Molrine, deborah.molrine@umassmed.edu
- For process development and manufacturing research, Bill Thomas, william.thomas@umassmed.edu
- For quality assessment, regulatory or business process proposals, Mark Leney, mark.leney@umassmed.edu

By providing seed funding to outstanding faculty members, this fund facilitates the development of faculty-to-faculty networks within the University system.

MassBiologics of the UMMS is the only FDA licensed biologics production facility owned and operated by a university in the United States. It has unique discovery, preclinical, clinical, regulatory, quality assessment and GMP manufacturing expertise. The academic affiliation of MassBiologics also allows it to serve as an incubator to innovate and improve the process of vaccine and biological and immunologic therapeutics development.

Current and future projects supported by this fund are envisioned to develop into larger initiatives that attract substantial funding from extramural sources, including the Federal Government, the Commonwealth, industry, foundations and others.

Process Development

Human Monoclonal Antibodies

UMASS MEDICAL SCHOOL
MassBiologics
Medicine for Better Lives

Process Development Overview

- Focus on proteins produced by CHO cells
  - Human monoclonal antibodies
- Cell culture, purification, formulations and analytical support
- 4 PhD's and 13 technicians
- Supplemented by MAb Manufacturing team

UMASS MEDICAL SCHOOL MassBiologics Medicine for Better Lives

- Upstream process development
- Downstream process development
- Analytical method development
- Formulation development
- Tech Transfer and Manufacturing support

UMASS MEDICAL SCHOOL MassBiologics Medicine for Better Lives

MBL Process Development
Platform Technology

- CHO cell expression host and vector
- Proprietary media and feeds
  - Chemically defined, animal component free
- Fed-batch culture method up to 5 gm/L
- Purification platform for MAbs
- Formulation platform for 25-100 mg/ml

UMASS MEDICAL SCHOOL MassBiologics Medicine for Better Lives

Upstream Process Development

Small Scale Shaken Cultures

Bench top DasGip Reactors

60 L Applikon Reactor

UMASS MEDICAL SCHOOL

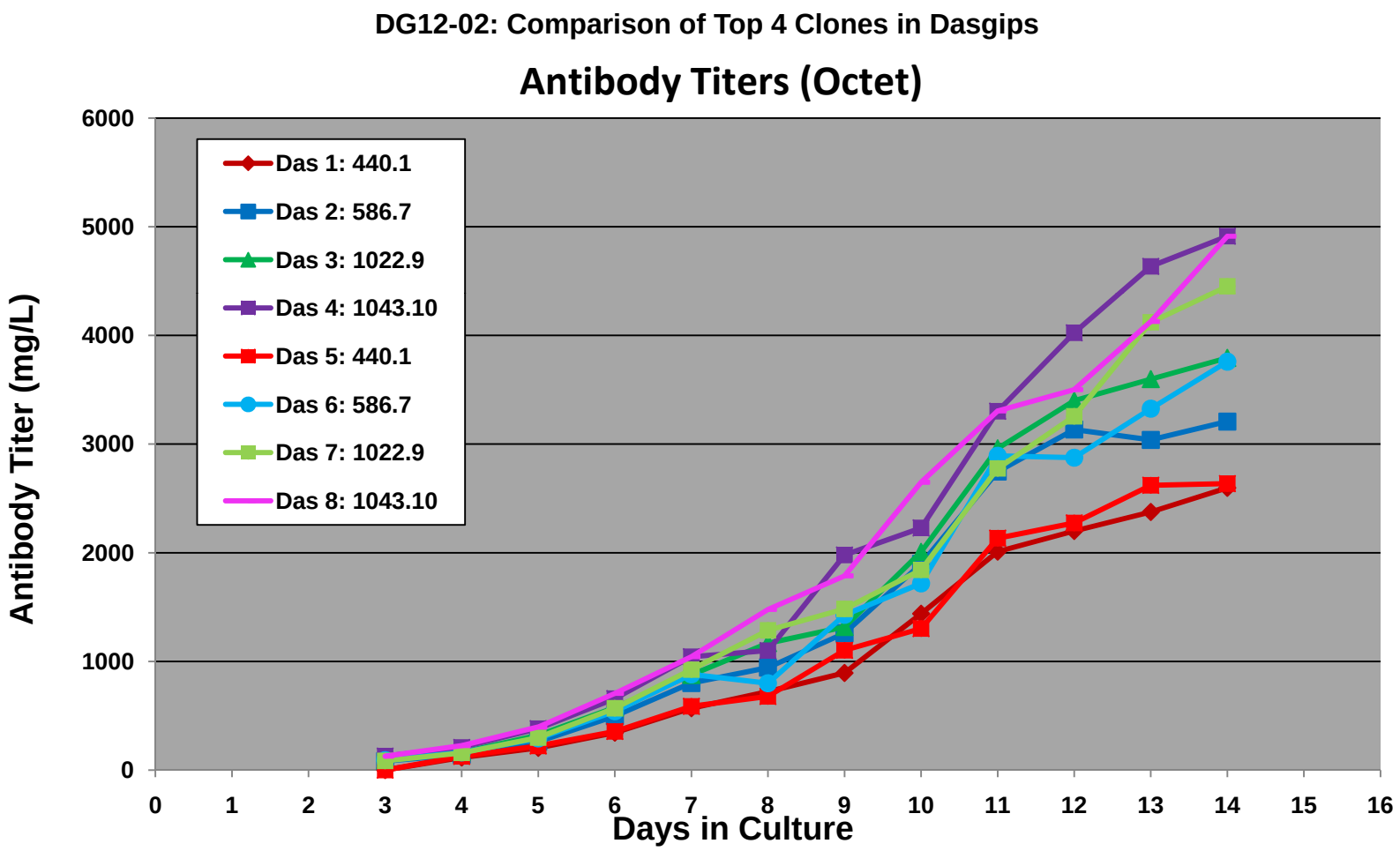
MassBiologics

Medicine for Better Lives

Upstream Process Development Activities

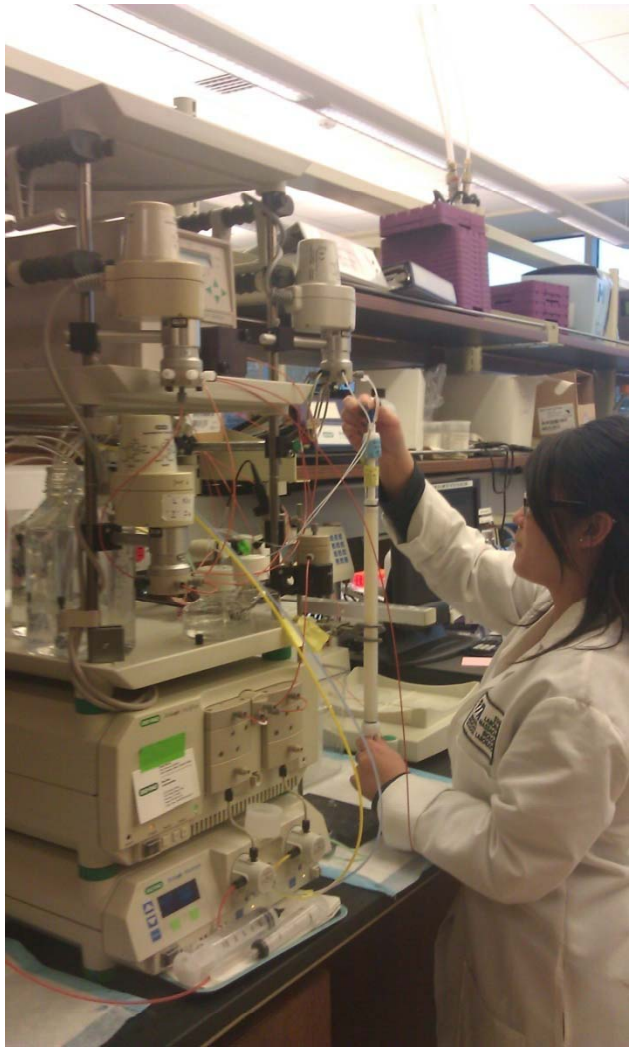
- Cell Line Development (transfection, cloning)
- Cell Line Characterization (growth, production kinetics, max cell density, specific productivity, stability, etc)
- Process for Seed-train and Bioreactor (pH, DO, Temp)
- Fed-batch Bioreactor Optimization (feeding, pH, DO, Temp)
- Material for Downstream and Analytical Process Development
- Process Scalability, Tox material production (IND), and Tech transfer (Ph I/II)

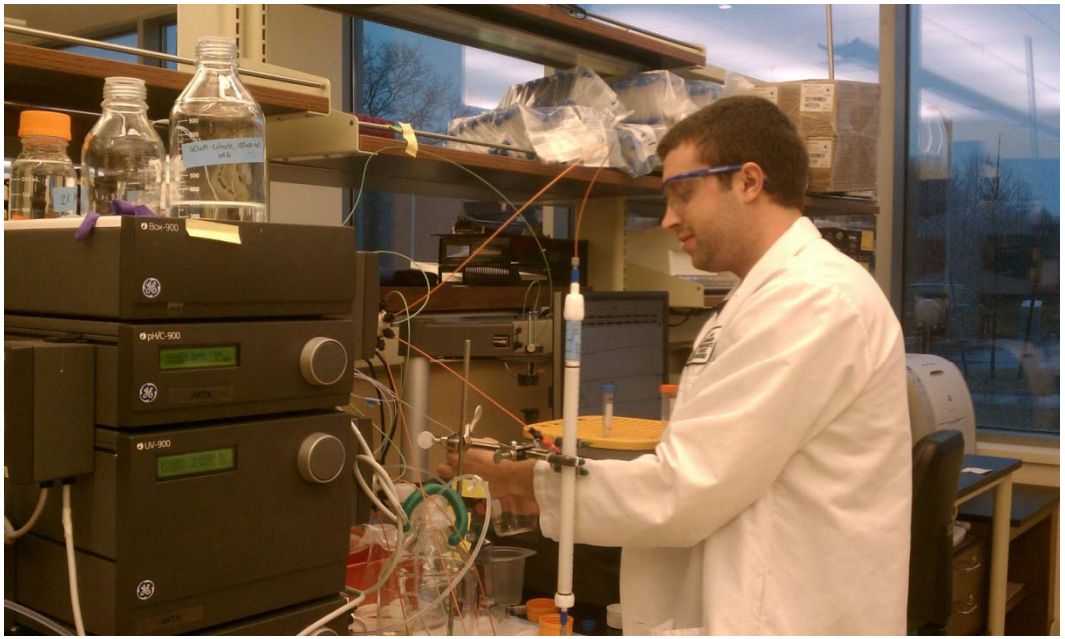
CHO Cell Line Selection



UMASS MEDICAL SCHOOL MassBiologics Medicine for Better Lives

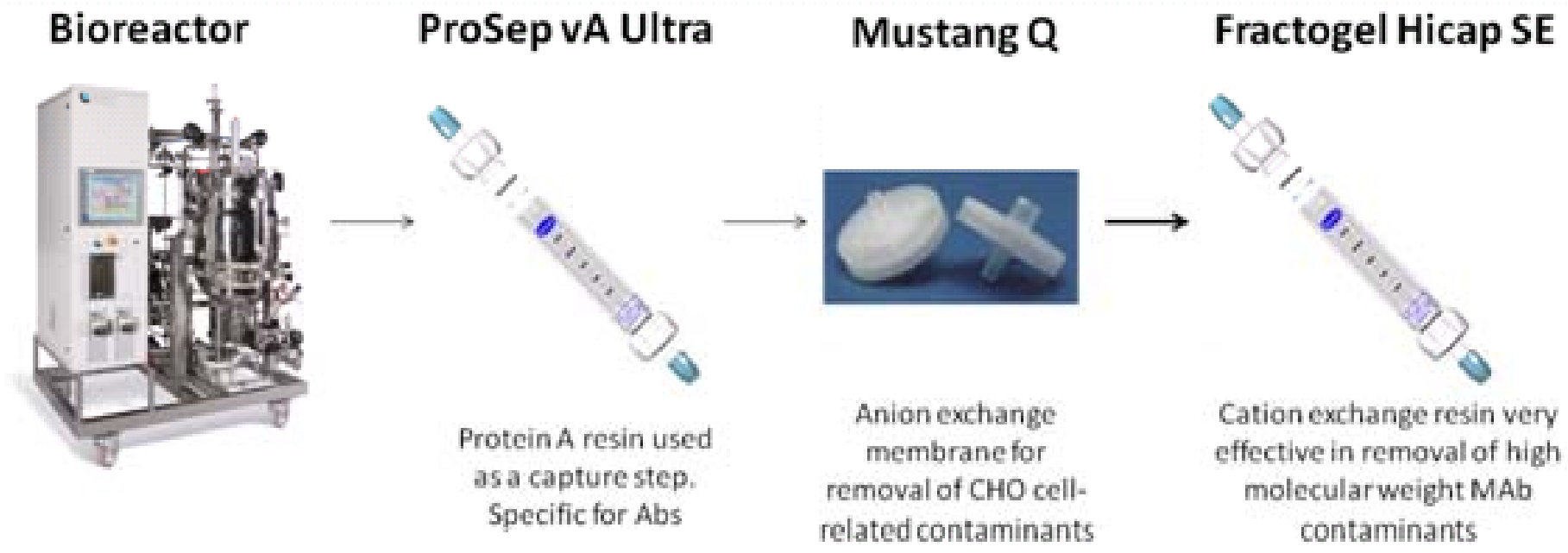
Downstream Process Development





UMASS MEDICAL SCHOOL
MassBiologics
Medicine for Better Lives

Current MBL Purification Platform



UMASS MEDICAL SCHOOL
MassBiologics
Medicine for Better Lives

Downstream Process Development

- Optimize chromatography steps
  - Establish set points, ranges and hold times
- Virus inactivation and removal studies
  - Prosep, low pH, nanofiltration
- MAb development purification scale >10 g
- Pre-clinical material (toxicology, reference standard)

UMASS MEDICAL SCHOOL MassBiologics Medicine for Better Lives

Analytical Development

- Antibody characterization
- Tox lot, reference standards, Mfg in-process samples
- Support Upstream, Downstream, and Formulation Development
- Development of New Assays, Methods
- Comparability Studies
- Improve Throughput of the Assays

Formulation Process Development

- Formulation development
- High concentration formulations (100 mg/L)
- High throughput analytical for Mabs
- Accelerated stability testing for formulation development
- Platform formulation
  - 20 mM citrate, pH 6.0, 150 mM NaCl, Tween 80

UMASS MEDICAL SCHOOL MassBiologics Medicine for Better Lives

Research, Process Development, GMP Manufacturing, Education and Training at

MassBiologics of UMMS

UMASS MEDICAL SCHOOL MassBiologics Medicine for Better Lives

MassBiologics, Product Discovery

Greg Babcock, Ph.D.
Associate Professor, Medicine, UMMS
Deputy Director, Discovery, MassBiologics

UMASS MEDICAL SCHOOL
MassBiologics
Medicine for Better Lives

Product Discovery

- Focus is the development of human monoclonal antibodies from initial concept to completion of preclinical activity to support an IND application

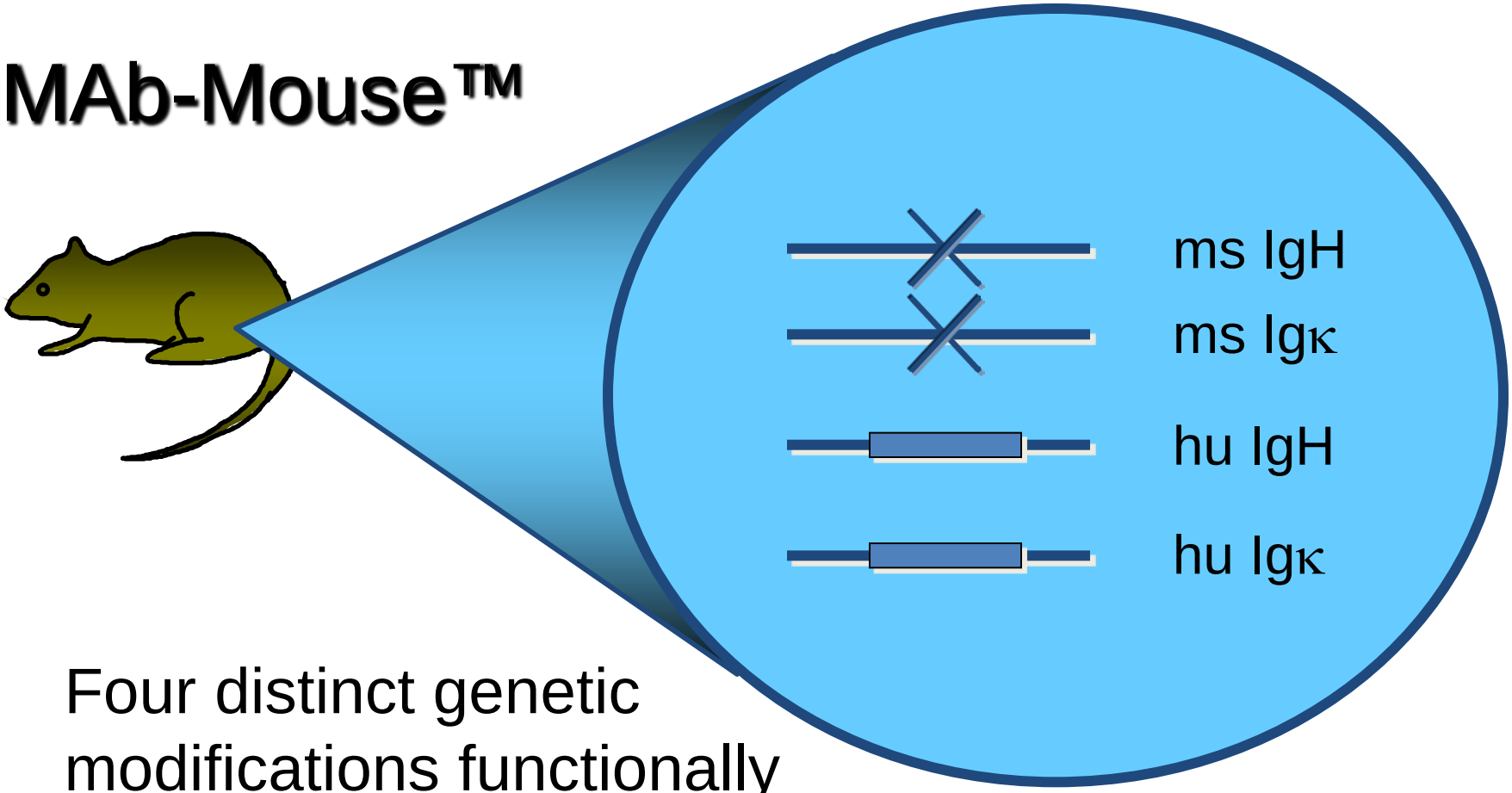
- Extensive experience in identifying novel antibody molecules

- Infectious disease targets (mostly but not all)

- Various technologies used for human antibody development

- Four human monoclonal antibodies developed from concept to phase 2 human studies

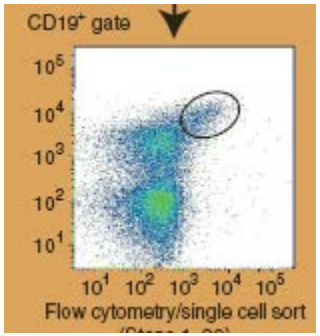
HuMAb-Mouse™



Four distinct genetic modifications functionally replace the mouse immunoglobulin loci with human immunoglobulin transgenes

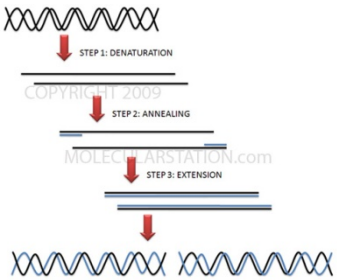
Antibody secreting cells

Draw blood Day 7 post vaccine

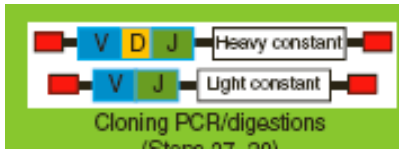


Stain PBMCs to isolate ASCs

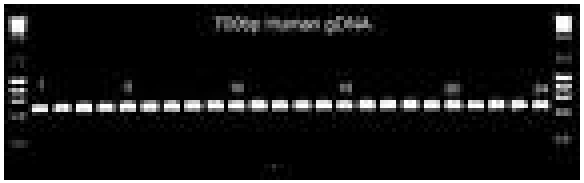
Sort individual ASCs into 96-well PCR plates



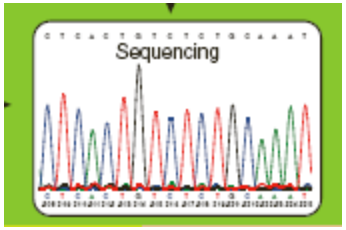
Perform 1-step RT-PCR on ASC-RNA (H+L)

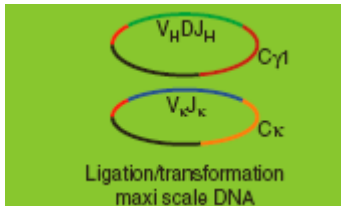


Perform separate cloning PCRs

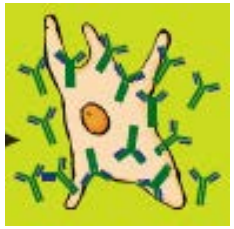


Run products on gel to determine positive clones





Ligate “valid” antibodies into expression vectors



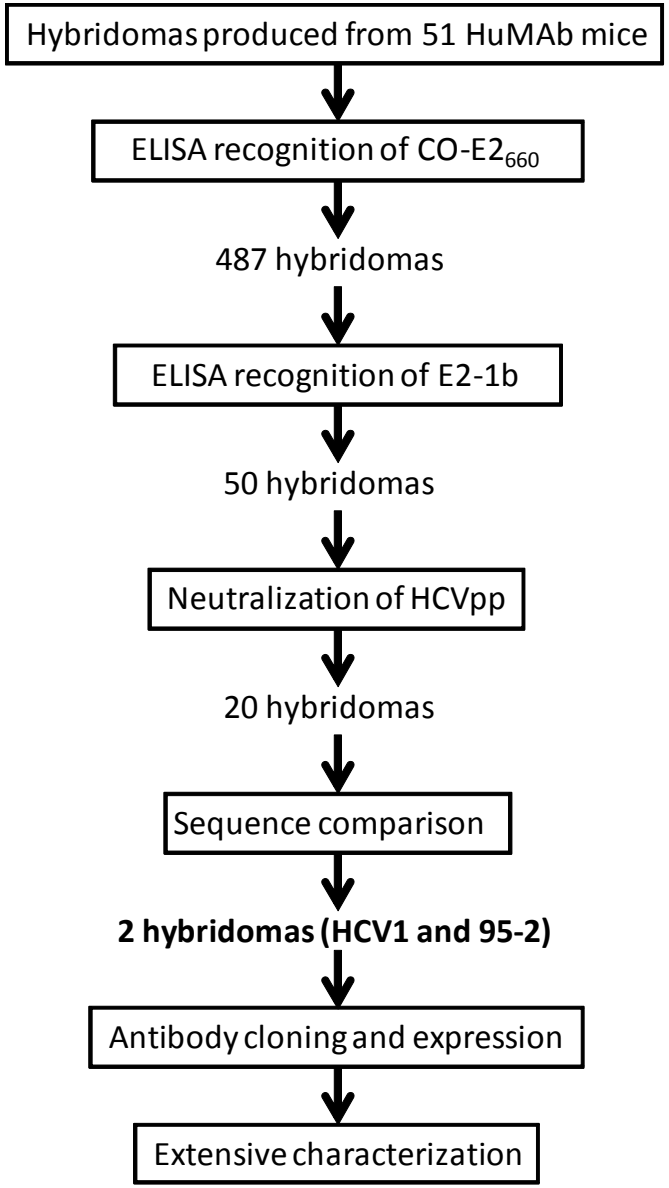
Transfect to produce antibody and screen against Tet/Dip toxoid via ELISA

MassBiologics Antibody Pipeline

Antibody	Pre-Clinical	Phase 1	Phase 2	Phase 3
Clostridium difficile antibody combination				Licensed to Merck
Rabies virus				Licensed to Serum Institute of India
Hepatitis C virus				
SARS virus				
anti-hSOD1 (ALS)				
Discovery Target #1 - Infectious Disease				
Discovery Target #2 - Infectious Disease				
Discovery Target #3 - Endogenous Target				

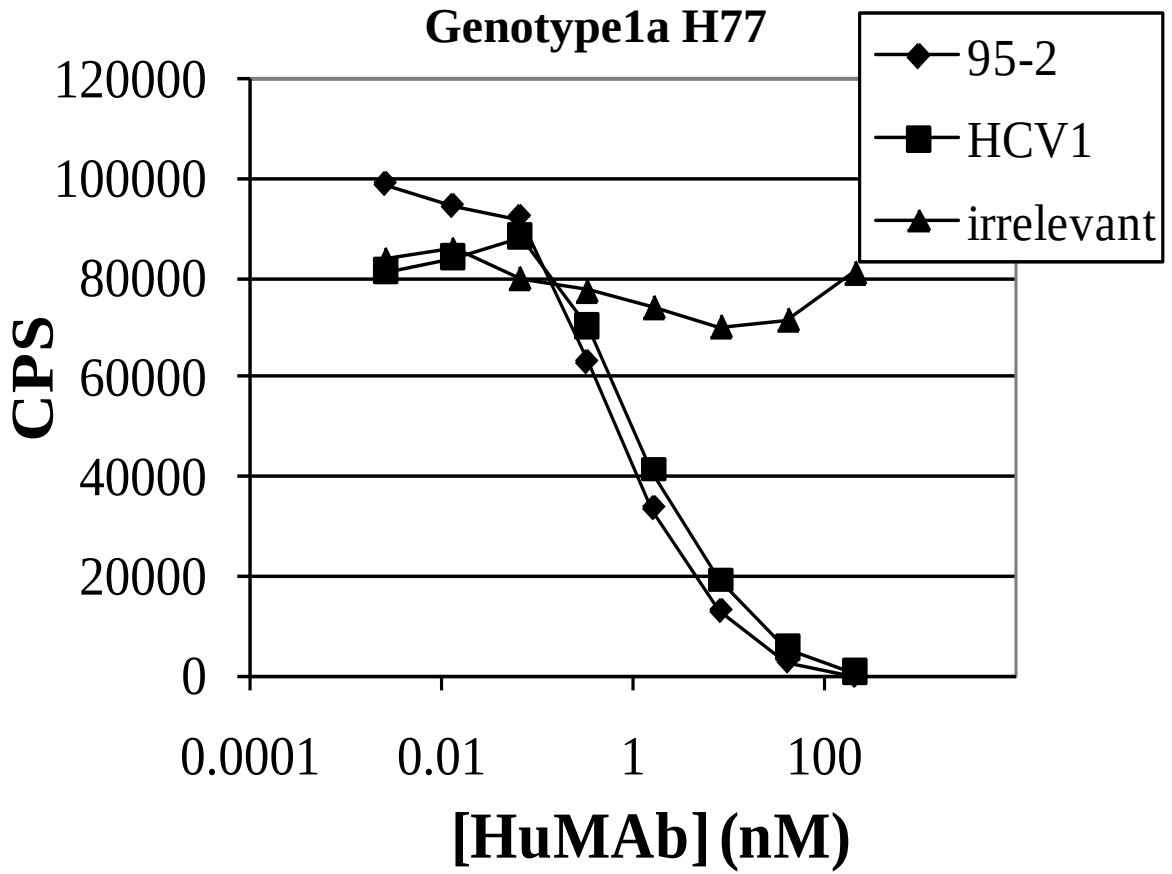
UMASS MEDICAL SCHOOL MassBiologics *Medicine for Better Lives*

Ex: HCV mAb Development



UMASS MEDICAL SCHOOL
MassBiologics
Medicine for Better Lives

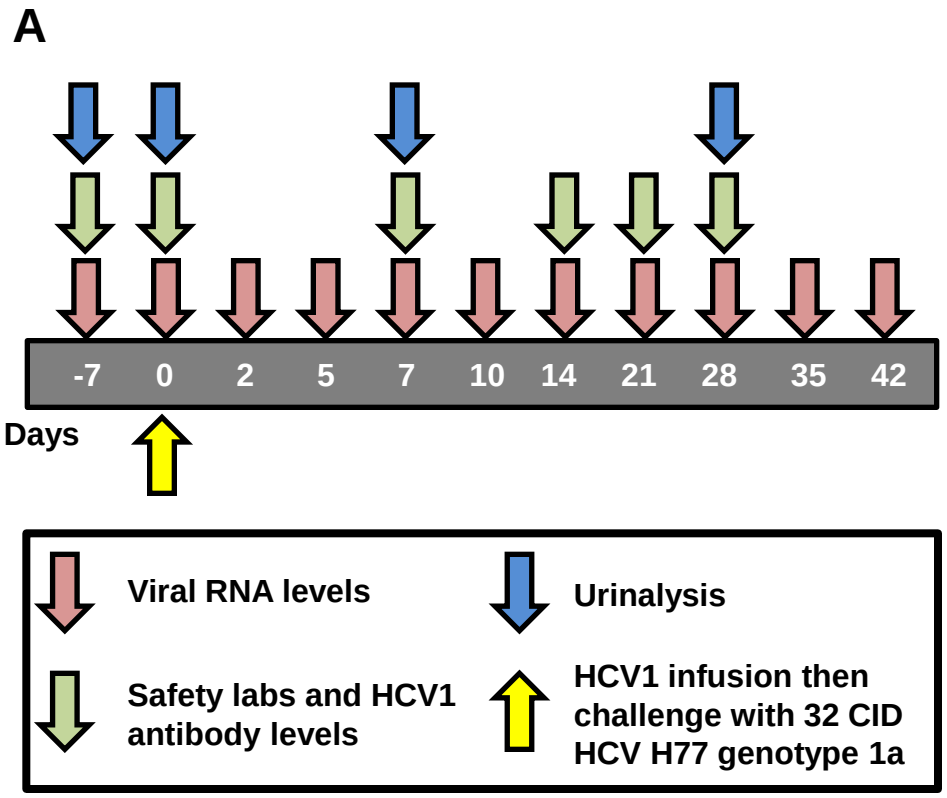
HCV mAb HCVpp Neutralization

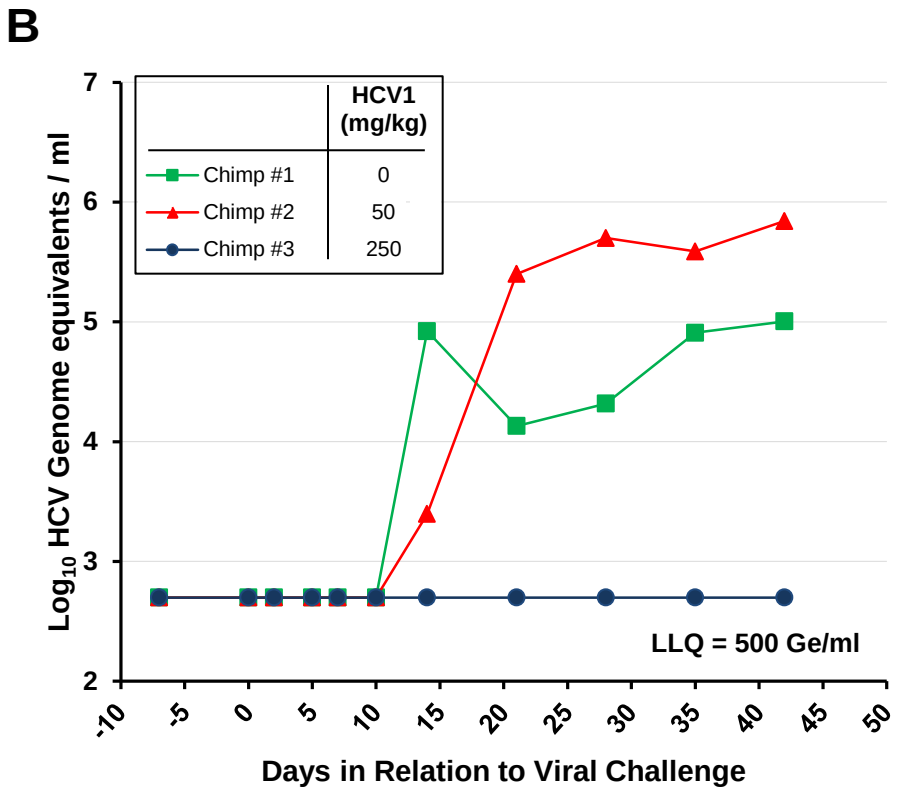


HCV1 neutralized all genotypes tested

UMASS MEDICAL SCHOOL
MassBiologics
Medicine for Better Lives

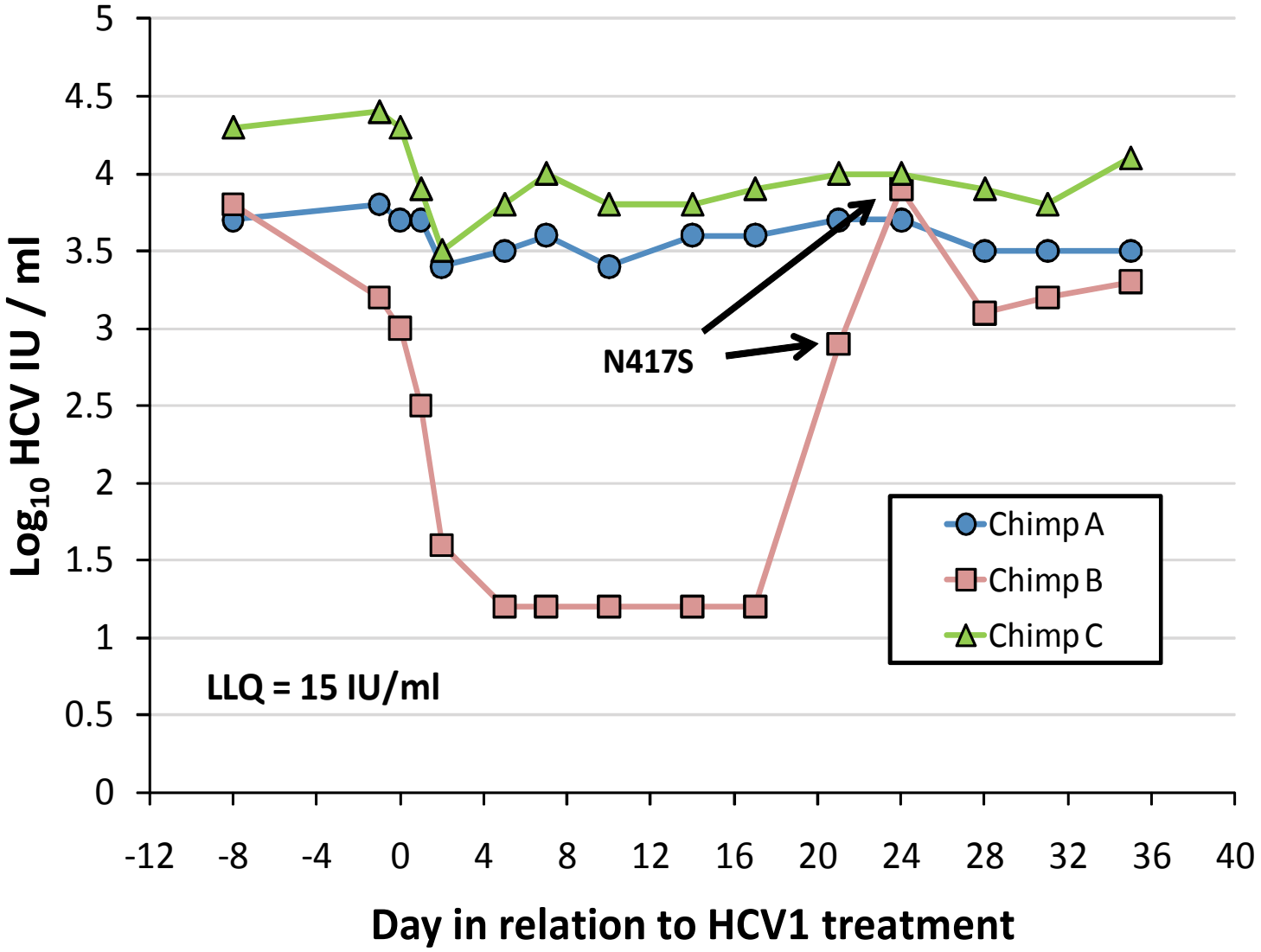
HCV1 Prevents HCV Infection of Chimpanzees





UMASS MEDICAL SCHOOL
MassBiologics
Medicine for Better Lives

HCV1 Treats HCV Infection of Chimpanzees



UMASS MEDICAL SCHOOL
MassBiologics
Medicine for Better Lives

Product Discovery

- Skilled in in vitro assays to determine mAb activities

- Adept at understanding requirements for animal studies to support human studies

-Preparing Pharm-Tox section of IND to the satisfaction of the FDA

- Proven track record of developing human monoclonal antibodies from bench to bedside

UMASS MEDICAL SCHOOL MassBiologics Medicine for Better Lives