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& BIOTECHNOLOGY RESEARCH

insight | innovation | application

Institute for Bioscience & Biotechnology Research

Retreat and Synergy Workshop

Lightening Talks

May 24 and 25, 2016

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Alexander (Sasha) Andrianov

- **Vaccine Delivery (Polyphosphazene Immunoadjuvants – SAR/Molecular level Mechanisms/Formulations)**
- **Macromolecular Drug Delivery (Polyphosphazene Synthetic Platform - Design of Multifunctional Carriers for Stabilization, extended release, vascular and cellular targeting of Proteins and RNAs)**
- **Self-Assembling Nanoparticulates (Non-Covalent Macromolecular Complexes - Stimuli Responsive Systems)**
- **Biomaterials (Ionic Complexation, Semipermeable Membranes, Multilayer coatings using synthetic functionalized materials)**

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My Trajectory

- **Vaccine Delivery – PP adjuvanted vaccine licensed, general understanding of mechanism and SAR obtained. Focused mechanistic-delivery modalities studies and collaborations with vaccine manufacturers.**
- **Drug Delivery – POC for multifunctional carriers using PP platform obtained. Collaborations on protein or RNA therapeutics.**
- **Biomaterials. Extend the potential of PP platform to biocompatible coatings and functional hydrogels. Collaborations on new biomedical and industrial applications.**

Brian Pierce

- Modeling structures and molecular recognition
  - TCRs
  - TCR-peptide-MHC interactions
  - Antibody-antigen, antibody-peptide
  - Loop modeling
- Structure-based protein design
  - Modeling effects of point mutants on affinities
  - Design TCRs for higher affinity and altered specificity
  - Design antibodies for greater potency and neutralization breadth
- Vaccine design
  - HCV: epitope-based immunogens and redesigned antigens
  - Database of virus-antibody interactions and viral variability
  - Exploratory design of coronavirus E RBD and other viral antigens

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My Trajectory

- Milestones/Goals
  - New tools, scoring functions, and web servers in modeling and design of immune interactions – high accuracy predictive docking and design
  - Successful antigen designs for virus subunit vaccines – move to in vivo testing and clinic
  - Integrate high resolution immune repertoire sequencing with modeling
  - New protein nanoparticle scaffolds for antigen presentation
  - Designed immunomodulators for cancer immunotherapy
- Key collaborations
  - Work with experimental researchers and facilities to generate and test designed proteins for binding and structure experimentally
  - Collaboration with TCR clinical researchers (e.g. Rosenberg Lab, NCI)
  - Work with industry biologics leaders (e.g. Medimmune, Roche, AbbVie, Amgen) or clinical researchers to design better antibodies
  - Collaboration with industry vaccine leaders (GSK, Novavax) to design vaccines
- Experimental resources/tools needed
  - Immune repertoire sequencing
  - Deep mutational scanning of antibody/TCR CDR loops for antigen binding affinity improvements
  - Antigen-specific antibody and TCR cloning

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Eric A. Toth

- Interests: structural biology, drug design
- Current projects:
  - SMART therapeutic
  - HCV vaccine
  - Kynurenine pathway therapeutics

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My Trajectory

- SMART
  - Where: licensed reagent/therapeutic for controlling oncogenic RAS activity
  - How: success of designs in progress + cracking the nut of protein delivery
- HCV:
  - Where: structure-based vaccine in the clinic
  - How: better resources for expressing recalcitrant glycosylated proteins; cryo-EM capabilities
- Kynurenine pathway therapeutics
  - Where: at least one legitimate pre-clinical/clinical candidate
  - How: better in vivo models of neurodegenerative diseases

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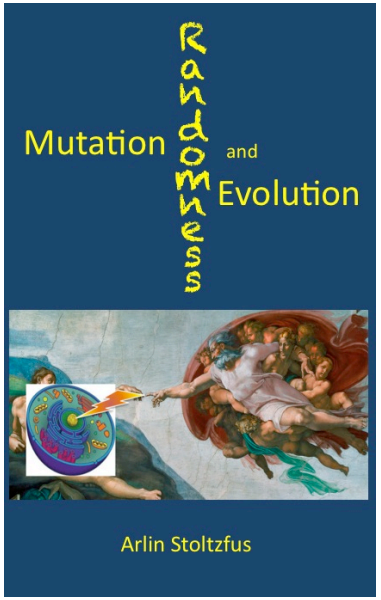
Arlin Stoltzfus

programming, data analysis, evolution

- Phylotastic – distributed web-services system + end-user tools to get quick & dirty species trees
- Mutation, Randomness and Evolution (book in draft)
- Modeling amino acid exchangeability with 100K measured fitness values from deep mutational scanning studies
- Open Data Initiative implementing at NIST
- Parallel amino acid changes

Phylotastic mobile app



Due in print, 2017

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To accelerate ...

- proving the quantitative importance of mutation biases in evolution:
  - Gold standard set of cases of molecular adaptation large enough to do statistics

- applying my skills to something more biomedically important:
  - interaction with molecular epidemiologists

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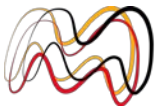
Roy Mariuzza

- Structural basis for recognition of cellular and viral ligands by natural killer (NK) cell receptors
- Evolution of the adaptive immune system: variable lymphocyte receptors (VLRs)
- Structural basis for recognition of self and viral antigens by T cell receptors (TCRs)
- Biophysical analysis of the TCR–CD3 complex and and TCR signaling
- Structure-based HCV vaccine design



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My Trajectory

- How do multiprotein cell surface receptors (e.g. TCR–CD3 complex) transmit signals across membranes upon binding protein ligands on other cells? (X-ray, NMR, cryo-EM)
- How can structural information on viral (e.g. HCV) antigens be used to increase the immunogenicity of broadly neutralizing epitopes and decrease the immunogenicity of decoy epitopes?

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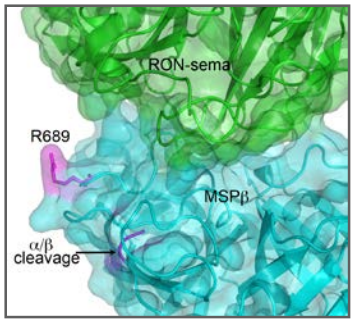
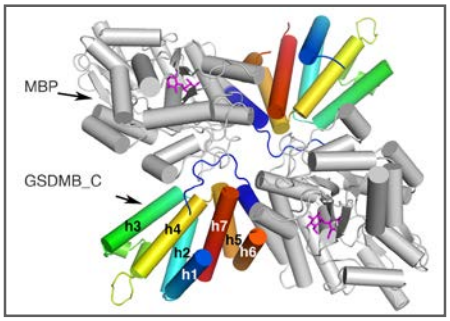
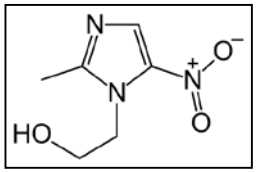
Osnat's ongoing research program

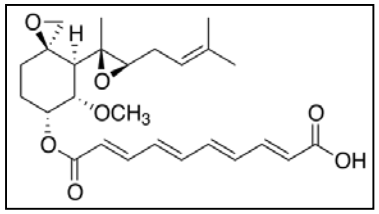
- **Missense SNP's implicated in Crohn's disease**
  - RON receptor tyrosine kinase - MSP interaction
  - Current main focus on the structure of gasdermin B
  - **NIGMS R01 award (with John Moult)**





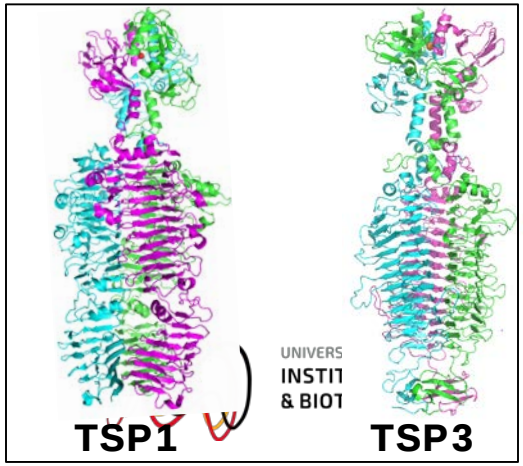
- **Antigiardiasis & antiamebiasis drug discovery**
  - Follow-up on HTS performed in collaboration with NCGC using their approved drug library
  - Currently optimizing fumagillin
  - **NIAID R21/R33 award (with Janak Padia)**





	Metronidazole	Fumagillin
MLC	8-10 μM	0.01 μM
ED_{50}	~50 (mg/Kg)	<0.6 (mg/Kg)

- **Structure-function of tailspikes from *E. coli* O157:H7 phage CBA120**
  - 4 proteins (TSP1-4)
  - Current focus of TSP2 and TSP3
  - **NIGMS R01 award (with Daniel Nelson)**



Five years Goals

- **Missense SNP's implicated in Crohn's disease**
- Obtain the structure of RON receptor tyrosine kinase in complex with full-length MSP and understand the structural basis for disease
- Obtained structures of full-length GSDMs and reveal the structural basis for disease and epithelial cell proliferation defects
- Establish whether the proteins could serve as targets for therapeutic interventions

Needed: good collaboration with cell biologists

- **Antigiardiasis drug discovery**
- Obtain 1-2 compounds with improved pharmacokinetic, toxicity, and stability properties
- Obtain FDA approval to advance the compounds to clinical trials

Needed: Luck and continued NIH support beyond R33

- **Structure-function of tailspikes from *E. coli* O157:H7 phage CBA120**
- Obtain the structures and substrate specificities of all 4 phage CBA120 tailspikes
- Identify a protein that could be engineered as biologic that degrades bacterial biofilm

Needed: collaboration to determine the high resolution structure of CBA120 by EM

Osnat

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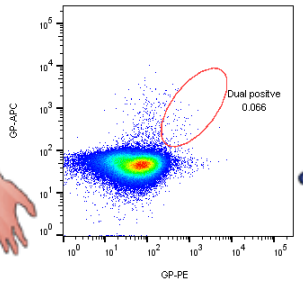
Yuxing Li Lab: Viral Immunology

Infected or Immunized individuals

Antibody isolation

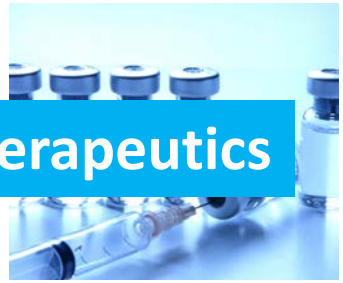


(HIV-1, Ebola) Neutralizing mAbs

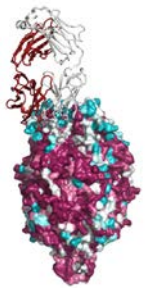
Antigen

Pathogenesis, immune evasion mechanism

Therapeutics

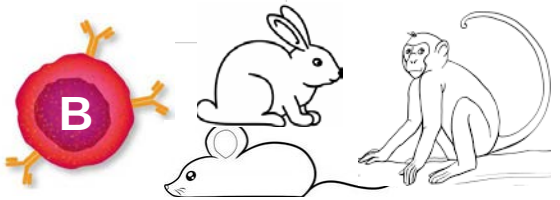


Ab-Ag interaction investigation e.g. epitope mapping, EM, X-ray crystallography



Immunogen design and testing, in vitro/ex vivo, in vivo

Vaccine



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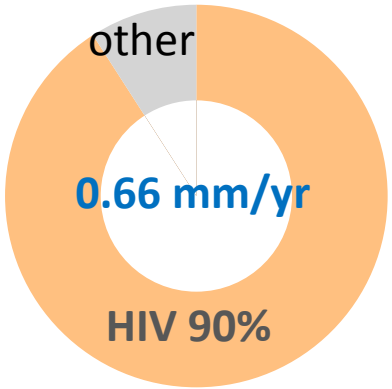
Burton, Nat. Rev. Immunol., 2:706-713, 2002

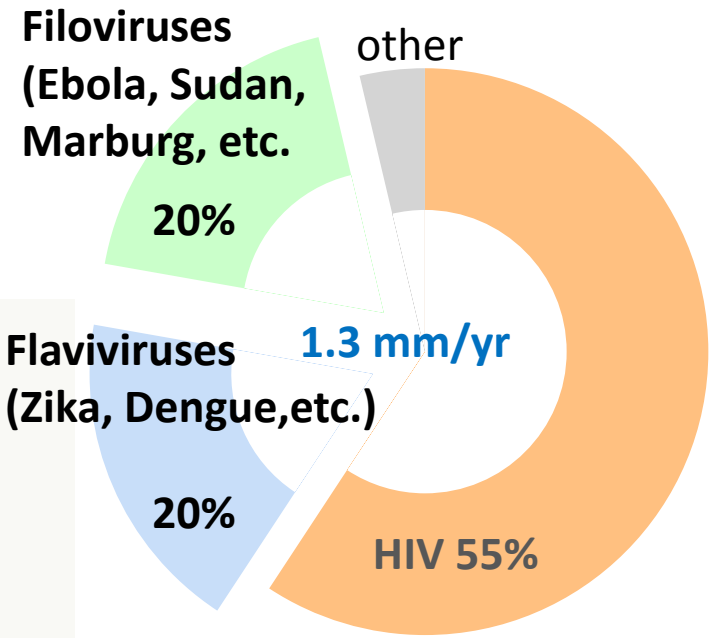
My Trajectory

Current budget



Vaccine

5 years later



Vaccine
Therapeutics (bNAbs)

Collaborators

NIH: John Mascola, Susan Moir
Mark Connors

Scripps: Rich Wyatt, Dennis Burton
David Nemazee, Andrew Ward,
Ian Wilson

Karolinska: Gunilla Karlsson Hedestam

IBT: Javad Aman

IBBR: Adi Ofek, Alexander Andrianov, Roy Mariuzza

Other/upcoming

Yuxing Li

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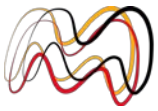
Ed Eisenstein

- Interests
  - Elucidating molecular mechanisms to engineer unprecedented behavior in biological systems
- Expertise
  - High-precision biomolecular interactions
    - Quantitative kinetic and thermodynamic approaches and modeling are applied to a range of simple to quite complex molecular interactions
  - Biomolecular engineering and design
    - Enhance natural proteins with new attributes for mechanistic studies and application
    - Design and construct novel biomolecules for cellular sensing and actuation
  - Plants as platforms
    - Use genome engineering to introduce novel modules into biological systems for biotechnology



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My Trajectory

- Goal: Routine and reliable (re)construction of biomolecules with novel properties
  - Accelerator: Robust design – build – test cycle for proteins, functional nucleic acids and cellular circuits
- Goal: Multi-modal intervention to understand and enhance biological systems
  - Accelerator: Synergistic interaction among diverse experts with shared goals
- Goal: Rewire complex genetic programs for biotechnology applications
  - Accelerator: Rigorous, highly parameterized models that yield more predictable outcomes

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John Orban

Keywords: structural biology, NMR, protein folding and design, conformational change, allostery

- **Fold malleability** – some proteins on the margin of stability can switch to other fold topologies in response to mutational and/or environmental triggers

- relevance to understanding the sequence/structure relationship, fold evolution, alternative splicing, SNPs, design of protein switches

- **Intrinsically disordered proteins** – ensembles on the margin of instability can shift conformational preferences in response to PTMs

- relevance to cancer; 30-50% of human proteins are predicted to be IDPs

- **Dynamic allostery** – ligand binding induces a conformational/dynamic change at a remote site with functional consequences

- relevance to understanding signaling mechanisms (T cell signaling, RAS signaling)

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Big questions / accelerators

- Is there an algorithm for predicting fold switching?

- *Enable design of protein switches; how folds evolved; effect of mutation on human disease*

- Can one predict ensemble preferences for IDPs and how these might change with PTMs?

- *Enable understanding of IDP "structure"-function relationships; human disease*

- Can one predict ligand-induced allosteric changes?

- *Enable better understanding of signaling processes; more sophisticated protein design of smart therapeutics that can sense-compute-respond*

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Shuwei Li

- Develop novel technologies for mass-spectrometry (MS) based bioanalysis (proteomics, metabolomics, glycomics)
- Develop POT (point-of-care) technologies for rapid detection of bacterial drug resistance
- Develop next-generation protein sequencing technology based on single molecule detection.

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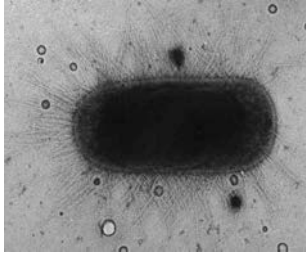
My Trajectory

- Apply MS based technologies (especially metabolomics) for clinical diagnostics.
- Commercialize POT technologies

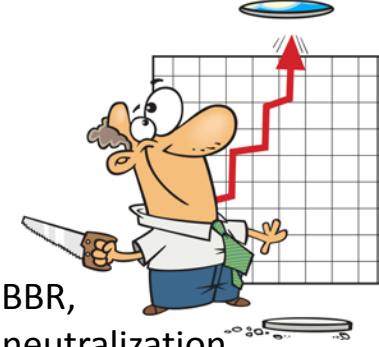
  Both goals require extensive collaboration with clinical scientists.
- Demonstrate next-generation protein sequencing platform with NIST scientists and resource (IMS fund)

Peter Fusco



- Establishing an Immunobiology Core at IBBR (expertise and interests)
  - Over 30 years of vaccine development experience from bench through licensure (NeisVac-C™, Certiva™, Scourmune®) in academia, small startups, and Fortune 500 corporation
  - Natural and recombinant proteins and polysaccharide conjugates for major bacterial, viral, and fungal diseases (DTaP, Mening, Pneumo, Strep, Hib, E.coli, Anthrax, Cdiff, Lyme, TB, Chlamydia, HIV, Flu, RSV, Dengue, Chikungunya, Candida, Aspergillus)
  - Functional vaccine assessment for correlates of protection and product stability
  - Why most investigational vaccines fail
  - Holy grail: chemistry to predict biology for vaccine potency
- Establishing anthrax vaccine development program (collaboration)
  - Polyphosphazene to replace alhydrogel as adjuvant for rPA
  - Combination with lipid A-based adjuvants and/or micro-needle patch delivery
  - Next generation anthrax vaccine for national stockpile requires fewer doses, accelerated response, and greater stability (reduce/remove cold chain)
- Establishing pneumococcal vaccine development program (collaboration)
  - Current standard of care for prophylaxis of pneumococcal disease (13-valent polysaccharide conjugate) losing efficacy due to serotype replacement (94+ serotypes)
  - $6.2 billion market (2015) needs protein-based vaccine replacement
  - Propose novel pneumolysoid adjuvanted with polyphosphazene

My Trajectory



- Immunobiology Core
  - Lab established to assess biological function for vaccines and therapeutics for IBBR, government, and industry partners – immunoassays, bioassays, toxin and viral neutralization
  - Relationship defined between chemistry and biological function – e.g., deamidation and vaccine potency
  - Facilitated by collaborations – e.g., IBBR and NIST for vaccines/therapeutics, IBBR and SOM for adjuvants, IBBR vivarium for immunogenicity, SOM and external labs for infectious challenge models
- Anthrax Vaccine
  - Improved anthrax vaccine to address government criteria for stockpile
  - Government (NIH/BARDA) interest/support for next generation product
  - Facilitated by collaborations within UMD – e.g., IBBR and SOM for adjuvants, IBBR vivarium for immunogenicity, NIH-sponsored infectious challenge by aerosol in established rabbit model for animal rule
- Pneumococcal Vaccine
  - Enhanced neutralization response to pneumolysin
  - Interest/partnership with Gates, WHO, industry
  - Facilitated by collaborations within UMD – e.g., IBBR for pneumolysoid constructs, IBBR and SOM for adjuvants, IBBR vivarium for immunogenicity in mice, SOM for pneumo infectious challenge model

Peter Fusco

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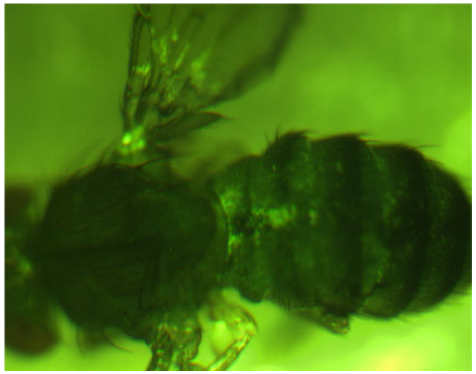
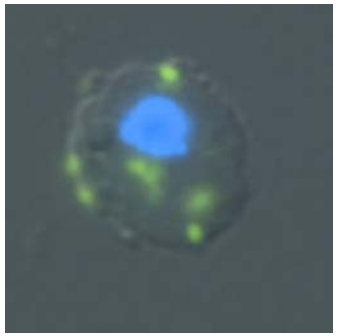
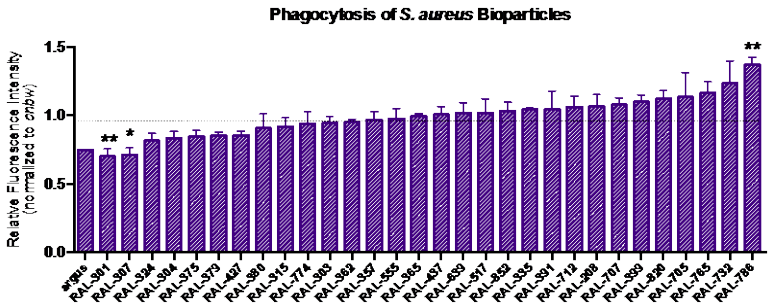
Louisa Wu, IBBR-CP

- Phagocytosis in Drosophila
- Antiviral immune responses in Drosophila
- Goal: identify new genes or pathways important for innate immunity
- Approaches: in vivo, genetic screens, genomic approaches (GWAS, hemocyte transcriptome)







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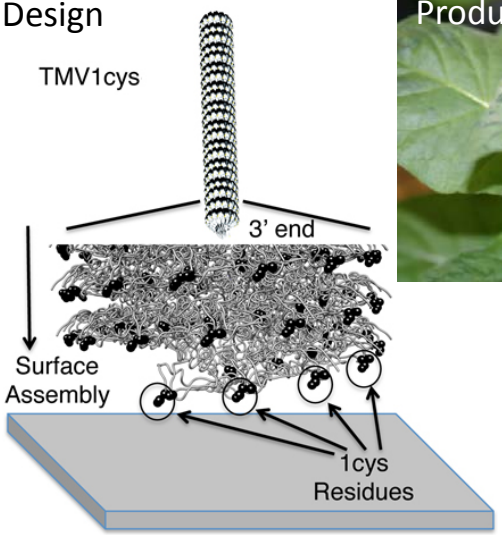
My Trajectory

- Systems biology level understanding of phagocytosis in Drosophila
- Understand what genes are important for specificity/recognition of different pathogens by hemocytes
- Look for any insights with doing GWAS in a model organism that might translate to human GWAS (collaboration with J Moult)
- Translate the work to mosquito immunity (in collaboration with DO'B)
- Not sure what will get me there faster…

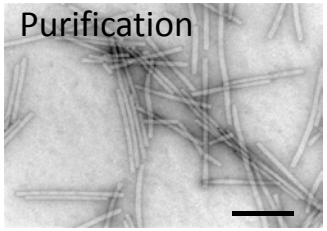
James Culver: Functionalization of Viruses and VLPs for Device Integration

Design

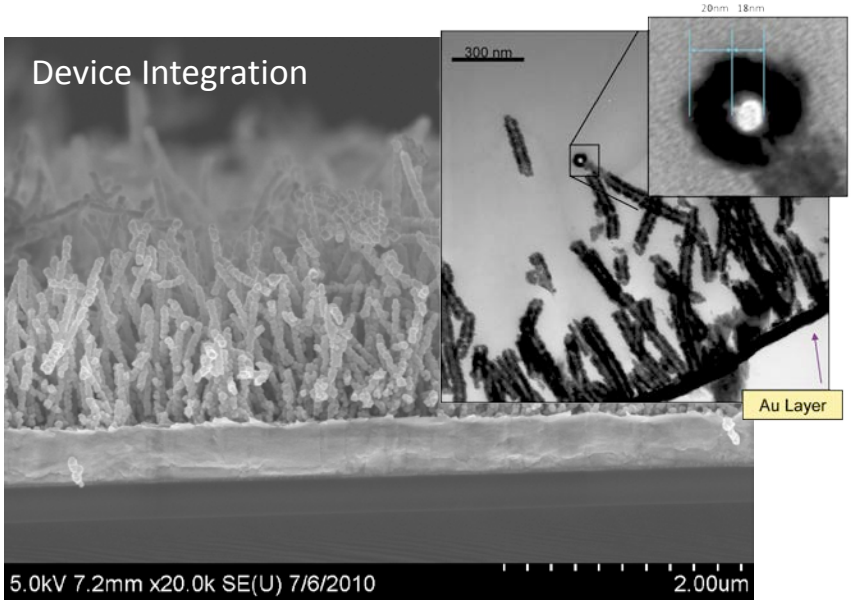


Production

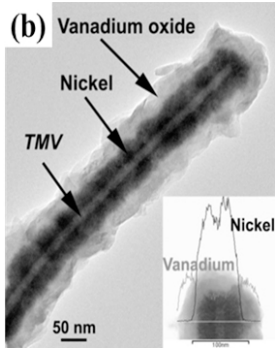
Purification



Device Integration

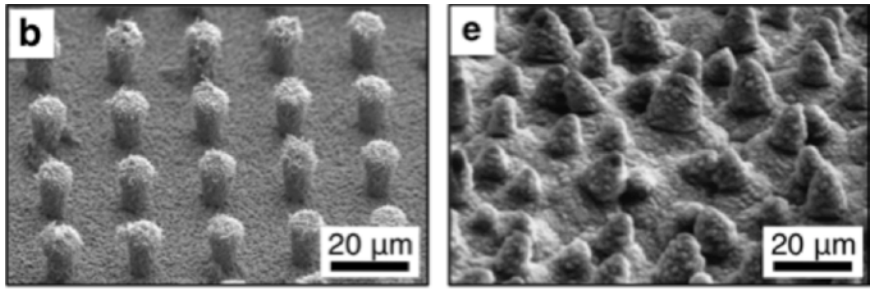


Batteries, Solar Cells, Fuel Cells
U.S. Patents 8,617, 869 & 8,383,237

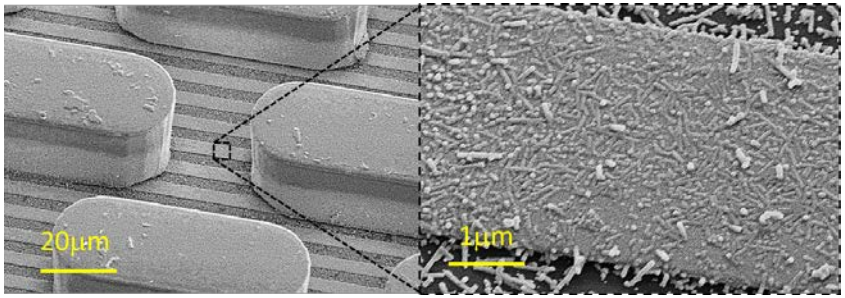


Harris, Ghodssi, Wang, Ehrman

Superhydrophobic Surfaces, Heat Exchangers
U.S. Patent 8,986,814 Ghodssi, Wang, McCarthy



Sensors – Label Free – Real Time – pM detection levels
Provisional Patent Filed Ghodssi



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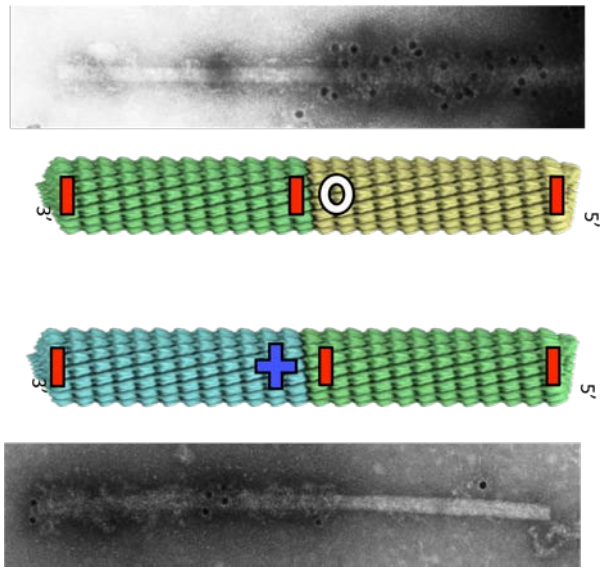
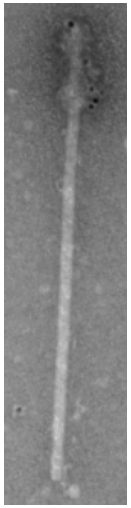
James Culver: Ongoing and Future Directions

Directed Assembly

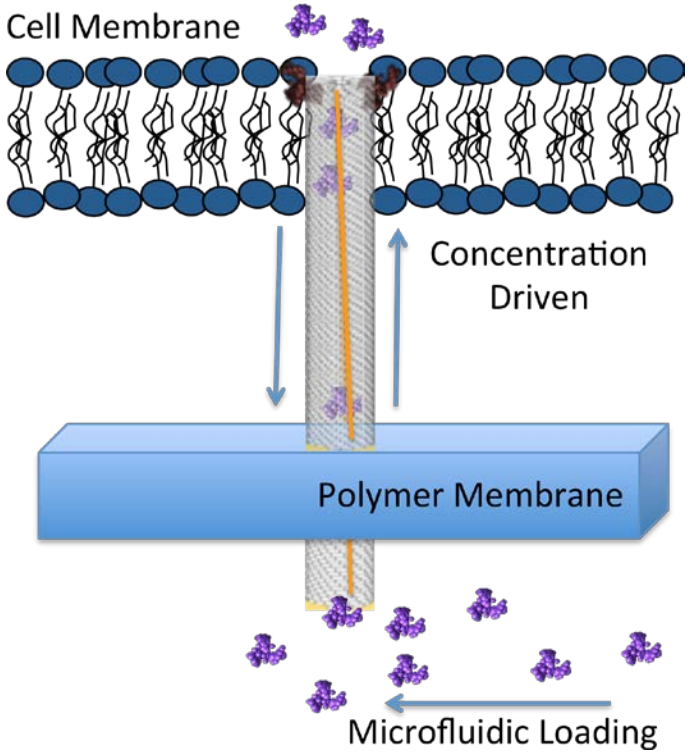


Nano Swabs

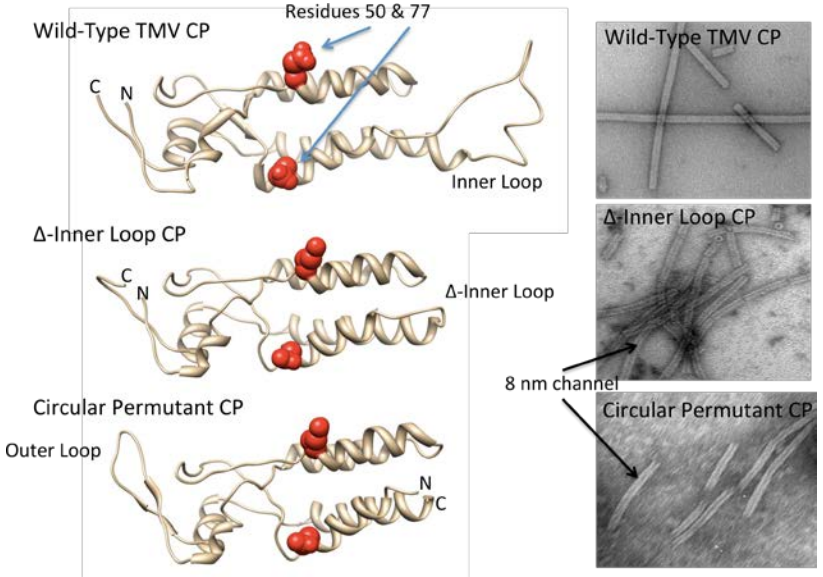


Cell - Device Communications: Cell Sampling and Control

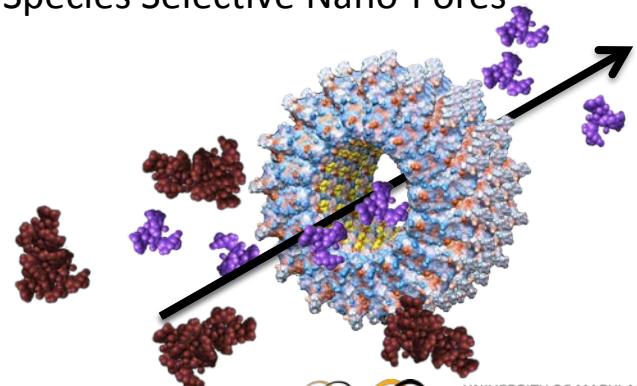
Future Goals



Inner and Outer Surface Modifications



Size and Species Selective Nano-Pores



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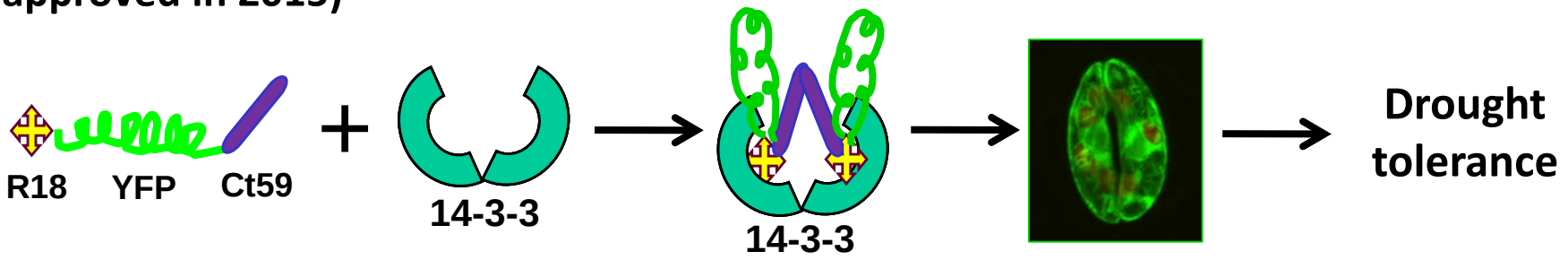
Shunyuan Xiao **Current Research**

Understanding & Engineering Stress Resistance in Plants

1. Membrane biogenesis and protein targeting in plant cells infected by powdery mildew fungi and engineering **novel resistance** (patent approved in 2015)

2. Engineer **drought tolerance** by manipulation of 14-3-3s in plants (patent approved in 2015)



3. Powdery mildew genomics----Genomes evolution and host adaptation

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Shunyuan Xiao

Future Research

Understanding & Engineering Stress Resistance in Plants

1. Plant nutrient transporters manipulated by pathogenic fungi

① Identification by genetic screens & sequencing

② Targeted mutagenesis in crops using CRISPR/Cas9

2. Reconstruction of immunity architecture of plant (Arabidopsis)

- Identification of novel immune components
- Making a universal host (susceptible to non-adapted pathogens)

3. Studying pathogenicity mechanisms of powdery mildew

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Greg Payne

- **Biofabrication of Functional Materials**
  - **What**? Build structure and function using materials and mechanisms from biology
  - **Why**? Biology is expert at building at the nanoscale and assembling over a hierarchy of length scales. Biology is poised to become the underpinning science for creating functional materials.
  - **How**?
    - Stimuli-responsive self-assembling biopolymers (chitosan, gelatin, alginate …)
    - Enzymes capable of cofactor-free synthesis (tyrosinase, transglutaminase …)
    - Advanced biology: protein engineering and synthetic biology
- **Redox-Based Molecular Communication between Biology and Electronics**
  - **What?** Establish "redox-connectivity" between biology and electronics
  - **Why?** Redox is a global modality that biology uses for communication and potentially provides an opportunity for systems-level interventions (analogous to defibrillation which intervenes globally through ionic mechanisms). Further, redox is accessible by electrochemistry.
  - **How?**
    - Impose electrical inputs at an electrode to probe-for or transfer chemical information
    - Employ diffusible mediators (electron shuttles) to convert the electrode inputs into redox "transmissions"
    - Receive and process the redox information from the output responses

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My Trajectory (Greg Payne)

- **Biofabrication Goals (Collaborations with Scientists; China)**
  - Broaden capabilities
    - Enlist more diverse biological materials and mechanism
    - Create more complex structures with controlled properties
    - Apply increasingly sophisticated biological methods to confer functionality
- **Redox-Based Molecular Communication Goals (Collaborations with Engineers)**
  - Deepen capabilities
    - Electrochemical methods
    - Signal processing (including reverse engineering)
- **“Killer” Applications (Collaboration with Practitioners)**
  - Sensing

Daniel Nelson – Summary of Projects

- **Development of Endolysins**
  - *Bacillus* (*B. anthracis* and *B. cereus*)
  - *Staphylococcus**(*S. aureus* and *S. epidermidis*)
  - *Streptococcus* (*S. pyogenes*, *S. pneumoniae*, *S. uberis**, *S. equi*, *S. suis**)
  - *Clostridium* (*C. difficile** and *C. perfringens*)
- **Biofilms**
  - *S. mutans, S. aureus, S. pyogenes*
- **Phage Structure/Function**
  - Tailspike proteins*
- **Development of Vaccines**
  - *B. anthracis*, C. difficile*, S. pneumoniae**
- **Azoreductases**
  - Tattoo removal
  - Bioremediation

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Daniel Nelson - Project Trajectory

- **Development of Endolysins**
  - Enzymes licensed to ContraFect, Elanco, Zoetis
  - Build on working relationship with Lysando (Roche)
  - First NDA will be watershed moment for the field
  - Development of 2nd generation endolysins
- **Biofilms**
  - Clinical trials for anti-biofilm “hep-lock”
- **Phage Structure/Function**
  - Progress structure/function science of bacteriohpage
- **Development of Vaccines**
  - Clinical trials in partnership with Integrated BioTherapeutics
- **Azoreductases**
  - Grants, corporate partners, spin out from I-Corps

Bill Bentley

- Synthetic Biology (rewiring signal transduction)
- Smart Probiotics (engineering motility, sensing)
- Animal on a chip (biological capcitor, sensors)
- Molecular Communication (devices)

My Trajectory

- Would like to electronically read and write to biological system (e.g. disease). Perhaps deliver therapeutic. Definitely as diagnostic. Need animal model.
- Would like to deliver commensal strains to treat disease. Need disease model.

Ofek Lab

- HIV-1 vaccine design
  - Structural basis for broadly neutralizing antibody (bNAb) lineage-dependent recognition of HIV-1 Env
  - Analysis of bNAb lineage development and virus co-evolution pathways in HIV-1 infection
  - Design of immunogens to guide development of lineage-specific anti-HIV-1 bNAbs
- HIV-1 bNAbs as immunotherapeutics and agents to clear the HIV-1 reservoir
- Filovirus vaccine design
  - Structural basis for protective and neutralizing antibody recognition of filovirus GP
  - Elicitation of pan-filovirus protective and neutralizing antibodies in nonhuman primates (NHP)
  - Design of filovirus GP immunogens to induce cross-reactive antibodies

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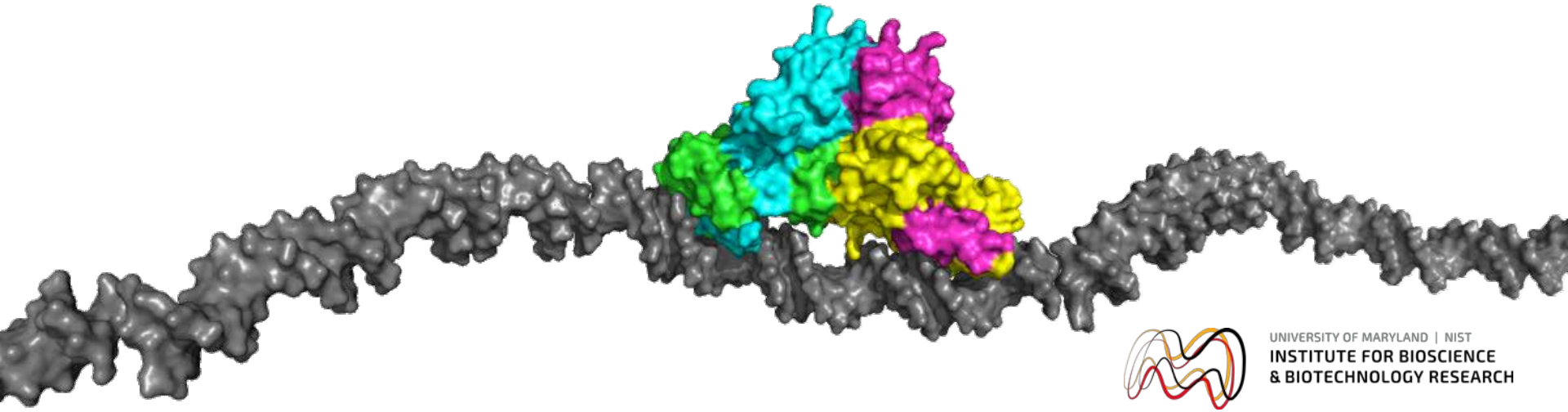
Ofek Lab, Trajectory

- Elicitation of lineage-specific antibodies that neutralize multi-tiered circulating HIV-1 strains with sufficient potency; faster if proper adjuvants, vaccine platforms, and associated mechanisms are investigated; faster with analysis of additional patient samples.
- Successful optimization of antibody potency and effector functions for use in immunotherapy and in reduction of latent HIV-1 reservoir; faster if markers of viral latency and mechanisms to reverse latency are investigated in parallel.
- Structural definition of pan-filovirus correlates of protection and associated design of pan-filovirus immunogens and therapeutic antibodies.

Ed Pozharski

- Biophysical and structural aspects of molecular recognition, including recognition of small molecules, DNA and protein-protein interactions
- Protein crystallography
- Evolution of bacterial transcription factors
- CBT: (diabetes) drug design



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My Trajectory

- Structural biology of large macromolecular complexes, including cryoelectron microscopy

John Moult

- Community wide experiments in computational biology.
- Computational studies of the relationship human genetic variation and disease (monogenic, complex trait, cancer).
- Analysis of mechanisms underlying Crohn's disease.
- Computational studies of protein structure and function.

My Trajectory

- Mechanism models of complex trait disease (*Current funding and collaboration with Lindley Darden, UMCP*).
- Community sourced models of specific diseases, particularly Crohn's (*Application pending*).
- Structure based analysis of mutations in monogenic disease and cancer (*Oriented to clinical pipelines, application awaiting dec*ision).
- Stability chaperones for protein folding disease (*IBBR)*
- Community experiments in genome interpretation (*Current funding*)

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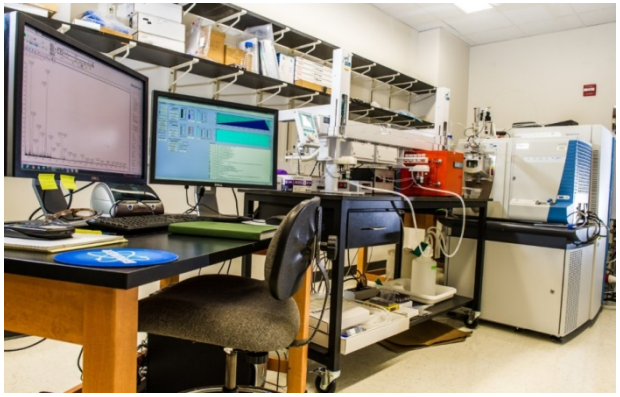
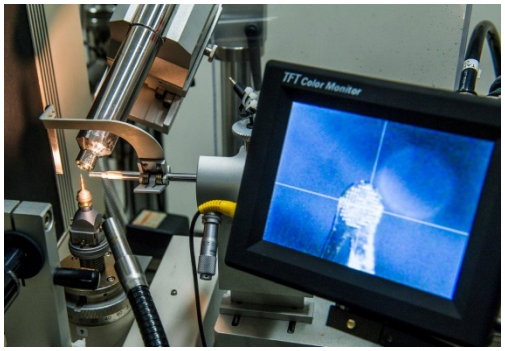
John P. Marino, Associate Director, Group Leader:
NIST Group Expertise & Capabilities in Biomolecular Measurements





NIST/Keck Laboratory for Structural Biology

600 MHz and 900 MHz NMR

Small Angle Scattering Laboratory

XRD, SAXS

Biomolecular Labeling Laboratory (BL^2)

Fermentation

Cell Culture

Mass Spectrometry Laboratory

HDX-MS

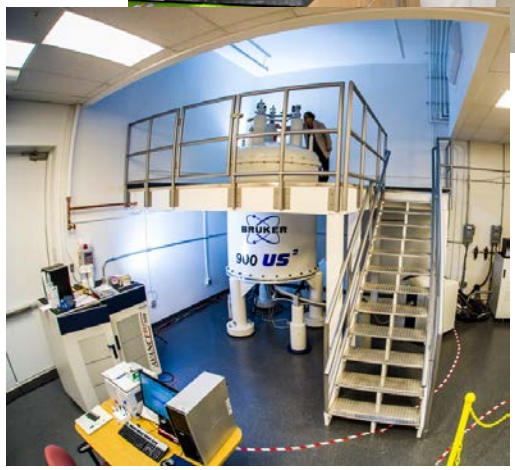
LC, CE-MS

Biophysical Tools

SPR, EIS,

Fluorescence

ITC, DSC



Research Focus

- Measurement science and standards to support the development and manufacture of biopharmaceuticals
- Proteomics tools for quantitative diagnostics of disease
- Hybrid Methods for Structural Biology: High-resolution, Small Angle Scattering, cryoEM, molecular modeling

Biomolecular Measurement Pillar @ IBBR
Where do we want to go in 5 – 10 years and how do we get there

The National Biotherapeutics Resource Center

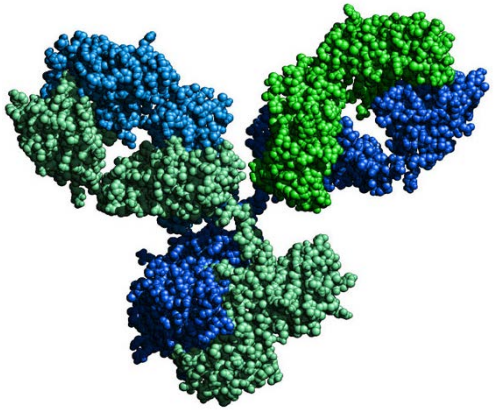
Biopharma Focus – fasting growing segment of the pharma industry

NIST and the University of Maryland have a opportunity to establish an internationally recognized research and education center (NBRC) dedicated to supporting development and manufacture of biopharmaceutical products through advanced measurement technologies and standards.

Structural Biology – Core Driver

Opportunity to develop and integrate NIST-IBBR into a local, hub that leverages internal strengths with national centers (NCNR and NCI- cryoEM) to become internationally recognized for hybrid methods in structural biology.

Focus on biopharmaceutically relevant proteins and protein complexes: (e.g. Glycoproteins and Membrane Proteins)



John P. Marino

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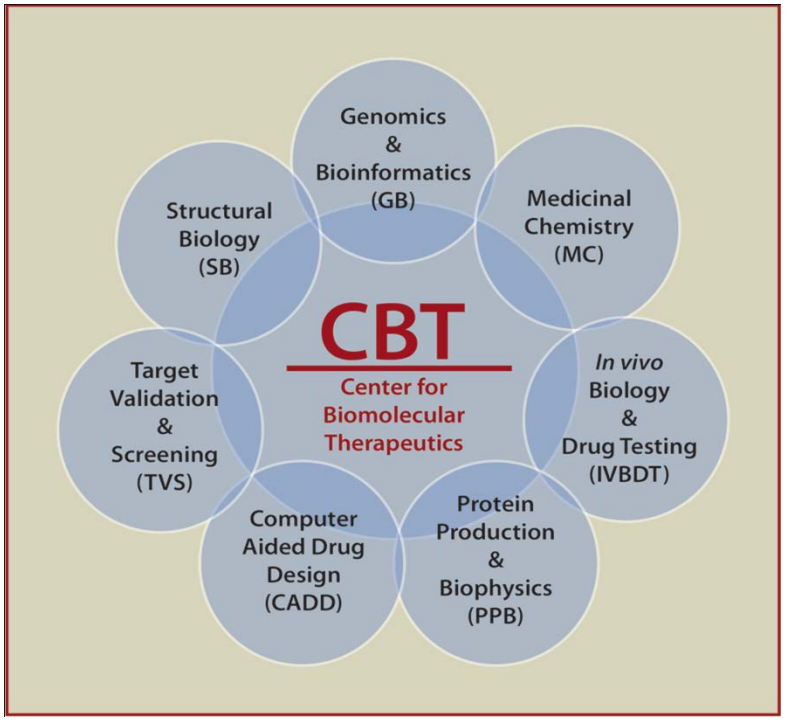
David Weber CBT

1. **Antibiotic:** Novel Antibiotics Targeting Lipid II
2. **Neurodegeneration:** Small molecule targeting to enhance cognition and prevent neurodegeneration
3. **CHKV:** Identify small molecule inhibitor of Chikungunya
4. **Melanoma**: Novel class of small molecule S100B inhibitors for the treatment of melanoma.
5. **Diabetes:** Targeting Grb10 interaction with insulin receptor for the treatment of diabetes



David Weber/CBT Trajectory

- Funnel novel biology and drug target innovations from UMB and other academic sources with greatest commercial potential and strategic fit with CBT's core scientific capabilities
- Translate to candidate small molecule drugs advanced to key commercialization milestones and stronger composition-of-matter patent protection
  - cryoEM
  - POC decision & $550-600K funding to reach POC milestone sufficient to generate Pharma interest
- Significantly increase value and improve prospects of developing pharma collaborations, company start up investments and licensing, as well as improve prospects for research grants

Tom Fuerst

- Interests
  - Development of next generation structure-based vaccines, immunotherapeutics, and delivery technologies
- Expertise
  - Virology, biochemistry, and recombinant genetic systems
    - Antibody-antigen relationships and corresponding qualitative and quantitative techniques to evaluate and measure binding interactions
    - Recombinant genetic systems for protein expression and characterization (viral, bacterial, and hybrid genetic systems)
  - Biomolecular engineering and development testing
    - Design and construction of optimal antigenic determinants to serve as immunogens to elicit broadly neutralizing antibody responses
    - Design and construction of recombinant antibodies and related molecules
    - Formulation and delivery of biomolecules to optimize effector functions, e.g., virus-like particles, recombinant vector systems, immunoadjuvants, etc.
    - Preclinical studies to demonstrate vaccine/immunotherapeutic efficacy
  - Culture systems for viral and bacterial systems
    - Culture systems associated with enveloped (e.g., vaccinia, flu, HCV, etc.) and non-enveloped (e.g., HEV, HRV, etc.) viruses
    - Culture systems for difficult bacterial organisms such as mycobacteria

My Trajectory

- Goal: Novel design and successful pre-clinical/clinical testing of structure-based vaccines, e.g., HCV, pan-filovirus, etc.
  - Funding from NIH, NGO, corporate R&D partnerships, endowment fund
  - Build programmatic strength and new targets
- Goal: Novel design and successful pre-clinical/clinical testing of SMART molecule therapeutics
  - Funding from NIH, corporate R&D partnerships, endowment fund
  - Build programmatic strength and new targets
- Goal: Novel design and successful pre-clinical/clinical testing of immunoadjuvant and delivery technologies for vaccines and immunotherapeutics
  - Funding from NIH, NGO, corporate R&D partnerships, endowment fund
  - Build programmatic strength and new targets
- Goal: Facilitate Institute-wide interdisciplinary programs
- Goal: Facilitate an Institute-wide grand scientific challenge

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Protein Production & Biophysics (PPB)

Protein Production

- ✓ Cloning and recombinant protein expression in *E. coli* and baculovirus expression systems (BVES)
  - DNA expression vector catalogue
- ✓ Purification of affinity tagged and native protein
  - Purified protein catalogue
- ✓ Uniform and selective isotope labeling

Biophysics

- ✓ Thermodynamic and kinetic stability, structure/dynamic properties, size, covalent modification
- ✓ Enzyme kinetics and binding
- ✓ Biophysical/biochemical techniques: **ITC, DSC, CD, Fluorescence, NMR, UV/Vis, DLS, AUC**…

Raquel Godoy-Ruiz, PhD
PPB Section Leader

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How I would like to see PPB section in 5 years….

- Mammaliam cell-mediated protein expression for structural studies
  - Ability to produce biologically active cell surface receptors and secreted glycoproteins
  - Spinner flasks or bioreactors
- Recombinant protein characterization by ESI-MS
- High-Throughput screening of stability and binding interaction by Differenctial Scanning Calorimetry (DSC) and Isothermal Titration Calorimetry (ITC)

EDUCATION & TRAINING

- Undergraduate Program in collaboration with USG
- IBBR High School Program

Raquel Godoy-Ruiz, PhD
PPB Section Leader

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