Undergraduate Biochemistry Experience

Education
- major is offered as both BA and BS
- faculty advisor is assigned from major declaration until graduation
- Dr. David Samols, program director: david.samols@case.edu

Community: CUBS (CWRU Undergraduate Biochemistry Society)
- virtual and in-person activities (e.g. ice-cream, pizza)
- mentorship program with upperclassmen
- study hours, study breaks, unwinding events
- interactions with faculty (mixers, presentations)
- monthly newsletter
- https://community.case.edu/biochem/home/
- email CUBS executives at: cwru-ubs-exec@case.edu
Biochemistry BA & BS

- students obtain experience in original research
  - research experience is required for the major
  - most students join research labs in Biochemistry or other departments in the School of Medicine
  - some students join labs in UH, CCF, VA, CAS
  - research approaches vary from working with purified molecules to animal models of disease

- most graduates go on to medical/dental/professional/graduate school, or to industry
Biochemistry Junior and Senior Years
SAGES, Research, and Capstone

Biochemistry Research

**BIOC 391**
- 3 unit Pass/Not Pass course requires >10 hours of lab time/week
- can take max of 9 units total
- hands-on experiments in a research laboratory
  (remote accepted during covid)
- does not have to be with Biochemistry faculty but must be “biochemical”

Biochemistry Capstone

**Bioc 393**
- written manuscript describing research efforts
- poster or oral presentation at departmental retreat

Biochemistry SAGES

**BIOC 373**
- lectures and discussions; how to prepare, read, and evaluate manuscripts;
  written and oral assignments
Research in the Department of Biochemistry

What is biochemistry?

“The study of chemical processes within and relating to living organisms” (wiki)
“Understanding biology from a molecular point of view”

Biochemistry faculty areas of research interest:

- antibiotic resistance
- cancer biology
- drug discovery
- epigenetics
- metabolism
- neurobiochemistry
- RNA biology
- transcriptional regulation
- etc.
What is the synergistic impact of 2 known drugs on melanoma growth?
- palbociclib (CDK4/6 inhibitor)
- everolimus (mTORC1 inhibitor)
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Hung-Ying Kao: Breast cancer disease mechanism and treatment

Targeting endocrine-resistant estrogen receptor-positive breast cancer-associated ER mutants

Promyelocytic leukemia protein (PML) in ER-positive breast cancer
Kao lab: Breast cancer disease mechanism and treatment

Sulforaphane antioxidants modify cysteines in PML

Sulforaphane can control abundance and localization of PML
Focco van den Akker: Bacterial antibiotic resistance and drug discovery

Diagram showing the interaction between different antimicrobial agents and bacterial resistance mechanisms.
van den Akker lab: Bacterial antibiotic resistance and drug discovery

Crystal structure of *P. aeruginosa* penicillin-binding protein 3 (PBP3) bound to novel β-lactam ceftobiprole (Kumar *et al*, 2020)
Prion diseases
- fatal neurodegenerative disorders
- unique: infectious agent is the prion protein
- prion protein refolding and aggregation disease mechanism
- methionine -> valine polymorphism at residue 129 predisposes to some human prion diseases
- approach: determine and compare structures of methionine vs valine versions of the human prion protein
Met129 Val129

Yee lab: Disease mechanisms
Drug Discovery

Prion protein crystal structures
- proteins with Met129 form intermolecular β-sheets
- proteins with Val129 do not

Prion peptide crystal structures
- peptides with Met129 form parallel β-sheets
- peptides with Val129 form tilted β-sheets
**Insulin**
- a peptide hormone secreted by pancreatic β-cells in response to high glucose
- binds to receptor and initiates the uptake of glucose by peripheral tissues
- low insulin causes diabetes; treatment is with insulin supplementation
- insulin is a small 2-chain globular protein that is stored as a Zn$^{2+}$-bound hexamer in the β-cells

**Nelson Phillips: Developing new insulin drugs**
Designing new insulin drugs
- more stable insulins will extend shelf life/storage of drug
- structure-function approach used in design of ultrastable single chain insulins
- need to maintain function (receptor binding)
- need to be more stable than “regular” insulin but not form insoluble amyloid fibrils

Phillips lab: Developing new insulin drugs
**Goal**
- understanding brain signaling pathways in decision-making, locomotion, and innate immunity

**Approach**
- use a cockroach model system
- use wasp venom (mixture of active compounds) that targets the cockroach brain -> causes changes in gene expression -> reveals signaling pathways
Arvidson lab: Brain signaling pathways

**Approach**
- elucidate the cockroach brain transcriptome upon wasp venom treatment
  -> identify expressed genes and their relative expression levels
- computational molecular modeling and molecular dynamics to probe structure-function relationships of expressed cockroach proteins

- structure-function relationships of identified wasp venom proteins
  - e.g. adenosine deaminase, hyaluronidase
Genetics
- DNA sequence in genes

Epigenetics
- regulation of gene expression
  (e.g. histone modification, DNA modification, nucleosome positioning)
How does the histone methyltransferase DOT1L regulate gene expression and embryonic development?

Comparing gene expression in wild-type and knockout cells

Comparing embryonic morphology in wild-type and knockout mice
Health is determined by both genes and environment.

“Big Data” approach:
- effect of genetic variation on RNA-binding proteins
- wearable technology to monitor health
Li lab: Determinants of health: genome and exposome

Regulatory variation and genetic control of RNA binding protein (RBP) in humans

Mutations alter post-transcriptional regulation by RNA-binding proteins
Research in the Department of Biochemistry

What is biochemistry?

“Understanding biology from a molecular point of view”

- development
- epigenetics
- metabolism
- neurobiology
- RNA biology
- transcriptional regulation
- etc.

- understanding disease
  - brain disorders
  - cancer
- drug discovery
  - antibiotics
  (overcoming resistance)
  - cancer
- optimizing health
- etc.
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