André K. Isaacs

Born in Kingston, Jamaica in 1981

Education:
Schooling in Jamaica
BA (Chemistry) from College of the Holy Cross
PhD (2011) from UPenn (Supervised by Jeffrey Winkler)
Postdoc (2011-2012) at UC Berkeley (Supervised by Richmond Sarpong)

Independent Career:
Assistant Professor (2012 – 2018), College of the Holy Cross
Associate Professor (2018 – till date)

PhD research: Design and development of cyclopamine-derived inhibitors of Hedgehog-signaling

Postdoc work: Synthesis of diterpenoids and radiolabeled chlorantraniliprole

Independent Research: Click chemistry, especially Cu-catalyzed cycloaddition of sulfonyl azides and terminal alkynes and differential fragmentation of the triazoles to form synthetically relevant electrophiles

Graduate Research

A brief discussion about the Sonic Hedgehog Protein (*SHH*)

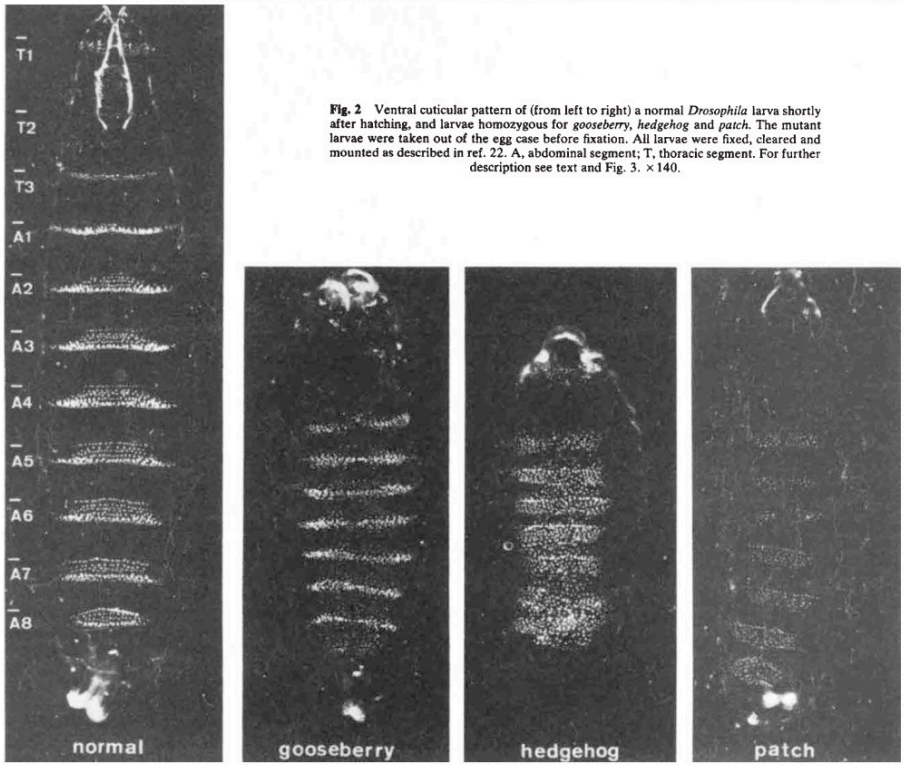
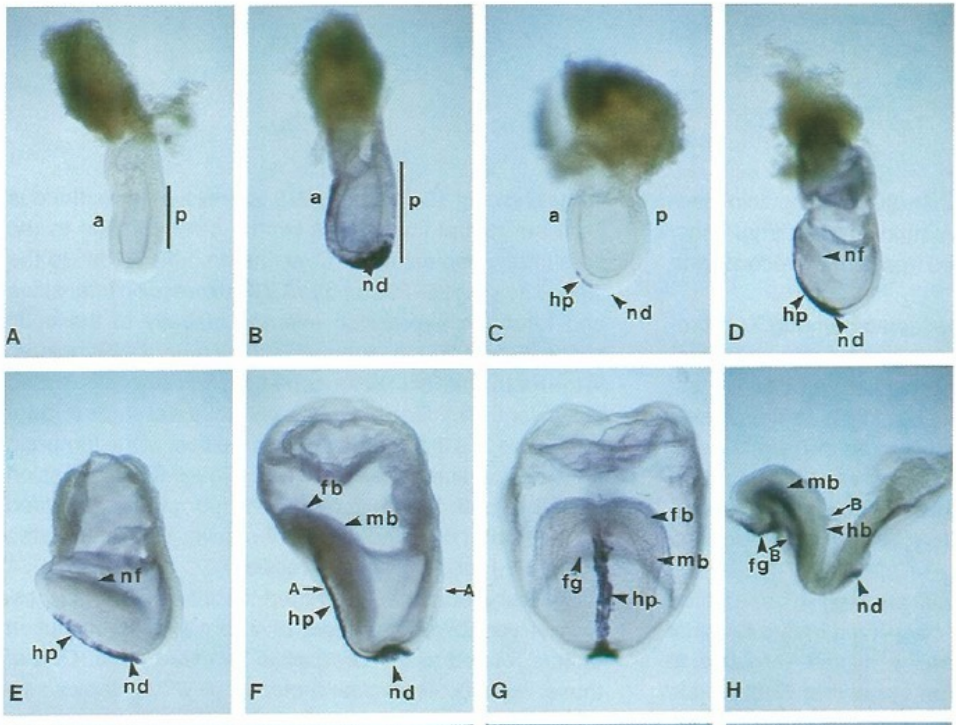


Fig. 2 Ventral cuticular pattern of (from left to right) a normal *Drosophila* larva shortly after hatching, and larvae homozygous for *gooseberry*, *hedgehog* and *patch*. The mutant larvae were taken out of the egg case before fixation. All larvae were fixed, cleared and mounted as described in ref. 22. A, abdominal segment; T, thoracic segment. For further description see text and Fig. 3. ×140.

Sonic Hedgehog, a Member of a Family of Putative Signaling Molecules, Is Implicated in the Regulation of CNS Polarity



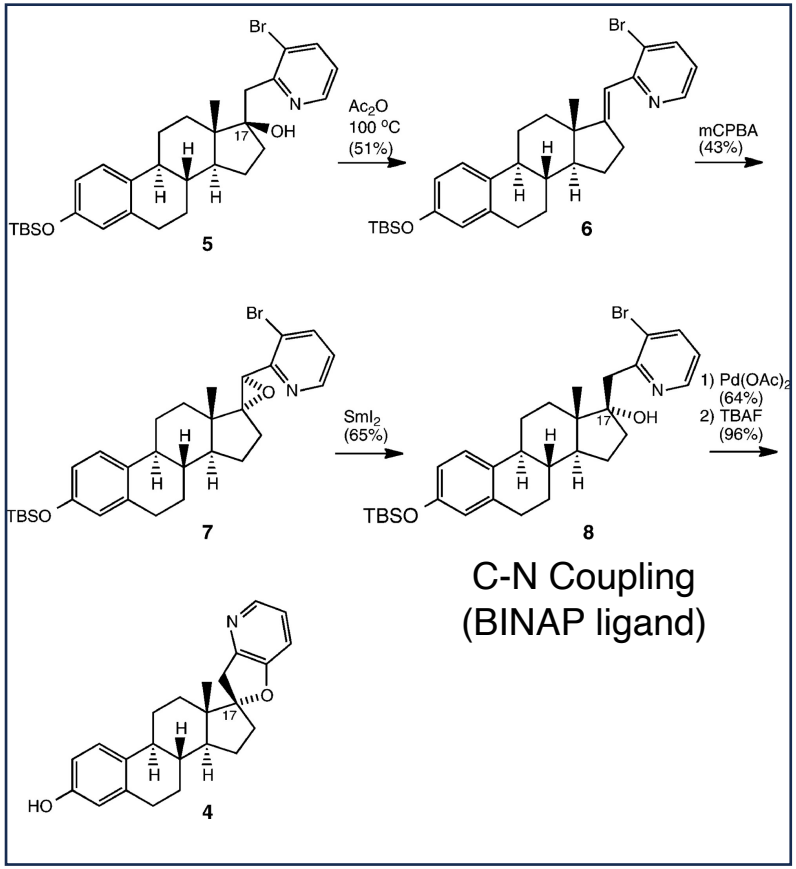
Originally named after a Drosophila protein (hh) that regulates organogenesis (formation of organs) during embryonic development – loss of gene causes formation of spikes in embryo – won 1995 Nobel prize in Physiology

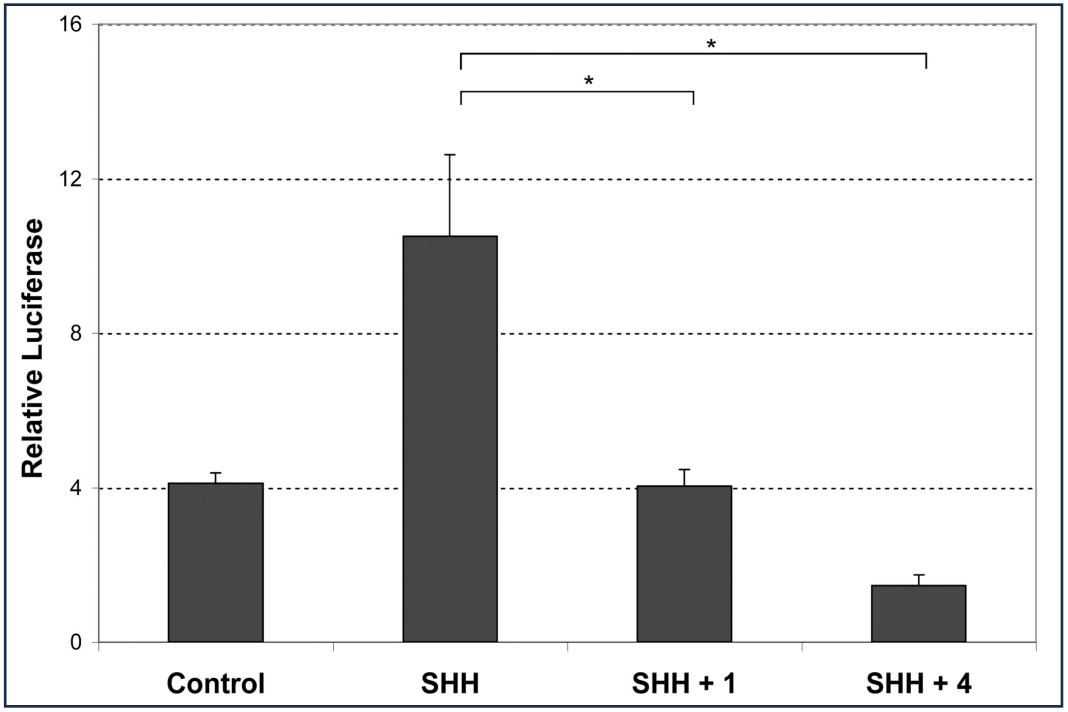
Later found in vertebrates (i.e. Zebra fish, mice, humans); **modulated by steroids**

Nature. **1980**, *287*, 795-801; *Cell*, **1993**, *75*, 1417-1430.

Graduate Research

Studies Directed toward the Elucidation of the Pharmacophore of Steroid-Based Sonic Hedgehog Signaling Inhibitors





Synthesized and tested various steroids to determine what pharmacophores are important for SHH inhibition using luciferase assays.
Determined 3-D structure less important than H-bonding

Isaacs, AK, Xiang, C, Baubet, V, Dahmane, N, and Winkler, JD. *Org. Lett.* **2011** *13*(**19**), **5140-5143**

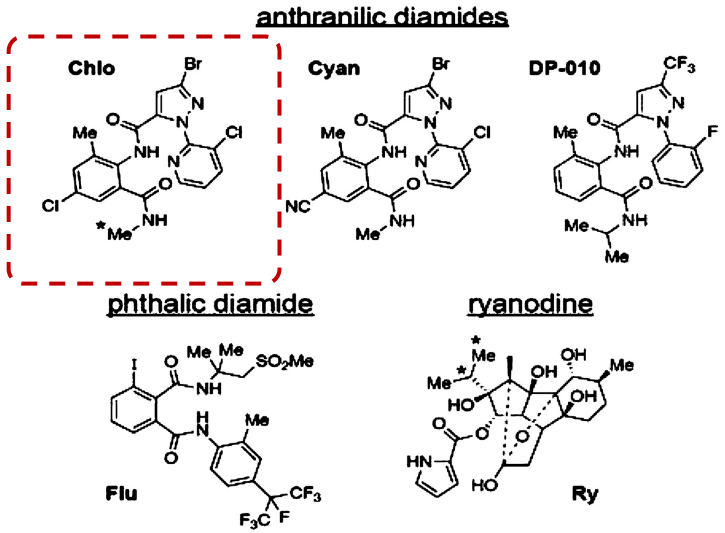
Chemical Research in Toxicology

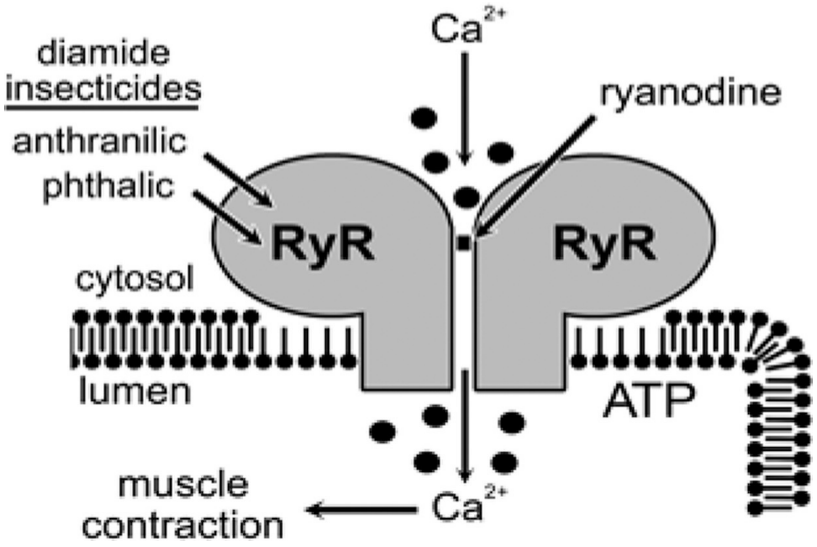
Insect Ryanodine Receptor: Distinct but Coupled Insecticide Binding Sites for [*N*-C^3H_3]Chlorantraniliprole, Flubendiamide, and [^{3}H]Ryanodine

André K. Isaacs,[†] Suzhen Qi,[‡] Richmond Sarpong,[†] and John E. Casida*,[‡]

Postdoc Research

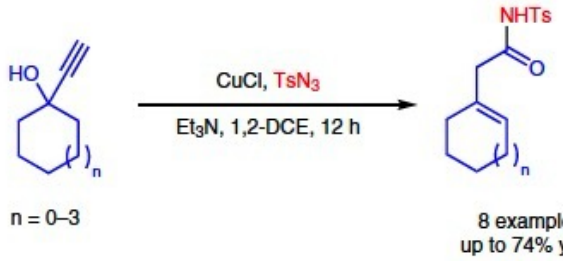
- diamides are a major class of insecticides
  - two classes: anthranilic and phthalic
- bind to insect ryanodine receptors (RyR) for intracellular release of Ca^{2+}
- synthesized [*N*-C^3H_3]Chlorantraniliprole for use in radioligand binding studies
- first direct evidence that anthranilic and phthalic diamide insecticides bind at different but allosterically coupled sites





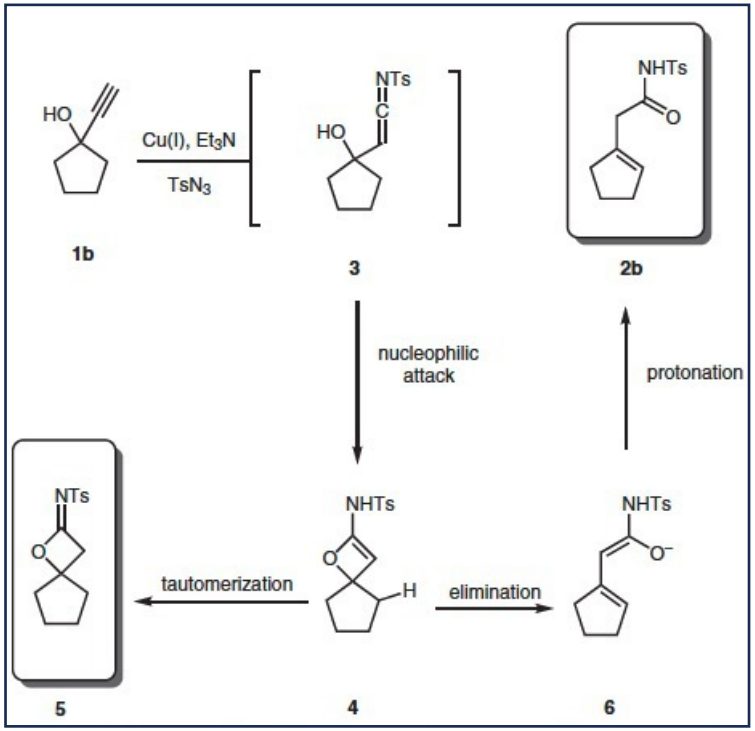
Independent Career I

Cu(I)-Catalyzed Synthesis of β,γ-Unsaturated Amides



Entry	Substrate 1	Product 2	Yield (%)
1	1a	2a	70
2	1b	2b	30[b]
3	1c	2c	33
4	1d	2d	35
5	1e	2e	65
6	1f	2f	70
7	1g	2g	74
8	1h	2h	51

Accesses unsaturated amides through CuAAC and subsequent rearrangements



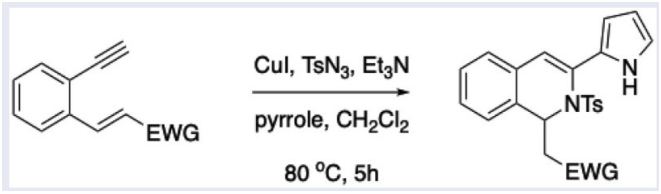
Bosse, AT, Tsougranis, GH, DeTroia, CD, Tejidor, FJ, Isaacs, AK. *Syn. Lett.* **2018,** *29*, **463-466**

Independent Career

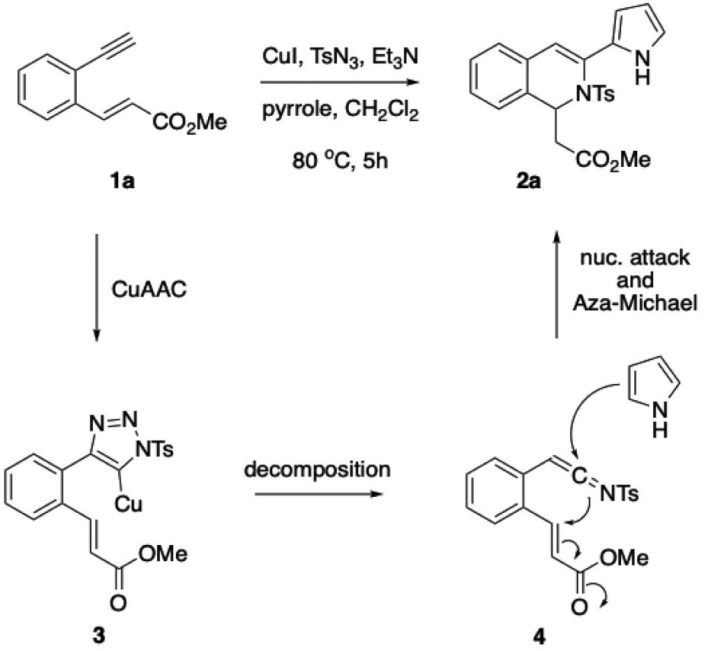
SYNTHETIC COMMUNICATIONS®
2022, VOL. 52, NO. 5, 755–763
https://doi.org/10.1080/00397911.2022.2050758

Copper-catalyzed three-component synthesis of pyrrole-substituted 1,2-dihydroisoquinolines

Matthew D. Floyd, Lianne Y. Ryan, Jessica L. Hendsey, Joshua M. Nicholson, Andrew T. Palaia, and André K. Isaacs

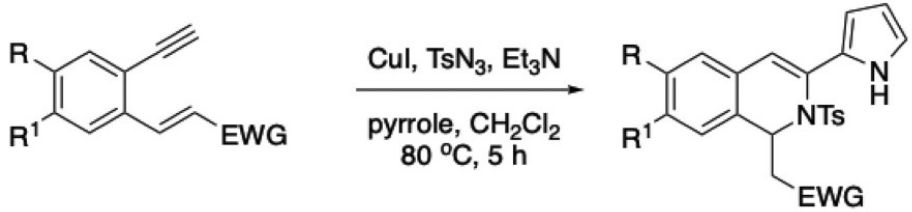


Project goal: *accomplish the synthesis of 1,2-dihydroisoquinolines via Cu-catalyzed click chemistry through a ketenimine*



Scheme 3. Proposed mechanism.

Selected scope



1i: R = H; R^1 = OMe, EWG = CO_2Me
1j: R = F; R^1 = H, EWG = $COCH_3$
1k: R = CH_3; R^1 = H, EWG = $COCH_3$
1l: R = F; R^1 = H, EWG = CN
1m: R = R^1 = OMe, EWG = CO_2CH_3

2i: 57%
2j: 71%
2k: 60%
2l: 58%
2m: 65%

Publications in Outreach and Education

Comment | Published: 16 May 2023

How to attract the next generation of chemists

André K. Isaacs

Nature Reviews Chemistry **7**, 375–376 (2023) | Cite this article

"Getting the next generation to participate in chemistry will require dismantling normative approaches to education and mentoring.

Inclusive pedagogy that incorporates social issues and innovative teaching with special attention to historically excluded groups are keys to unlocking the full potential of future scientists."

Publications in Outreach and Education

Social Media as a Tool

- Start by meeting students where they are (e.g. social media)
- Powerful tool to engage with younger generations' culture and social concerns
- Provides a platform for scientific communication (e.g. Hank Green)

We don't have to all turn to posting Tik Toks to explain chemistry, but can take lessons from the personalized and relatable methods for delivering scientific information that internet personalities employ

Publications in Outreach and Education

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Diversity is a Strength

- We must work to elevate the voices of successful minoritized chemists and bring diverse representation to the forefront
- Promote the expression of joy and balance in the classroom and the lab
- Students who are valued and supported will be more driven to do transformative scientific work

Broader representation and diverse engagement brings strength to the scientific community, allowing us to generate more questions, solve more challenges, and further advance knowledge

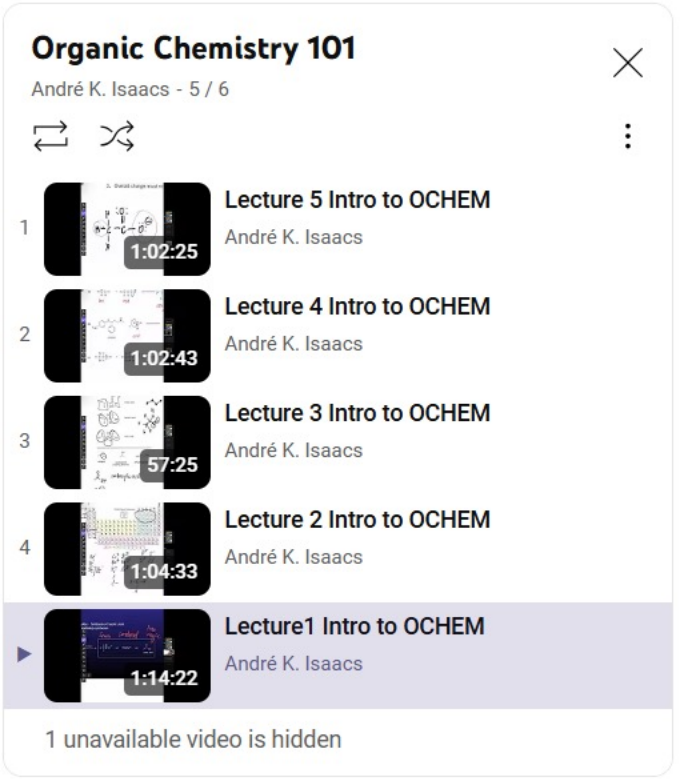
Outreach

Short videos on TikTok.
“Right now, students use social media so much, so I find myself on it too just to learn their vocabulary.”

Live course on TikTok and recorded lecture on YouTube.
Intro to Organic Chemistry

Students’ feedback:
He presented the material in a way that was like, ‘I want you guys to see how cool and exciting this is’.

Andre cofounded Outfront (Holy Cross) to support LGBTQIA+ faculty and students and increase their visibility on campus.



Alisha Jones - CV and Background

2006 - 2010:
B.S. Zoology, Miami University of Ohio
B.A. Chemistry, Miami University of Ohio

2010 - 2015:
Ph.D. in Chemistry, University of Washington

2015 - 2016:
Postdoctoral Researcher, University of Washington

2017 - 2022:
Postdoctoral Researcher, Helmholtz Zentrum München

2023 - present:
Assistant Professor of Chemistry, New York University

MIAMI UNIVERSITY

UNIVERSITY OF WASHINGTON 1861 LVX SIT

HELMHOLTZ MUNICH

NYU

Awards and Outreach

Awards:

2010: Presidents Distinguished Service Award
Miami University

2012: NSF GRFP, University of Washington

2012: Graduate Student Merit Fellowship
University of Washington

2013: 63rd Lindau Nobel Laureate Meeting in Chemistry
University of Washington

2019: 18 of the last 9 Award, Miami University
Celebrates 18 alumni of the last 9 years

Outreach:

Amongst other, she created the LiNC program at NYU

The LiNC Program: "serves the purpose of linking **STEM-focused high school students from traditionally excluded groups** with students who are just steps ahead of them to tackle the vast unknowns of the long noncoding RNA (lncRNA) world."

- Collaborative team of graduate students, undergraduate students, and high school students to probe RNA structure and RNA-protein interactions
- 4-6 high school students per year
- Provides a stipend and housing (for out of state students)

Research Focus during PhD

RNA structural biology

- RNA often adopts complex and diverse 3D shapes, essential for its functionality
- Describes the study of the three-dimensional (3D) structure of RNA
- Focuses on understanding the intricate shapes that RNA molecules adopt
- structure of RNA determines how it interacts with other molecules, including proteins, other RNA molecules, and small molecules

Research Focus during PhD

RNA-protein and RNA-ligand interactions

- **RNA-protein** and **RNA-ligand** interactions refer to the specific binding events between RNA molecules and proteins or small molecules (ligands).
- Interactions are essential for many biological processes, including gene regulation, RNA processing, and cellular signaling

RNA-based regulatory mechanisms

- **refers** to the various ways that RNA molecules regulate gene expression, RNA processing, and cellular function.
- RNA-based regulation is a dynamic and essential aspect of cellular control, influencing processes such as development, stress responses, and disease states.

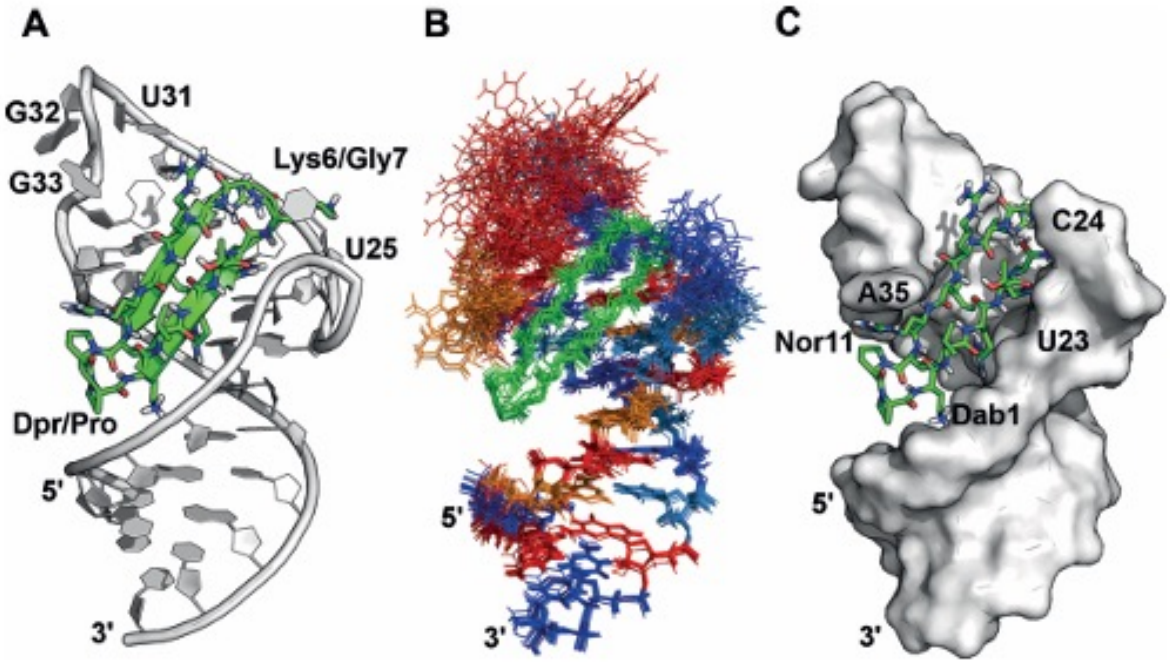
An ultra-high affinity ligand of HIV-1 TAR reveals the RNA structure recognized by P-TEFb

M. D. Shortridge†, P. T. Wille†, **A. N. Jones†**, A. Davidson, J. Bogdanovic, E. Arts, J. Karn, J. A. Robinson, G. Varani

- **HIV-1 TAR RNA** refers to a specific region of the RNA genome known as the **T**rans-**A**ctivation **R**esponse element
- The **TAR RNA** is a **stem-loop** structure located near the 5' end of the HIV-1 RNA genome.
- Function: **TAR RNA** plays an important role in the HIV's ability to replicate and regulate the transcription of the viral genome.
- Mechanism: The **TAR RNA** serves as a binding site for the viral protein **Tat** (**T**rans-**A**ctivator of **T**ranscription), which is critical for the virus's replication.
- **Tat** binds to **TAR RNA** → enhances transcription of the HIV-1 genome → more viral RNA and proteins produced.
- The **stem-loop** structure of **TAR RNA** is a secondary structure which is important for its interaction with the **Tat** protein.
- **Stem-loop** is highly conserved among different strains of HIV-1 → important target for antiviral therapies
- HIV hijacks the normal cellular machinery, including **P-TEFb** (**P**ositive **T**ranscription **E**longation **F**actor **b**, protein which regulates transcription elongation) to facilitate the transcription of its RNA genome during the viral life cycle

An ultra-high affinity ligand of HIV-1 TAR reveals the RNA structure recognized by P-TEFb

M. D. Shortridge†, P. T. Wille†, **A. N. Jones†**, A. Davidson, J. Bogdanovic, E. Arts, J. Karn, J. A. Robinson, G. Varani



Structure of JB181 bound to HIV-1 TAR RNA

This work:

- Rational design of macrocyclic peptide JB181
- JB181 mimics the arginine-rich motif of **Tat** and binds **TAR** with ultra-high affinity (K_D(HIV) < 0.180 nM) and specificity.
- Despite its strong binding, JB181 only moderately inhibits **Tat**-dependent transcription and **P-TEFb** recruitment.
- Structural analysis suggests that targeting the **TAR** loop, rather than just the UCU bulge, is crucial for effective inhibition of SEC recruitment.

Nucleic Acids Research, **2019**, *47*, 1523–1531

PostDoc Work

2017 – 2022

Postdoctoral Researcher with Prof. Dr. Michael Sattler

Helmholz Zentrum München, Germany

Prof. Dr. Michael Sattler

PostDoc Work

PostDoc Work

2017 – 2022

Postdoctoral Researcher with Prof. Dr. Michael Sattler

Helmholz Zentrum München, Germany

Advisor is an expert in:

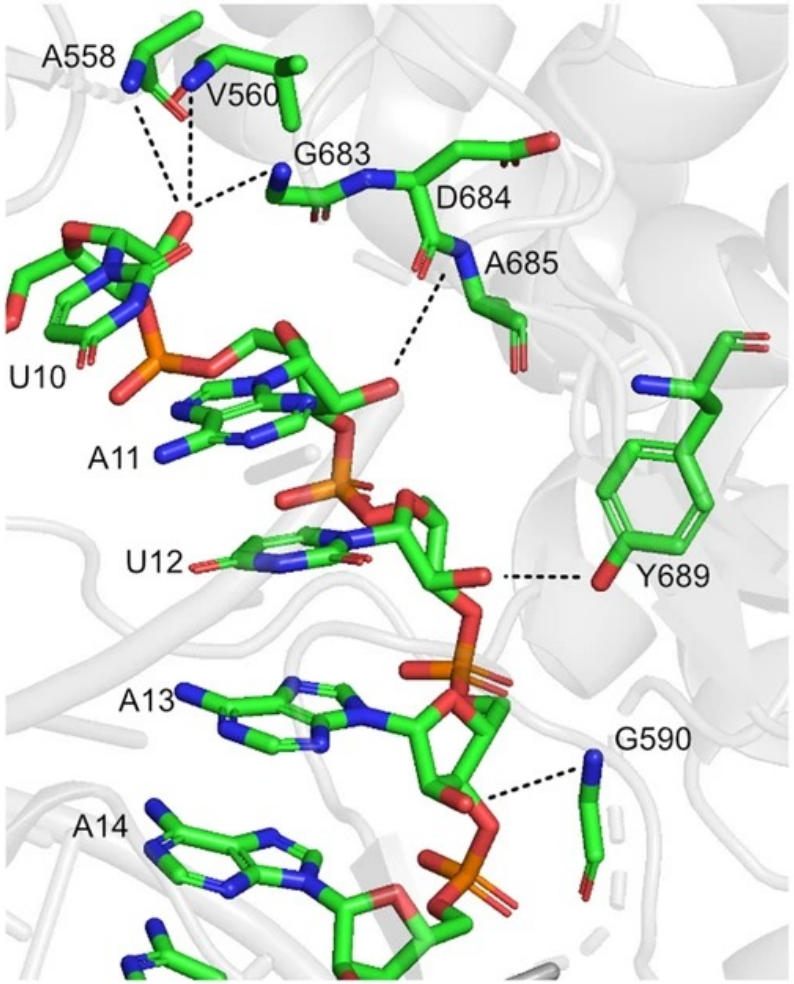
- Intergrades structural biology
- Biomolecule NMR spectroscopy
- RNA-mediated gene regulation
- miRNA processing

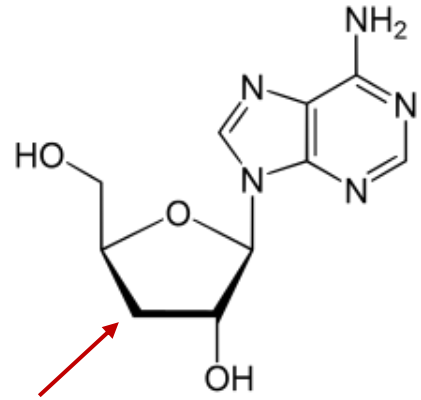
Prof. Dr. Michael Sattler

- Worked on SARS-CoV-2 research, cancer biology, immunology, and fundamental RNA research
- 13 publications associated with postdoc advisor

Characterization of SARS-CoV-2 replication complex elongation and proofreading activity

- SARS-COV-2 uses one of the fastest RNA-dependent RNA polymerase (RdRp) Nsp12, for copying the RNA genome
- Elongation process with RdRp is susceptible to errors → mutation → more difficult to drug than SARS-CoV-1
- This work: Taking advantage of the error prone nature of SARS-CoV-2's RdRp
- Authors found that 3'-OH and 2'-OH are critical for RdRp template recognition and elongation
- Nsp12 forms contacts (i.e. H-bonds and electrostatic interactions) with RNA through the 2′OH group of the ribose
- A 2'-OMe-terminated chain failed to be degraded by exonucleases that perform a proofreading function
- Any 3'-deoxy nucleic acid terminated chain failed to be degraded





Missing 3'-OH

Cordycepin

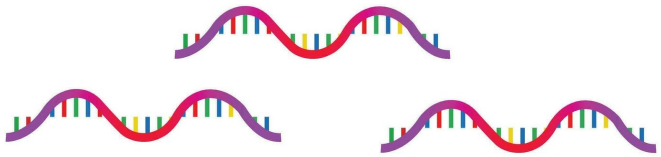
Jones, AN, et al, *Scientific Reports*, **2022**, 12, 9593

Independent Research

- Main Focus: Investigations and structural characterizations of long noncoding RNA (lncRNA, >500 nucleotides, do not encode for protein)
- Inherent flexibility of RNA enables it to take on many shapes, and subsequently functions
- But: Crystallization becomes challenging → X-ray crystallography or cryo-electron microscopy unfeasible
- Alternative: NMR spectroscopy to determine RNA structure.
  Problem: NMR is more effective for short strands of RNA, not lncRNAs.
- Ultimate goal: Identify a structure that can be blocked with a therapeutic agent

lncRNAs

Degradation

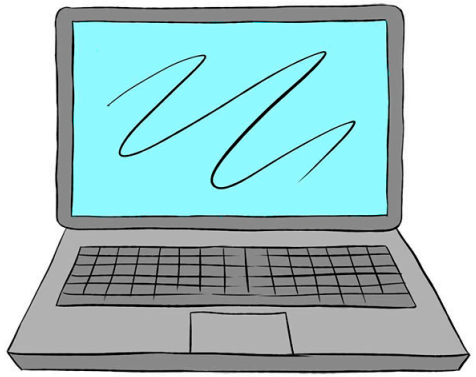


Shorter RNA strands

NMR Spectroscopy

Determine 3D structure of shorter strands

Computational modeling



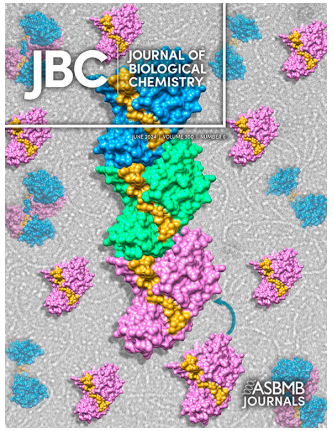
Join small 3D back to lncRNA to determine structure

Selected Publications

JBC REVIEWS · Volume 300, Issue 6, 107317, June 2024 · *Open Access*

Probing RNA structure and dynamics using nanopore and next generation sequencing

Emma Bose ‡ · Shengwei Xiong ‡ · Alisha N. Jones



bioRχiv
THE PREPRINT SERVER FOR BIOLOGY

Characterization of RBM15 protein binding with long noncoding RNAs

Emma Bose, Caleb Mayes, Lance Ellis, Corrine Baker, Sofia Tambalotti, Shengwei Xiong, Yaa Pokua Osei Sarpong, Marwan Shalaby, Lucas Barry, Frank Lewis, Johnson Joseph, Talaidh Isaacs, Derik McCarthy, Dana Katz, Jingyang Wang, Victoria Zirimu, Luis Vargas, Julian Von Hofe, Glen Aguilar, Katherine Buchan, Lei Zheng, Gregory Wolfe, Alisha N Jones

doi: https://doi.org/10.1101/2023.07.20.549950

RNA Chemical Probing Reagents and Protein Amino Acids: a Double-Edged Sword

bioRχiv
THE PREPRINT SERVER FOR BIOLOGY

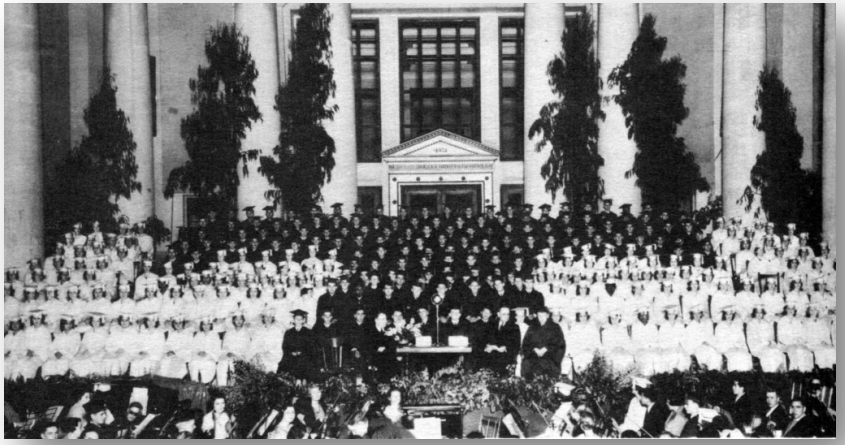
Lucy Fallon, David Klingler, Daniel Cohn, Liza Marcus, Alisha N Jones

doi: https://doi.org/10.1101/2024.03.21.586119

Lloyd Ferguson – Early Life

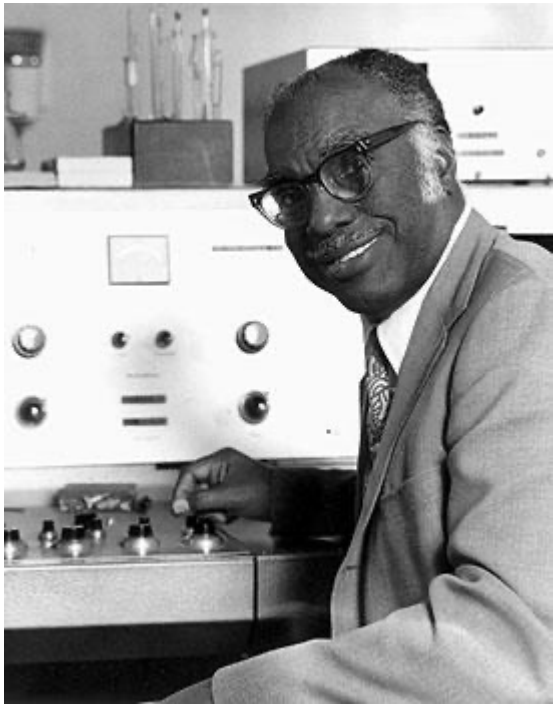
- Born & raised in Oakland, CA
- Bought a chemistry set and built a shed *<u>at age 12</u>* to serve as his home laboratory
- *<u>Before entering high school</u>*, already had inventions for a…
  - Moth repellent
  - Spot remover
  - Lemonade powder
- Graduated Oakland Tech at 16
- Worked as a railroad porter to earn money for college

Lloyd Ferguson
(age 16)



Oakland Tech Class of 1935
(one year after Lloyd Ferguson)

Time at UC Berkeley

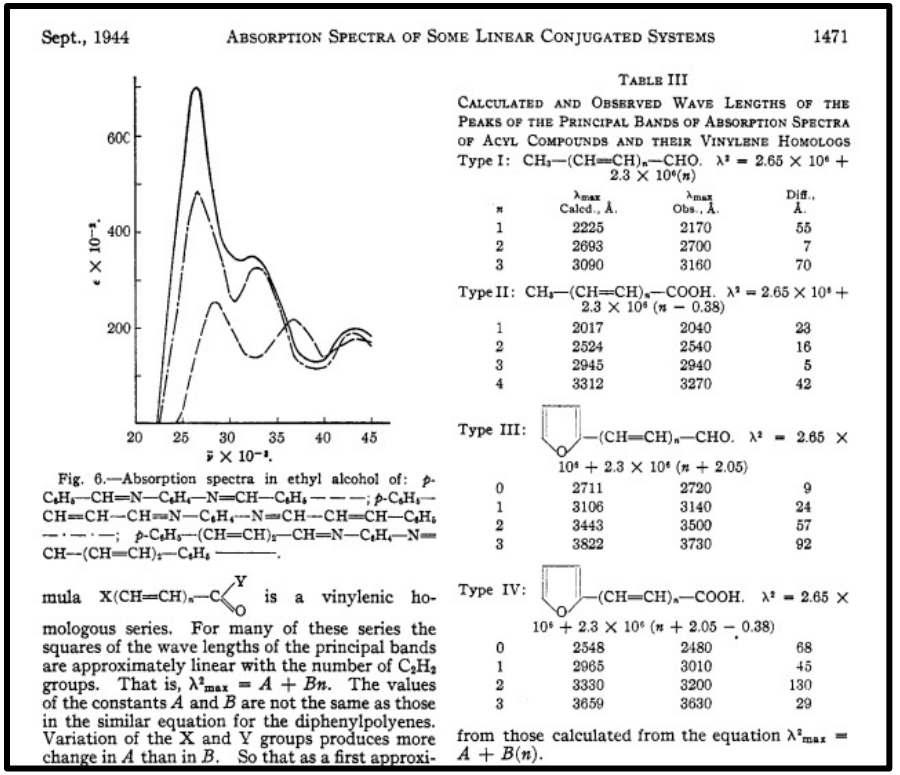


- Graduated with a B.S. from UC Berkeley in **1940**
- First Black person to earn a Ph.D. in chemistry from UC Berkeley, only 3 years after finishing undergrad (**1943**)
- Thesis: **Absorption Spectra of Some Linear Conjugated Systems**
- Advisor: Gerald E. K. Branch (also worked with Nobel Laureate Melvin Calvin)

No Path to Industry

"Later, when I was about to get my Ph.D. degree, I noticed that none of the recruiters set up interviews with me. Then, I realized that it was going to be a little difficult in getting a job [...]"

Accepted a teaching position at the North Carolina Agriculture & Technology College (NCATC)



Sept., 1944 ABSORPTION SPECTRA OF SOME LINEAR CONJUGATED SYSTEMS 1471

Fig. 6.—Absorption spectra in ethyl alcohol of: *p*-C_6H_5—CH=N—C_6H_4—N=CH—C_6H_5 — — —; *p*-C_6H_5—CH=CH—CH=N—C_6H_4—N=CH—CH=CH—C_6H_5 —·—·—; *p*-C_6H_5—(CH=CH)$_2$—CH=N—C_6H_4—N=CH—(CH=CH)$_2$—C_6H_5 ———.

mula $X(CH{=}CH)_n{-}C\langle^{O}_{Y}$ is a vinylenic homologous series. For many of these series the squares of the wave lengths of the principal bands are approximately linear with the number of C_2H_2 groups. That is, $\lambda^2_{max} = A + Bn$. The values of the constants A and B are not the same as those in the similar equation for the diphenylpolyenes. Variation of the X and Y groups produces more change in A than in B. So that as a first approxi-

TABLE III

CALCULATED AND OBSERVED WAVE LENGTHS OF THE PEAKS OF THE PRINCIPAL BANDS OF ABSORPTION SPECTRA OF ACYL COMPOUNDS AND THEIR VINYLENE HOMOLOGS

Type I: $CH_3{-}(CH{=}CH)_n{-}CHO$. $\lambda^2 = 2.65 \times 10^6 + 2.3 \times 10^6(n)$

n	λ_{max} Calcd., Å.	λ_{max} Obs., Å.	Diff., Å.
1	2225	2170	55
2	2693	2700	7
3	3090	3160	70

Type II: $CH_3{-}(CH{=}CH)_n{-}COOH$. $\lambda^2 = 2.65 \times 10^6 + 2.3 \times 10^6 (n - 0.38)$

1	2017	2040	23
2	2524	2540	16
3	2945	2940	5
4	3312	3270	42

Type III: —$(CH{=}CH)_n{-}CHO$. $\lambda^2 = 2.65 \times 10^6 + 2.3 \times 10^6 (n + 2.05)$

0	2711	2720	9
1	3106	3140	24
2	3443	3500	57
3	3822	3730	92

Type IV: —$(CH{=}CH)_n{-}COOH$. $\lambda^2 = 2.65 \times 10^6 + 2.3 \times 10^6 (n + 2.05 - 0.38)$

0	2548	2480	68
1	2965	3010	45
2	3330	3200	130
3	3659	3630	29

from those calculated from the equation $\lambda^2_{max} = A + B(n)$.

Independent Career as a teacher and educator

1943: accepted a position as an assistant professor at North Carolina Agricultural and Technical College (NCATC), a historically black college (HBCU) in Greensboro, North Carolina

none of the major chemical companies would interview African Americans or consider them for employment.

1945: joined as faculty at Howard University in Washington, D.C.

1955: full professor at Howard University

1958-1968: head of the chemistry department at Howard University

1958: established the first Ph.D. program in chemistry at any HBCU

1953: received Guggenheim Fellowship to do research at the Carlsberg Laboratory in Copenhagen and ETH Zurich.

1961: received NSF funding to go back to ETH Zurich.

1971-1972: visiting professor at the University of Nairobi in Kenya

1965: moved to Cal State L.A. as a professor in the Department of Chemistry and Biochemistry

1984-1985: visiting professorship at Bennett College, an HBCU for women in Greensboro, North Carolina.

1968-1971: chair of the Department at Cal State L.A.

1972: one of the founders of the National Organization for the Professional Advancement of Black Chemists and Chemical Engineers (NOBCChE)

1973-1984: established and served as director of the Cal State L.A.'s Minority Biomedical Research Support (MBRS) program

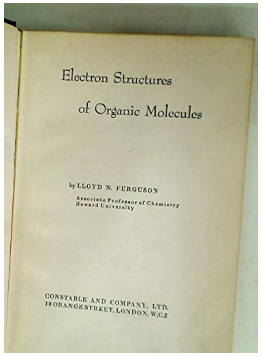
NCATC (HBCU)

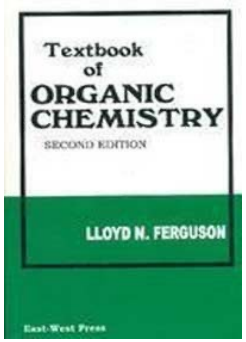
Howard University (HBCU)

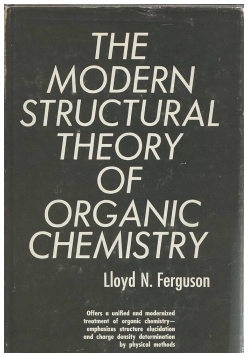
Cal State L.A.

Independent Career as a researcher

- Author of more than 50 scientific journal publications and six books







- Elucidated the relationships between molecular structure and biological activities
- Focused on structural basis of sweetness
- Work in cancer chemotherapy and the molecular structure of biologically-active compounds.

Key Role of Mentorship and Opportunity

Important to contextualize the exercise and what we hope to get from it.

- For me, two major goals:
  1. Awareness
  2. Appreciation
- To take it forward important to consider the part we play in it and what we can do.

“He continued with the railway until graduate school when Glenn Seaborg offered him a position working in the [Donner] radiation laboratory.”

"Later, when I was about to get my Ph.D. degree, I noticed that none of the recruiters set up interviews with me. Then, I realized that it was going to be a little difficult in getting a job […]”

It was not typical for undergraduates to stay on for their doctoral work in the College. Students were (and still are today) encouraged to go onto other institutions for breath of learning and experience. Dr. Ferguson had to request permission from G.N. Lewis to continue his studies at the College.

It just so happened at that time, an announcement of a teaching position came into the department at a Black school in North Carolina, Agriculture & Technology College (NCATC). So the secretary gave it to me and I investigated and found out it seemed to be a good institution at which to work. I applied for the job and got appointed assistant professor there in Greensboro."

Ways We Can Get Involved

- Easiest: restart our BASIS team

→ We need someone to take on organizing and people to commit to going

- Finding and making opportunities

→ Connecting with existing on-campus initiatives

  → Underground Scholars/Underground Scholars Initiative

  → Incarceration to College

  → Power Bay Area

- Many other opportunities!