

## Overview

### Laboratory of Immunobiochemistry

Ronald L. Rabin, MD

April 29, 2021

# Mission: assure safety and efficacy of allergenic products

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- Biologics License Application (BLA) and Investigational New Drug (IND) review
- Represent FDA to domestic and international academic or government organizations
- Expert advice to other FDA Centers
  - CDER
  - CDRH
  - CDER (anti-PEG IgE study)
- Allergen extract potency and lot release of standardized extracts and new products
- Research

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# Review of Biologic License Applications (BLA) and Investigational New Drug (IND) Applications

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- Chemistry, Manufacturing, and Control (CMC) reviewers
- Integral to review process as IND progresses Phase 1 → Phase 3 → BLA
- Inspections of manufacturing sites prior to BLA approval
- Comprehensive reviews of manufacturing processes for quality and consistency
- Review of BLA Annual Reports and Supplements

# Represent FDA to domestic and foreign organizations

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- AAAAI annual meeting of the Board of Directors (Washington, DC)
- AAAAI Committee on Standardization
- Paul Ehrlich Institut Seminars
- European Medicines Agency: co-authors on position papers
- European Academy Asthma and Clinical Immunology (Rabin)
  - Advisory Board for the EAACI Research and Outreach Committee
  - Co-author on two EAACI reviews on Covid19 vaccine allergy
- Editorial Board (Rabin)
  - *Clinical and Experimental Allergy*
  - *Frontiers in Allergy*

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# Natural allergen extracts

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- Standardized extracts
  - Controlled for potency and stability
  - Potency measured as relative to a US standard
  - Unitage correlates to biological potency
    - mass units
    - BAU or AU/mL
    - specific allergen
- Non-standardized
  - Unitage uninformative (PNU/mL or w/v)

## Standardized products (n = 19)

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- House dust mites
  - Insect venoms
  - Cat hair and dander
  - Grass pollens
  - Short ragweed pollen
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- Non-Standardized products (n > 1000)



# LIB Reference reagent laboratory

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- Lot release
  - Standardized allergen extracts for injection (diagnosis and therapy)
  - Tablets for sublingual immunotherapy (SLIT)
  - Oral immunotherapy for food allergy
- Distribute and maintain US reference reagents for standardized allergen extracts
- International Standards Organization (ISO) 17025 accreditation
  - Stringent documentation and SOP protocols
  - Annual accreditation
- Improve methods of standardization
  - Fel d 1 and Amb a 1 (cat and ragweed) ELISA

# Staffing

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## Senior Staff

- Ronald L. Rabin, MD      Lab Chief
- Jay E. Slater, MD      Director, DBPAP
- Alexander Zhovmer, PhD      Principal Investigator

## Staff Fellows/Staff Scientists

- Philippa Hillyer, PhD      Staff Scientist
- Eric Levenson, PhD      Staff Fellow
- Michael (Brad) Strader, PhD      Staff Scientist
- Xuefei Ma, Ph.D. (July 2021)      Staff Scientist

## Reference Reagent Lab

- Aaron Chen, MS
- Katia Dobrovolskaia
- Robert Zagorsky
- Mona Febus

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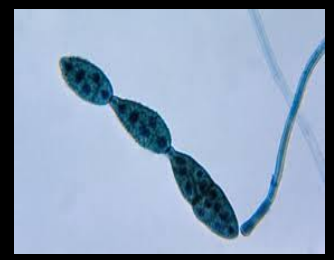
# Immunotherapy: complex natural products

Images for Decoration



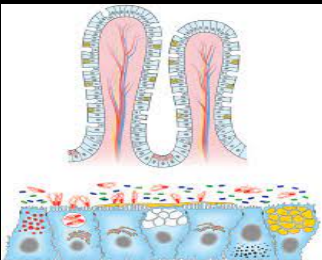
- Unselective aqueous extractions of natural source material (pollens, insects, animals, foods, venoms)
- Diagnostic products
  - Environmental allergens: skin testing
  - Food allergens: oral food challenge
- Therapeutic products
  - Insect venoms and extracts
  - Weed, tree, grass pollen extracts
  - Animal hair and dander extracts
  - House dust mite extracts
  - Peanut flour

Images for Decoration

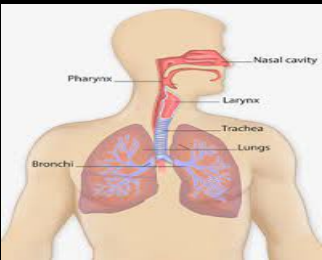


# Allergic disease: complex pathophysiology

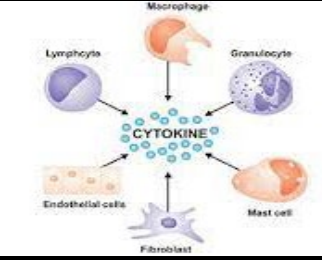
Images for Decoration



Cartoon of bronchial mucous membrane



Cartoon of human respiratory tree



Cartoon of interaction between cells and cytokines

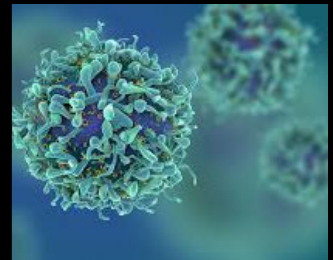


Cartoon illustration of a human encircled by chromosomes

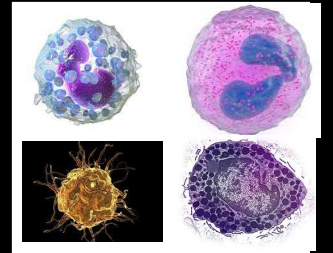
- Genetic predisposition
- Multiple organ systems
- Innate and adaptive immunity
- Viral infection
- Microbiome

Images for Decoration

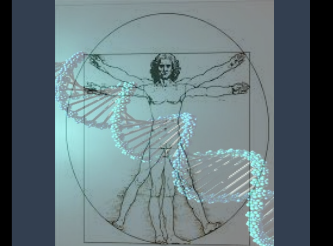
Electron micrograph of a T cell



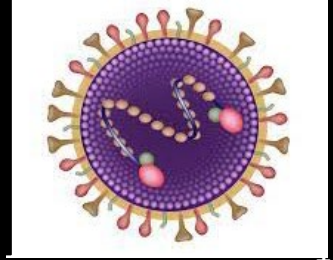
Microscopic images of eosinophils, basophils



Da Vinci's "Vetruvian Man" with overlay of DNA



Cartoon illustration a cell and nucleus



# Future of allergen immunotherapy

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- Targeted populations (e.g. children to prevent allergic march)
- Virus like-particles<sup>1</sup>
- Short or intermediate length peptides
- Complex mixtures for oral immunotherapy for food allergies<sup>2</sup>
- Immunotherapy/biologics combinations
- Adjuvants
- DNA vaccines

1. <https://www.globenewswire.com/news-release/2020/01/29/1976690/0/en/Allergy-Therapeutics-publishes-encouraging-new-data-for-peanut-allergy-vaccine-candidate-in-The-Journal-of-Allergy-and-Clinical-Immunology.html>

2. [https://www.jacionline.org/article/S0091-6749\(19\)30900-5/fulltext](https://www.jacionline.org/article/S0091-6749(19)30900-5/fulltext)

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- Adjuvants

- DNA vaccines

→ Protein chemistry

Innate and adaptive immunology

1. <https://www.globenewswire.com/news-release/2020/01/29/1976690/0/en/Allergy-Therapeutics-publishes-encouraging-new-data-for-peanut-allergy-vaccine-candidate-in-The-Journal-of-Allergy-and-Clinical-Immunology.html>
2. [https://www.jacionline.org/article/S0091-6749\(19\)30900-5/fulltext](https://www.jacionline.org/article/S0091-6749(19)30900-5/fulltext)

# Summary

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- Slater lab studies allergen protein structure
  - Focus on indoor environmental allergens
- Rabin lab research is on viral respiratory infections, interferons, and how allergens affect the antiviral response
  - Rabin and Slater lab share common interests in pet and indoor environmental allergens
- Zhovmer lab studies food allergy
  - All three labs share an interest in mucosal response to allergens



End

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