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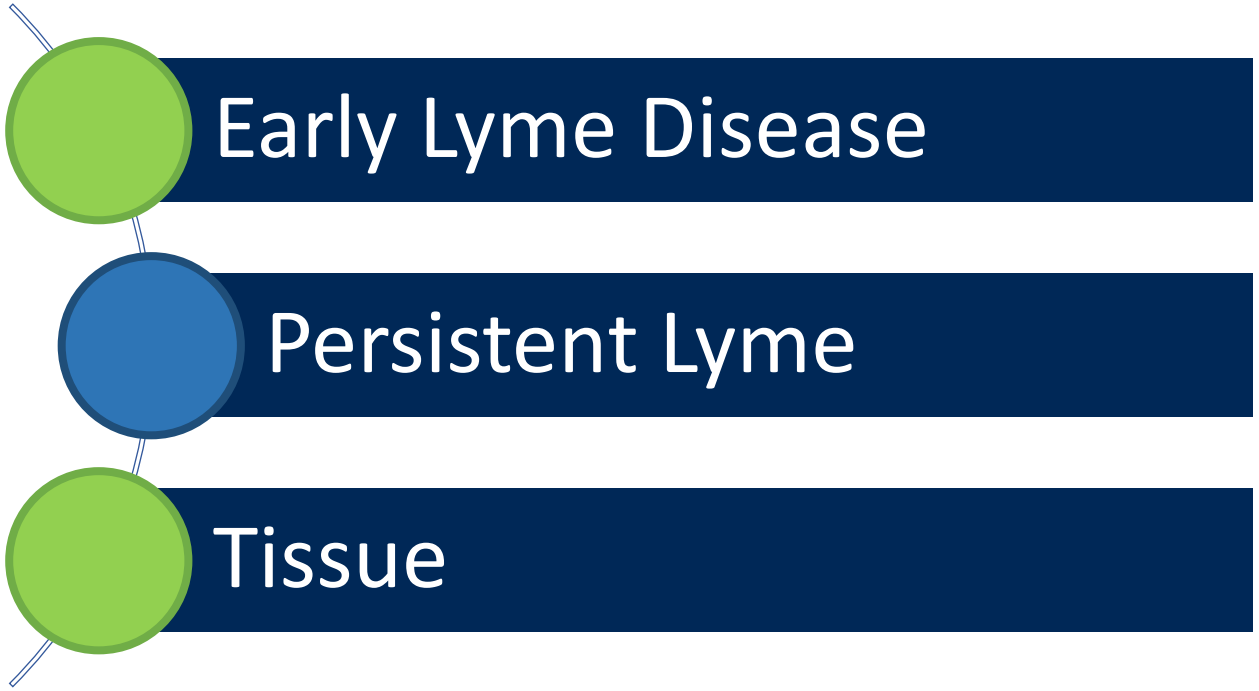
A BAY AREA LYME FOUNDATION PROGRAM

The Need for Well-Characterized Samples



Liz Horn, PhD, MBI
Lyme Disease Biobank
June 30, 2023

Well-characterized Samples are Key to Advancing Research

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Sourcing well-characterized samples takes time/effort/resources

- Purpose of collection (eg diagnostic test development, disease pathophysiology, clinical trial)
- Types of sample(s), from which patient population(s), and at what timepoints
- Existing samples or prospective collection/ collaborators and partners
- Steps to acquire or collect samples (build in time for administrative/legal/regulatory tasks and governance)
- Prospective collection is time and resource (human and $) intensive
- Limited federal funding for infrastructure projects like biobanks

Well-characterized samples are essential

- Standardized protocols/ chain of custody/ pre-analytic variables
- Clinical information, patient questionnaires, standardized instruments
- Laboratory/ diagnostic test results
- Additional data sources (eg patient registries)

Samples that are not well-characterized may not be very useful!

Individual vs Centralized Collections

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- *Fragmentation*
- *Sample acquisition required for each project*
- *High costs/ redundant infrastructure*
- *Limited sharing/ incentives to not share*
- *Limited ability to compare results*
- *Variable collection quality*

- *Centralization adds efficiencies*
- *Multiple projects per blood draw*
- *Lower costs for centralized resource*
- *Designed to share/ attract new researchers*
- *Ability to compare results with same samples*
- *Consistent quality across collection*

>1200 Participants Enrolled

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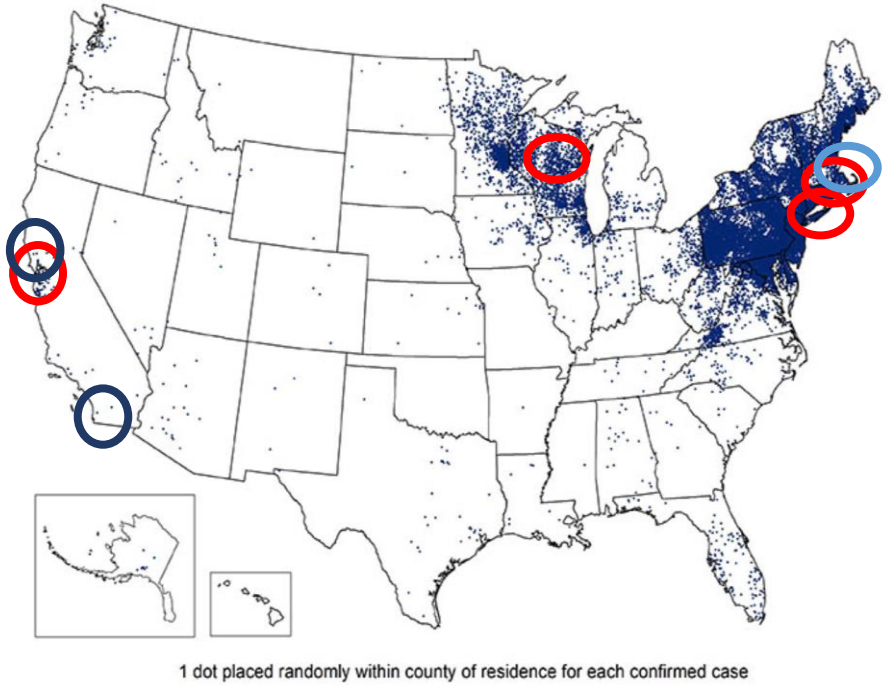
- East Coast, Upper Midwest, and California
- Trusted resource with transparent protocols
- Samples available
  - Each donation supports **~50** research projects
  - **>85 approved** projects in academia and industry
  - >**17,000** aliquots distributed since 2016
- 11 publications using LDB samples or data



Early Lyme
Later Lyme/ Other TBI
Persistent/Chronic Lyme

Through June 21, 2023

https://www.bayarealyme.org/biobank/news-publications/

Early Lyme Collection (825 available)

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- Signs and symptoms of early Lyme in endemic areas with and without erythema migrans (EM)
- Whole blood, serum, and urine with Case Report Form at each visit
- Collecting in family practice/regional medical centers
- Testing all samples at the end of the collection season
- Samples used for Lyme diagnostics development

Red/Pink All Over (common)

Bulls-eye (uncommon)

https://journals.asm.org/doi/10.1128/jcm.00032-20

Large Numbers of Samples Needed

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- Only ~30% of cases are laboratory confirmed (28% have EM/ clinical diagnosis without laboratory confirmation)
- Ongoing need to collect due to sample depletion of lab confirmed

Classification Category for Cases	Total (2014-2021)
Laboratory Confirmed Lyme Disease (LD)	119
Probable LD	114
Suspected LD	56
Symptomatic No Lesion (SNL)	120
Endemic Controls	330
Total Collected	739

409 Cases

Key : *Laboratory Confirmed LD* : Positive by CDC's standard two-tiered testing (STTT) algorithm or 2 positive ELISA's with EM>5 cm; *Probable LD* : EM>5 cm (clinical diagnosis) and negative by STTT; *Suspected LD* : EM≤5 cm and negative by STTT; *SNL* : No lesion and negative by STT.

https://journals.asm.org/doi/10.1128/jcm.00032-20

Persistent Collection (~150 Available)

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- People with persistent Lyme in CA
- Whole blood, serum, urine with case report form
- 15 projects for novel diagnostics (direct detection, RNA and protein assays) and biomarker exploration
- Researchers provide data back to the resource

LDB Tissue Bank

- Post-mortem donations (14) and tissue (12) from surgeries
- Robust clinical information including redacted medical records
- Option to link MyLymeData profile to tissue sample
- No cost to patients and families
- Tissue analysis pipeline to characterize tissue (evidence of infection and/or evidence of inflammation)

Post-Mortem Tissues

- Aortic Arch
- Bladder
- Blood
- Bone Marrow
- **Brain** (~11 regions)
- Cartilage and Synovium (knee)
- Cerebral Spinal Fluid
- **Heart**
- Liver
- Lymph Node (mesenteric)
- Muscle (deltoid and quadriceps)
- Nerve (sciatic and tibial)
- **Spinal cord**
- Spleen

Purple: Additional Processing by Andrew Dwork, MD, New York Foundation for Mental Hygiene

https://www.bayarealyme.org/biobank/patient-information/

Tissue Analysis Pipeline

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Pipeline Process Steps | Collaborator Experiments

Post-Mortem Tissue Evaluation: *Fixed and Frozen Tissue*

- Neuropathologic Evaluation
  - IHC/ additional staining
- Pathogen Evaluation
  - IFA staining and PCR
- Pathogen Sequencing
  - Metagenomic NGS
  - Capture Sequencing
- Potential Biomarkers
  - *Borrelia* Biomarkers
  - Host Biomarkers

IHC=Immunohistochemistry
IFA=Immunofluorescence
NGS=Next Generation Sequencing

A Call to Action to Standardize Evaluation of Microbes in Tissue from Alzheimer's Patients

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alzheimer's association | Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

REVIEW ARTICLE | Open Access

Establishment of a consensus protocol to explore the brain pathobiome in patients with mild cognitive impairment and Alzheimer's disease

Research outline and call for collaboration

Richard Lathe, Nikki M. Schultek, Brian J. Balin, Garth D. Ehrlich, Lavinia Alberi Auber, George Perry, Edward B. Breitschwerdt, David B. Corry, Richard L. Doty, Robert A. Rissman, Peter L. Nara, Ruth Itzhaki, William A. Eimer, Rudolph E. Tanzi, the Intracell Research Group Consortium Collaborators

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