Ecology and Evolution of the Fungi *Coccidioides immitis* and *Coccidioides posadasii*, Causative Agents of Valley Fever

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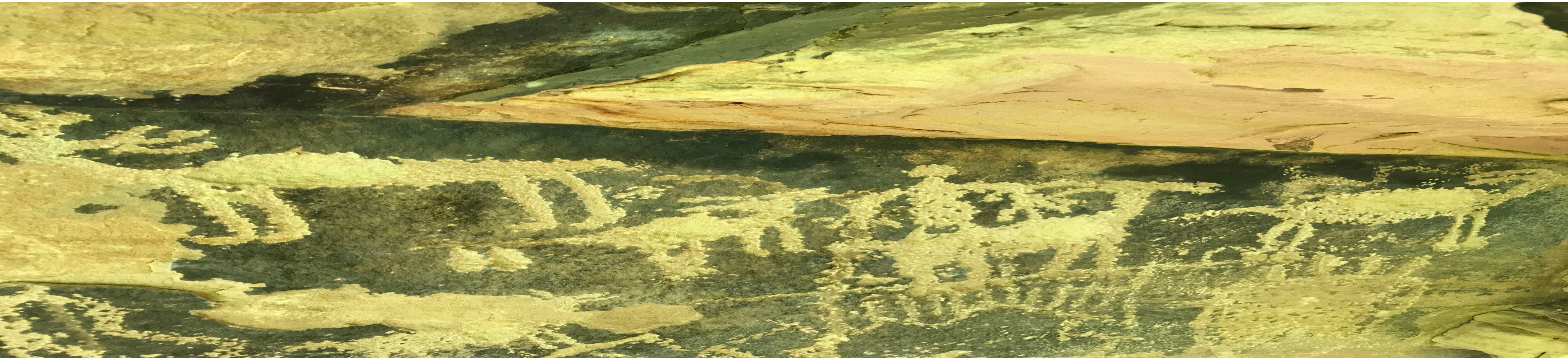
The Pathogen and Microbiome Institute

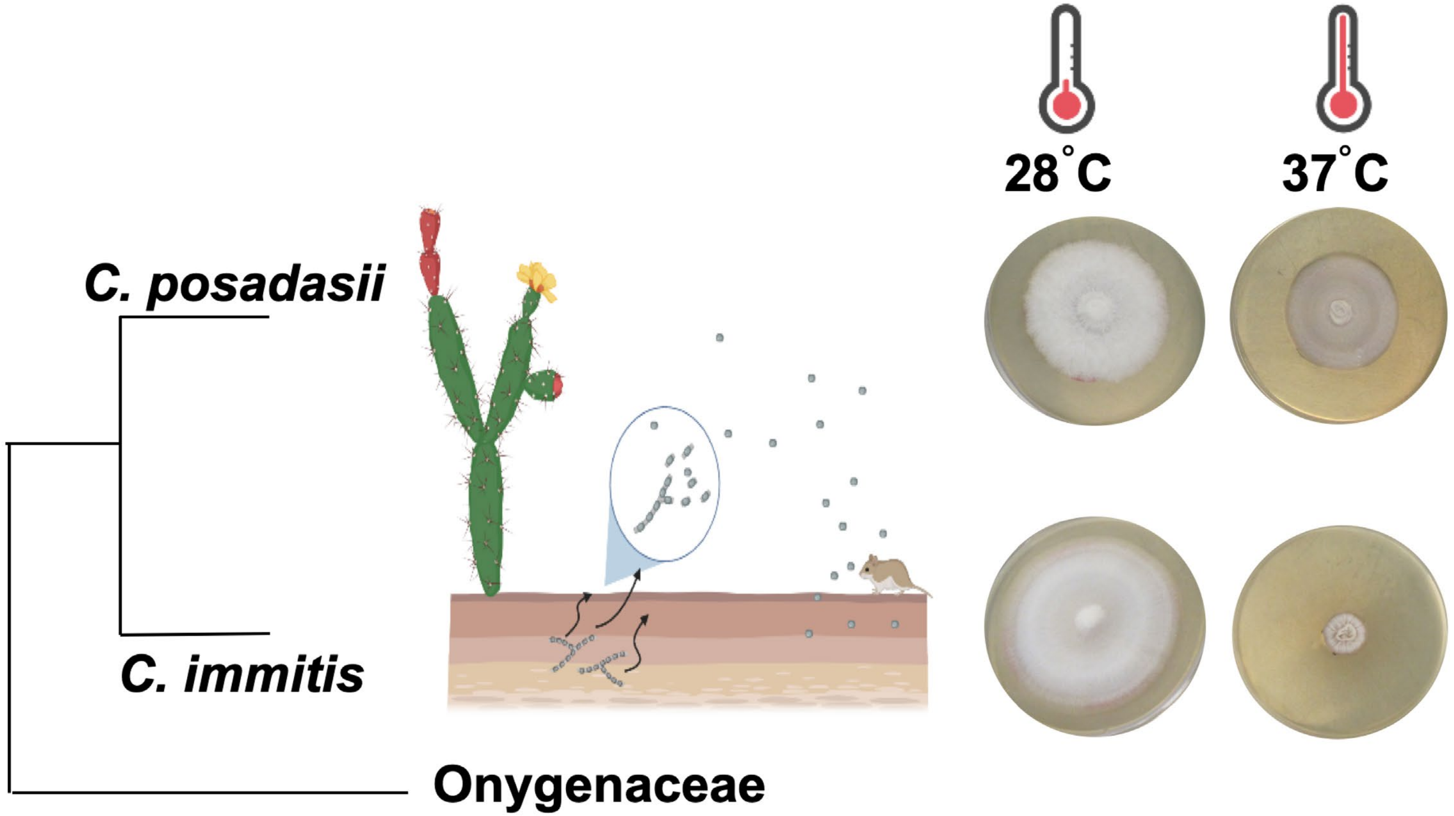
Land Acknowledgement

Northern Arizona University sits at the base of the San Francisco Peaks, on homelands sacred to Native Americans throughout the region. I honor the past, present, and future generations, who for millennia have lived in the region where I conduct my research

Baa ahééh nisin, díidí



Two species: *C. immitis* and *C. posadasii*

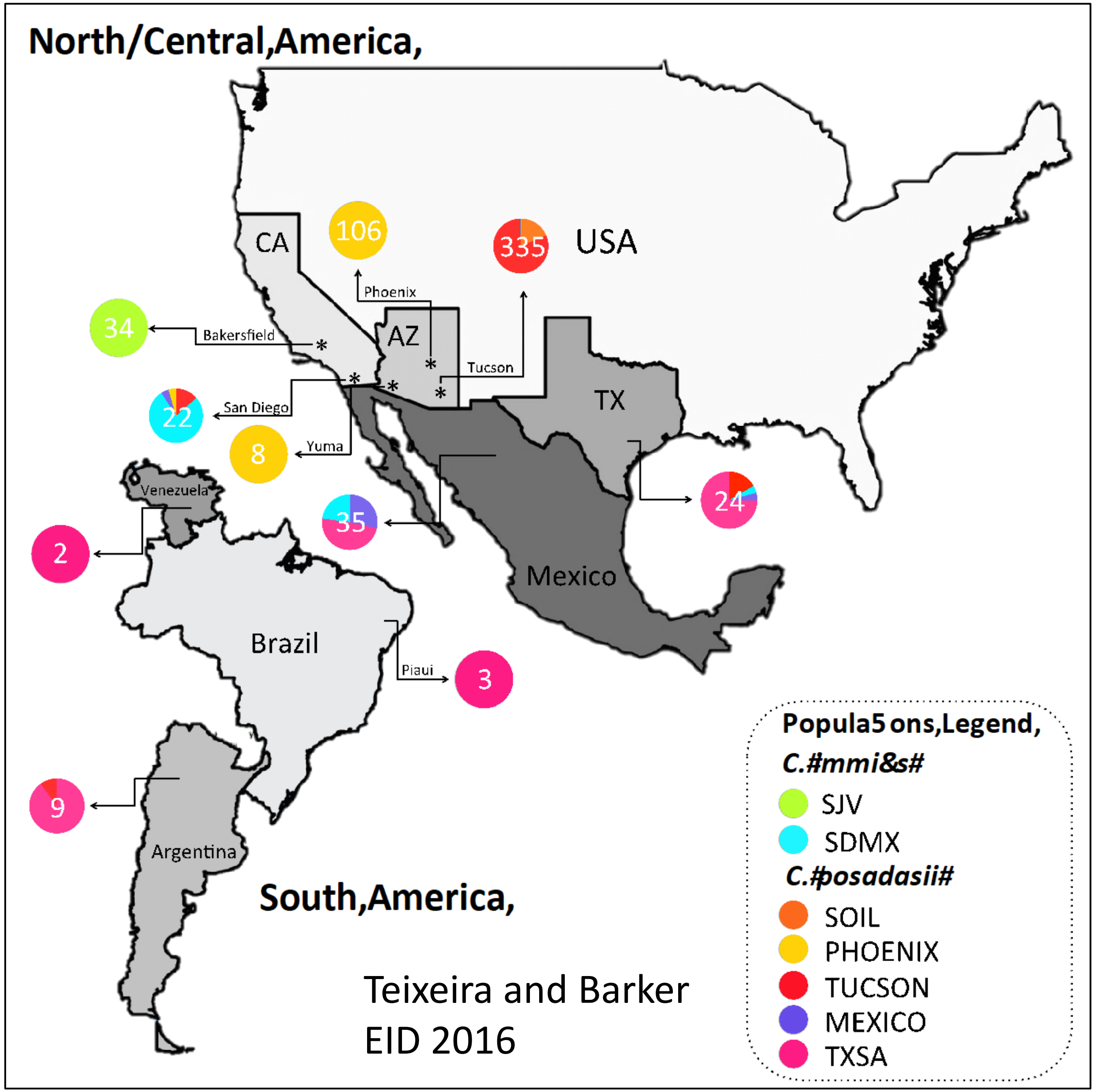


Mead *et al.* J Fungi 2020

Strong Biogeographic Patterns among Clinical Isolates using PCR-based markers

C. immitis: California to Baja, Mexico

C. posadasii:
Southwest US
Mexico
Brazil/Argentina



Teixeira and Barker
EID 2016

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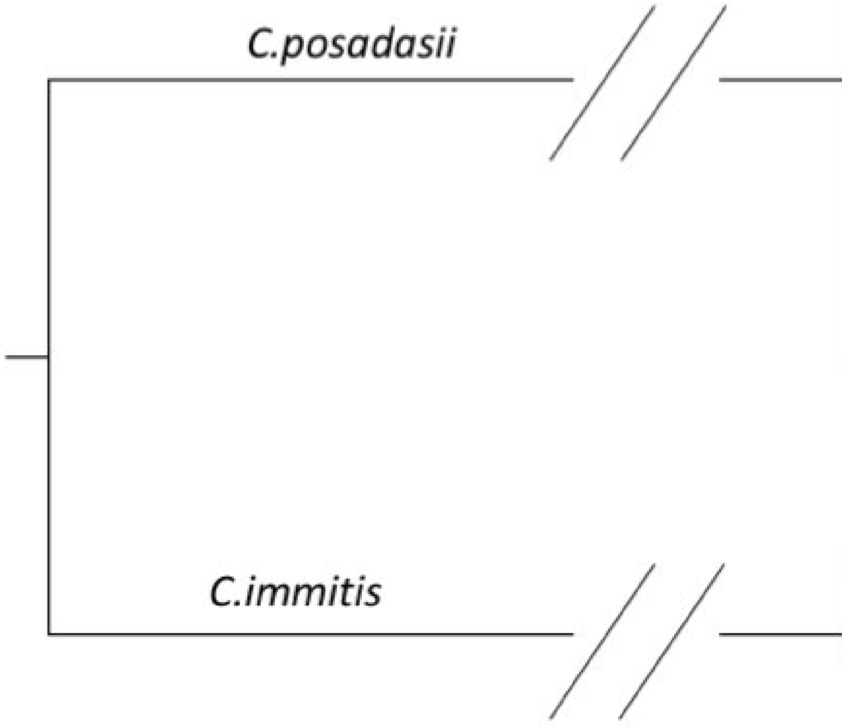
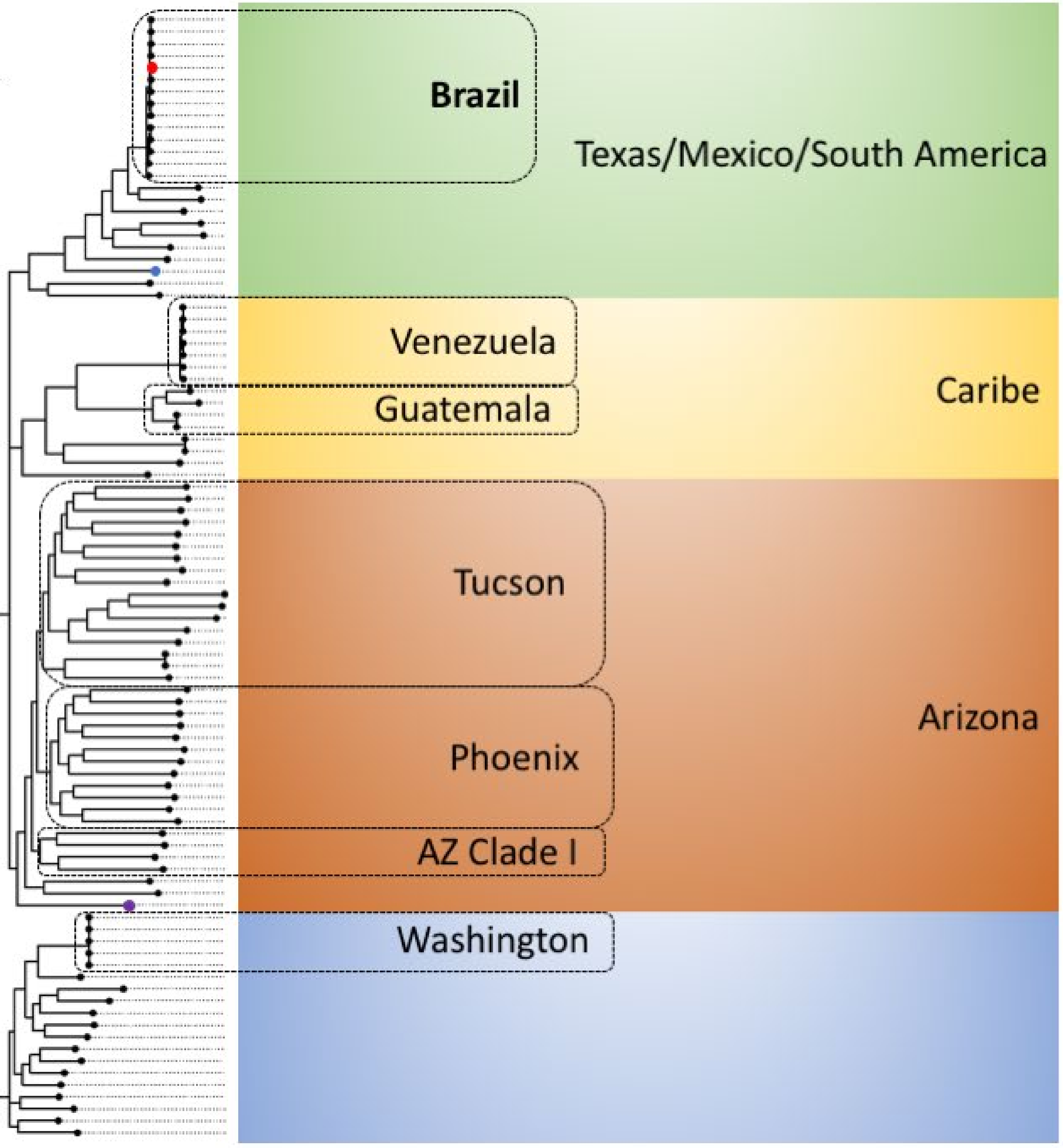




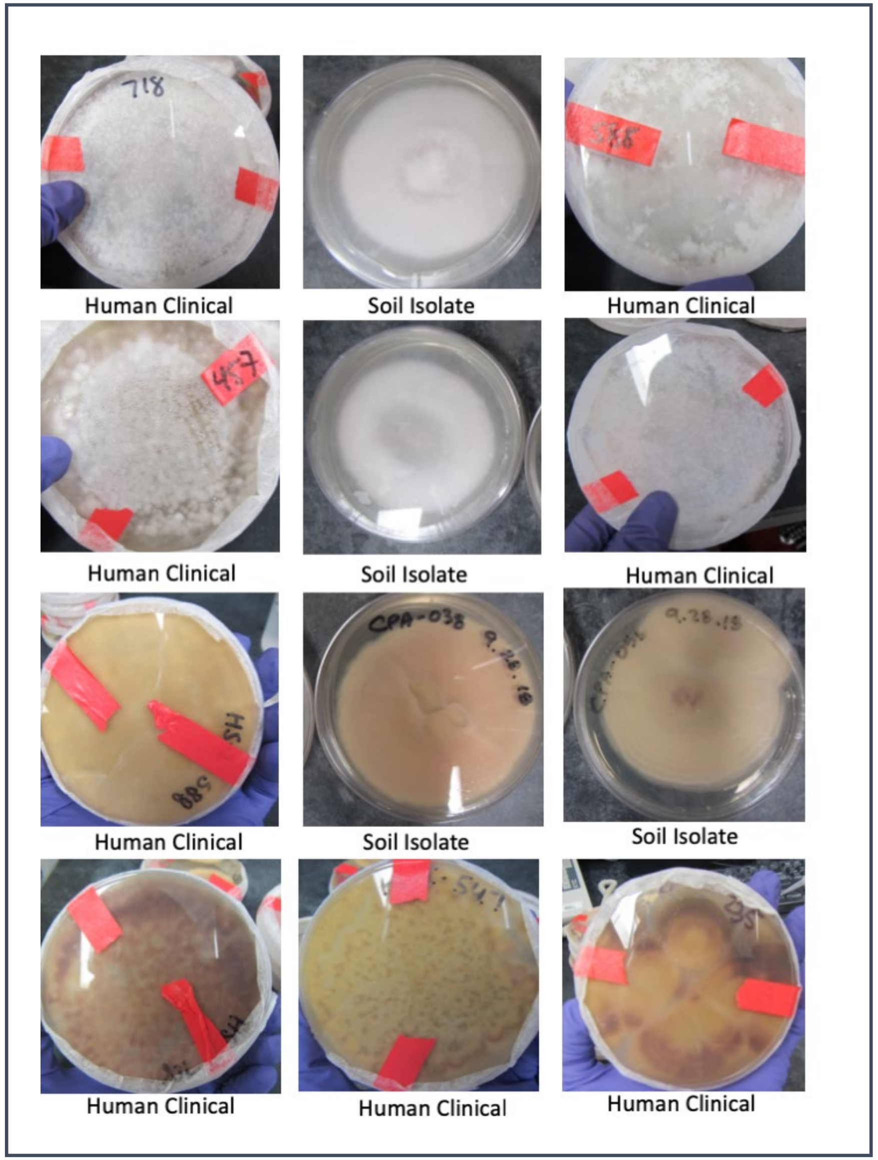
Local Adaption or Founder Effect?

Hector and Laborin 2005

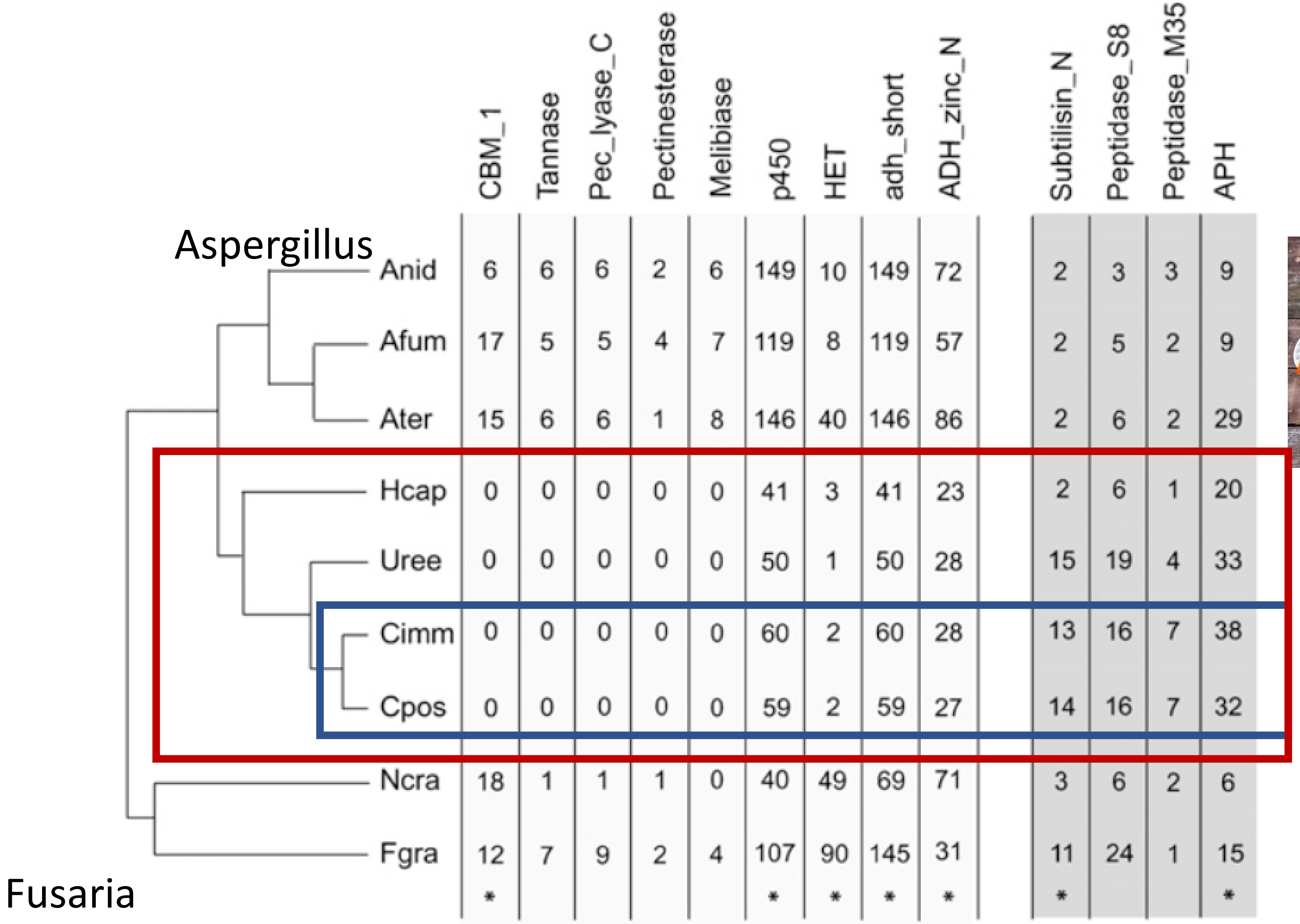
- Coccidioides immitis and C. posadasii show distinct biogeographic population structure
- Population structure varies- some regions harbor isolates with recombining population structure and some appear more clonal.
    - Does this reflect newly established populations?
    - Founder effect?
    - Local adaptation?

Importance of understanding genetic variation

- Pathology
  - Differences in pathogenicity?
    - Diagnosis of coccidioidomycosis does not require knowing which species caused the disease
    - Variation in severity not well characterized
  - Differences in treatment?
    - Vaccine targets
    - Antifungal drug resistance
- Epidemiology
  - Different associations/ interactions
  - Different outbreak pattern



Loss of plant-associated gene families, expansion of keratin degradation indicates a close interaction with animals



	CBM_1	Tannase	Pec_lyase_C	Pectinesterase	Melibiase	p450	HET	adh_short	ADH_zinc_N	Subtilisin_N	Peptidase_S8	Peptidase_M35	APH
Anid	6	6	6	2	6	149	10	149	72	2	3	3	9
Afum	17	5	5	4	7	119	8	119	57	2	5	2	9
Ater	15	6	6	1	8	146	40	146	86	2	6	2	29
Hcap	0	0	0	0	0	41	3	41	23	2	6	1	20
Uree	0	0	0	0	0	50	1	50	28	15	19	4	33
Cimm	0	0	0	0	0	60	2	60	28	13	16	7	38
Cpos	0	0	0	0	0	59	2	59	27	14	16	7	32
Ncra	18	1	1	1	0	40	49	69	71	3	6	2	6
Fgra	12	7	9	2	4	107	90	145	31	11	24	1	15
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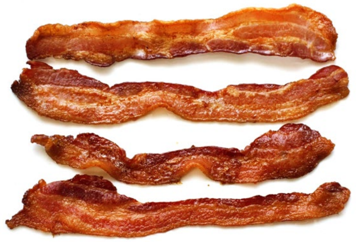


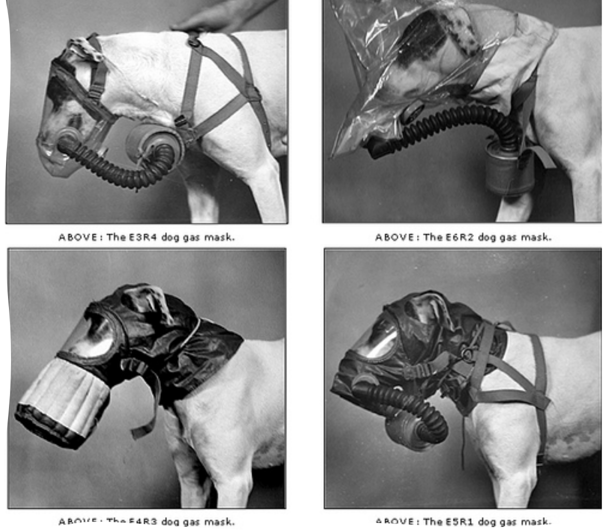
Sharpton et al. 2009
Genome Research

Linking Genomics with Ecology

- Determine loss and gain of genes
  - Proper annotation
  - Reference genomes
- Identify gene family expansions
  - Sequencing of close relatives
- Genes under positive selection
  - Define novel antigens
  - Immune escape
- Expression of transcripts
  - In vivo, life stages, nutrient sources
- Species and Population specific patterns

Environmentally acquired infection

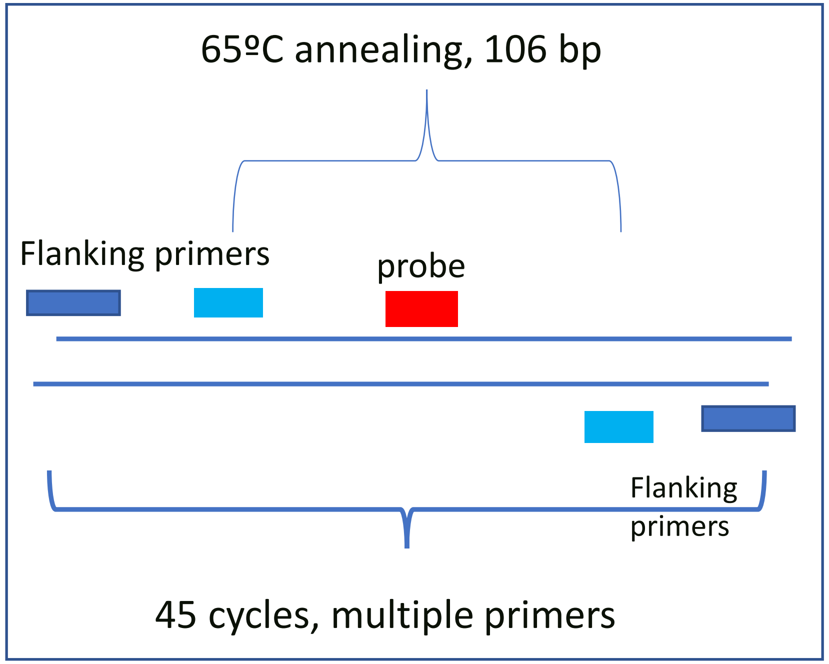
- **Infection results from inhaling arthroconidia in soil/dust/air – <u>understanding ecology and environmental reservoir is critical</u>**
- **No evidence for transmission from infected host (except rare cases, e.g. organ transplant)**
- **Data on environmental niche limited: limits climate modeling and predictive ability**
- **Pathogen that infects apparently healthy mammals (reptiles?)**



To understand ecology, we needed a higher throughput way to find *Coccidioides* positive sites

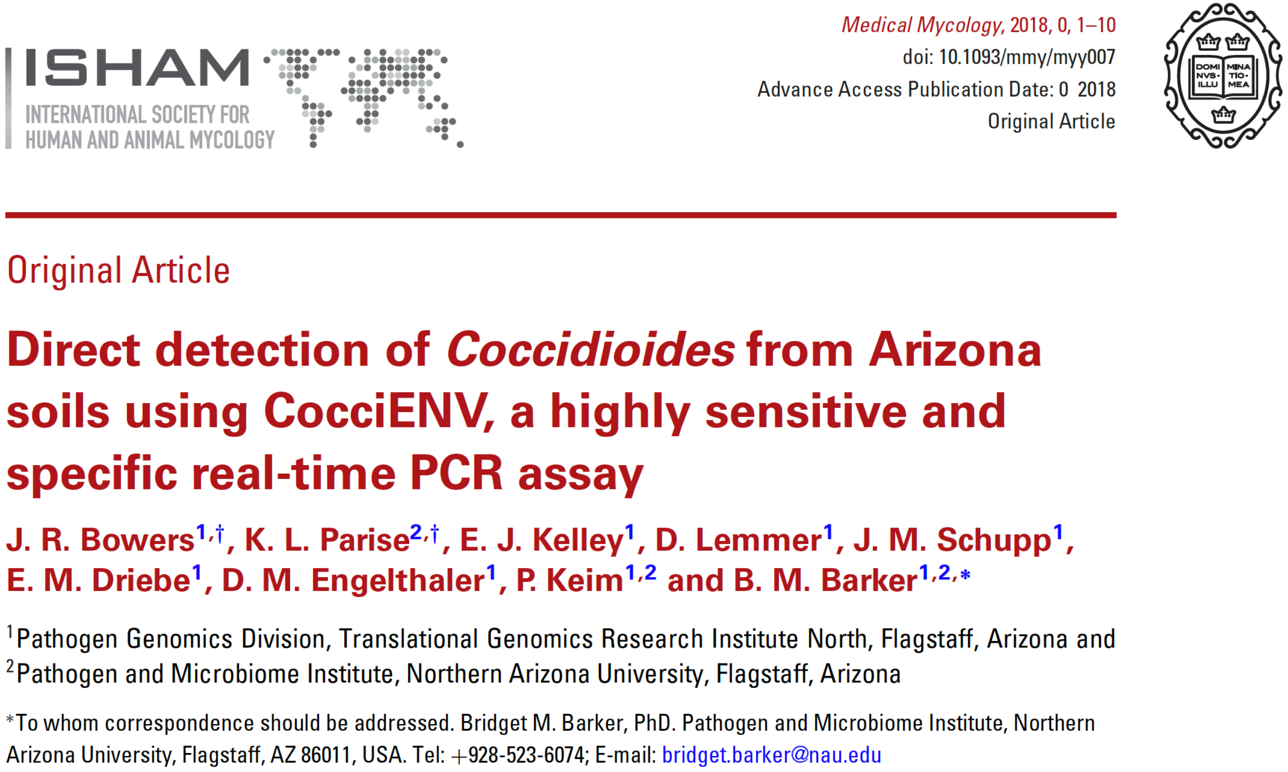
- Previous molecular methods gave many false negatives AND positives
- Culture-based is labor intensive (or doesn’t work)

CocciENV: TaqMan probe real-time PCR developed from clinical assay



70-250 copies per genome

Probe specific for *Coccidioides*



ISHAM INTERNATIONAL SOCIETY FOR HUMAN AND ANIMAL MYCOLOGY

Medical Mycology, 2018, 0, 1–10
doi: 10.1093/mmy/myy007
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Original Article

Original Article

Direct detection of *Coccidioides* from Arizona soils using CocciENV, a highly sensitive and specific real-time PCR assay

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Now we have a tool to explore the environment!

Regions colonized by *Coccidioides* are hot, dry, alkaline soil; occupied by other endemic species

Biotic

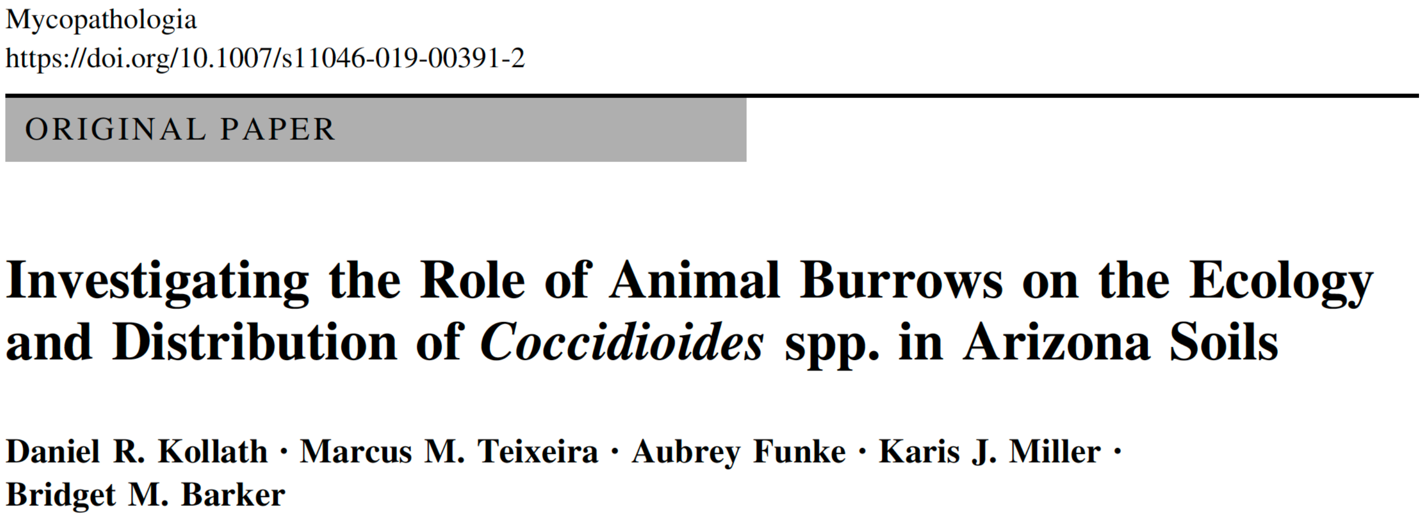
- Many animal species found in North and South American only
  - Armadillos
  - Various reptile species
  - Heteromyid rodents
    - Pocket mice
    - Kangaroo rats
- **Other Microbes**
- Arid lands characterized by biocrusts

Abiotic

- Seasonal moisture, with long periods of drought
- Extreme high temps
- Desert soil
  - Impacted by anthropogenic disturbance
  - pH 7.5-8 is common
  - Salts and minerals

Host or burrow as preferred environment?

Burrows often represent point sources of infection in outbreaks, AND a majority of positive samples



Mycopathologia
https://doi.org/10.1007/s11046-019-00391-2

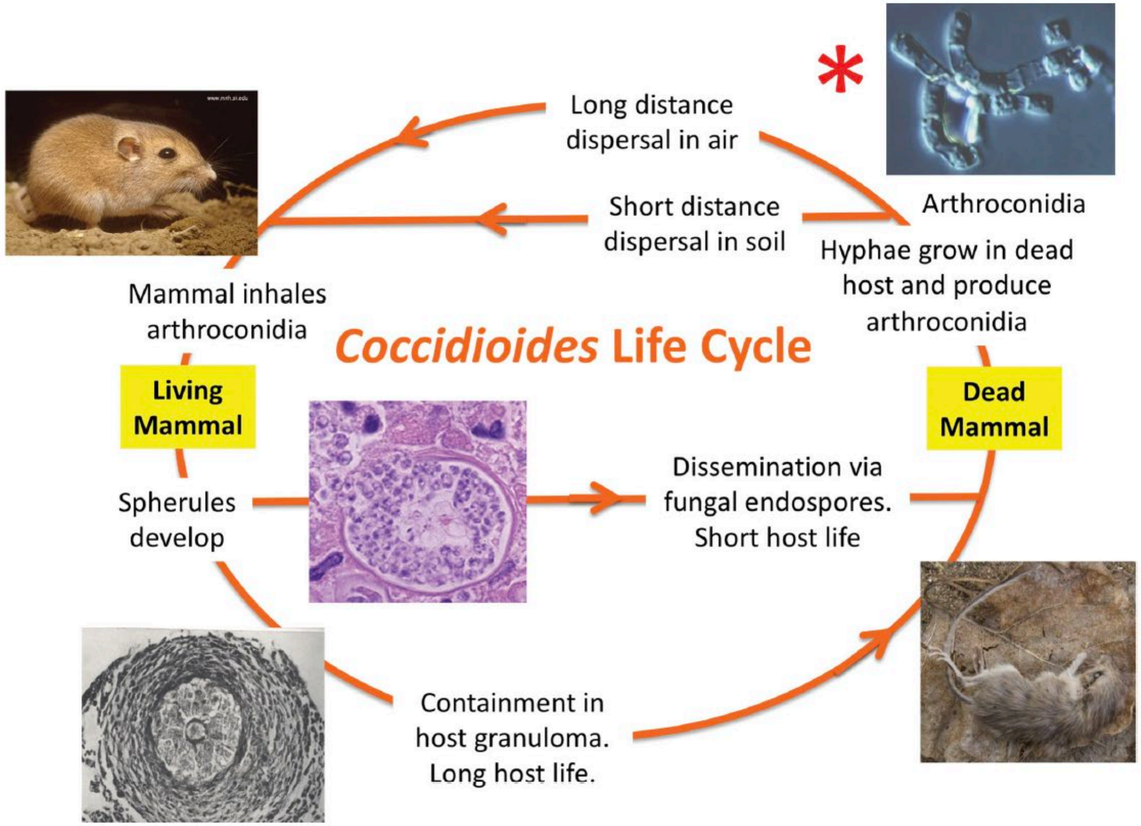
ORIGINAL PAPER

Investigating the Role of Animal Burrows on the Ecology and Distribution of *Coccidioides* spp. in Arizona Soils

Daniel R. Kollath · Marcus M. Teixeira · Aubrey Funke · Karis J. Miller · Bridget M. Barker

Endozoan-based life cycle of *Coccidioides*

- The endozoan, small-mammal reservoir hypothesis and the life cycle of *Coccidioides* species
- Basic concept- the spherule is an evolutionary dead end if not able to return to the soil
- Climate affects the abundance of small mammals too



Coccidioides **Life Cycle**

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Long distance dispersal in air

Short distance dispersal in soil

Arthroconidia

Hyphae grow in dead host and produce arthroconidia

Mammal inhales arthroconidia

Living Mammal

Dead Mammal

Spherules develop

Dissemination via fungal endospores. Short host life

Containment in host granuloma. Long host life.

Taylor and Barker. Medical Mycology 2019 57:S16-20

Longterm monitoring of positive sites

- Sites remain positive for decades
- Majority of isolates retrieved from single site are clones
- But patient isolates are mostly different genotypes

- Developing methods to assess whole genomes without culture
- Qs: Do genotypes change over time? How?

Pathogen and Microbiome Institute – PMI

Executive Director: Paul Keim

Barker Lab

Ashley Jones, Research Associate: Lab manager, CRISPR

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Ana Braga, PhD candidate, Cocci and wildlife

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Kaitlyn Parra, Research Technician: Mycobiome, CRISPR

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