

Impact and Control of Valley Fever - A Workshop

Environmental background and significance

John W. Taylor
UC Berkeley
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November 2022



CALIFORNIA

- UC Berkeley
 - Rob Wagner
 - Lily Montoya
 - Justin Remais
 - Jennifer Head-Zhutenneger
- UC San Francisco
Anita Sil
- UC Berkeley
Rachel Brem



ARIZONA

Northern Arizona University
Bridget Barker

University of Arizona
John Galgiani

NEW MEXICO

University of New Mexico
Paris Salazar-Hamm
Don Natvig

Environmental background and significance



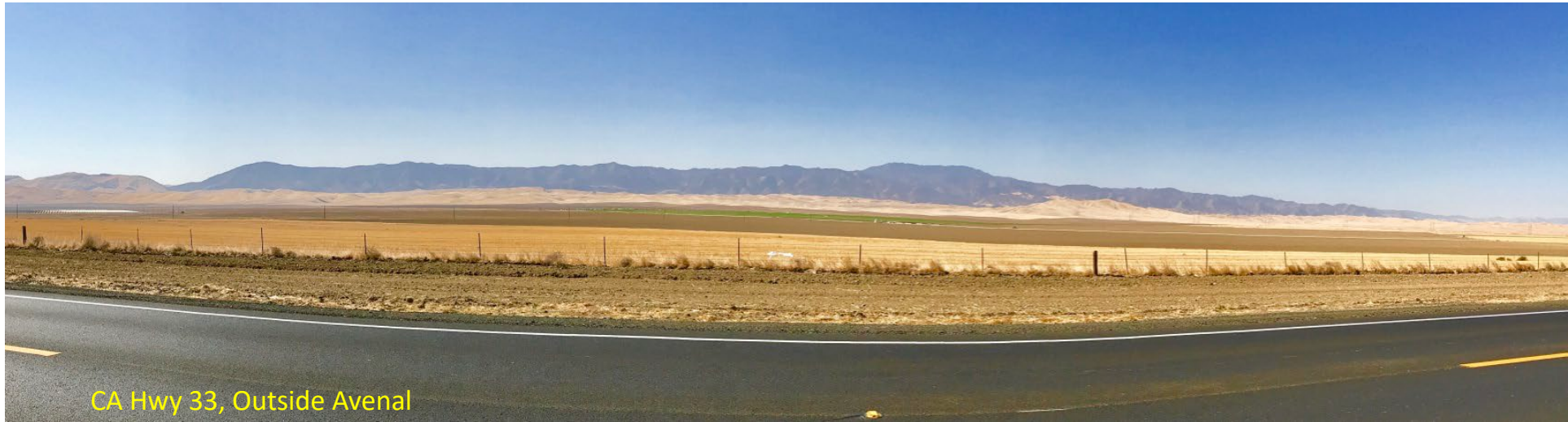
Pioneering studies

Traditional Environmental Cycle

Genomics

Revisionist Environmental Cycle

Hypothesis testing



Myrnie Gifford, 1938

Coccidial granuloma = San Joaquin Valley Fever



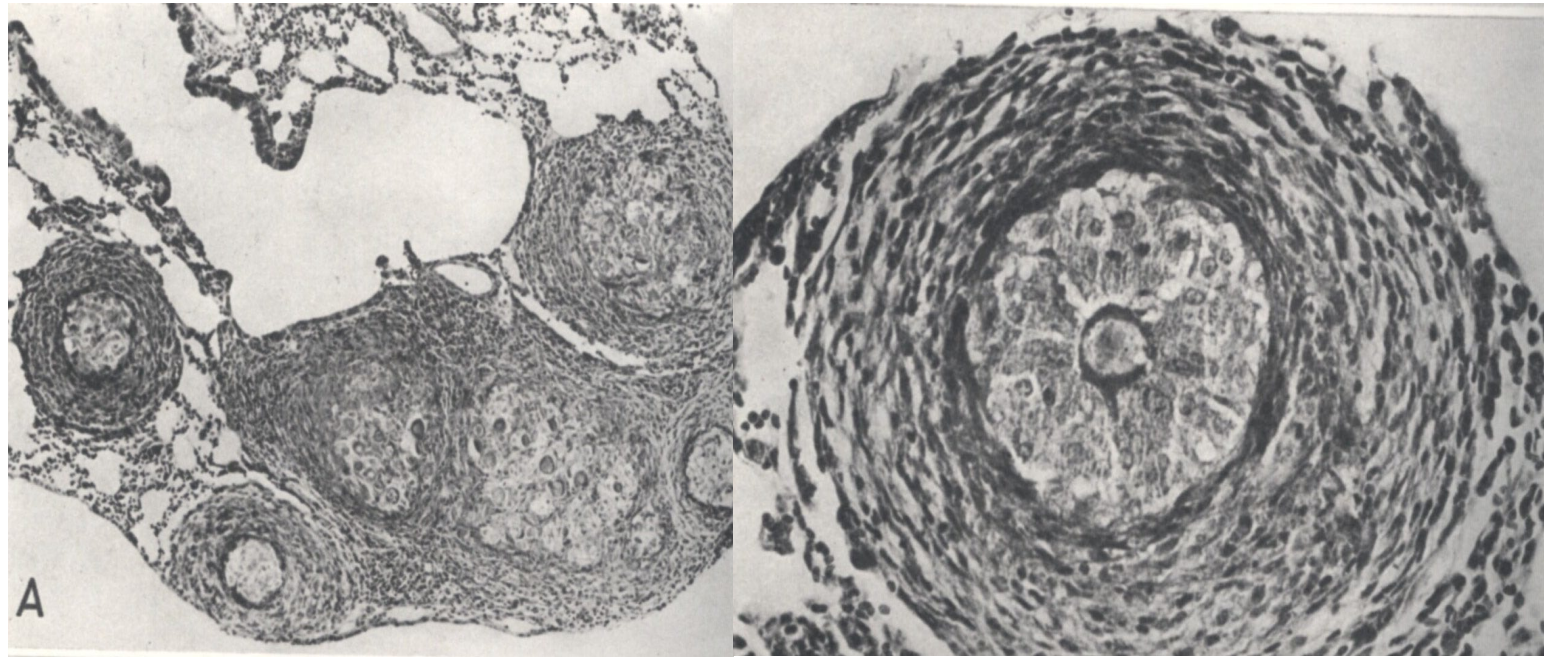
1830 1850 1870 1890 1910 1930 1950 1970 1990 2010

Coccidioides in granuloma in mouse lung

1942



Chester W. Emmons



Ashburn and Emmons 1942. *Archives of Pathology* 34:791-800.

Emmons and Ashburn, 1942

Public Health Reports

Vol. 57 • NOVEMBER 13, 1942 • No. 46

THE ISOLATION OF *HAPLOSPORANGIUM PARVUM* N. SP.
AND *COCCIDIOIDES IMMITIS* FROM WILD RODENTS.
DIOIDOMYCOSIS^{1,2}

L. L. ASHBURN, Passed Assistant
Public Health Service



Pocket Mouse
Perognathus.....

Dipodomys.....



Kangaroo Rat
Total.....

Total trapped	Lesions	Only <i>C. immitis</i> isolated	Only <i>H. parvum</i> isolated	<i>C. immitis</i> and <i>H. parvum</i> isolated	Total animals	
124	{ Seen Not seen	11 1	18 60	5 2	34 63	13%
29	{ Seen Not seen	3 -----	1 5	2 -----	6 5	17%
10	{ Seen Not seen	----- -----	5 -----	----- -----	5 -----	
27	{ Seen Not seen	1 -----	----- 1	----- -----	1 1	
113	{ Seen Not seen	----- -----	----- 2	----- -----	----- 2	
303	-----	16	92	9	*117	

*Cultures from 11 additional animals were contaminated and the pathogens, if present, were lost.

Emmons, 1943

Journal of Bacteriology, 1943, 45:306

WASHINGTON BRANCH
ONE HUNDRED AND TWENTY-NINTH MEETING
GEORGE WASHINGTON MEDICAL SCHOOL
JANUARY 26, 1943

A RESERVOIR OF COCCIDIOIDOMYCOSIS IN WILD RODENTS. C. W. EMMONS
Emmons, National Institute of Health, U. S. Public Health Service. Pulmonary

. . . it may be primarily a disease of rodents . . . certain species of rodents constitute a natural reservoir of coccidioidomycosis . . .

Plunkett and Swatek, 1957

Ecological studies of *Coccidioides immitis*.
Orda A. Plunkett and F. E. Swatek
In: Ajello, L. et al. 1957. Proc. Symp. Coccidioidomycosis.
Public Health Service Publication 575.

May 1954, outbreak with 5 UCLA anthropology students

Soil Samples from the midden -- positive.

80 burrow samples taken near the midden – all negative.

440 native rodents near the midden -- all negative.

Environmental background and significance

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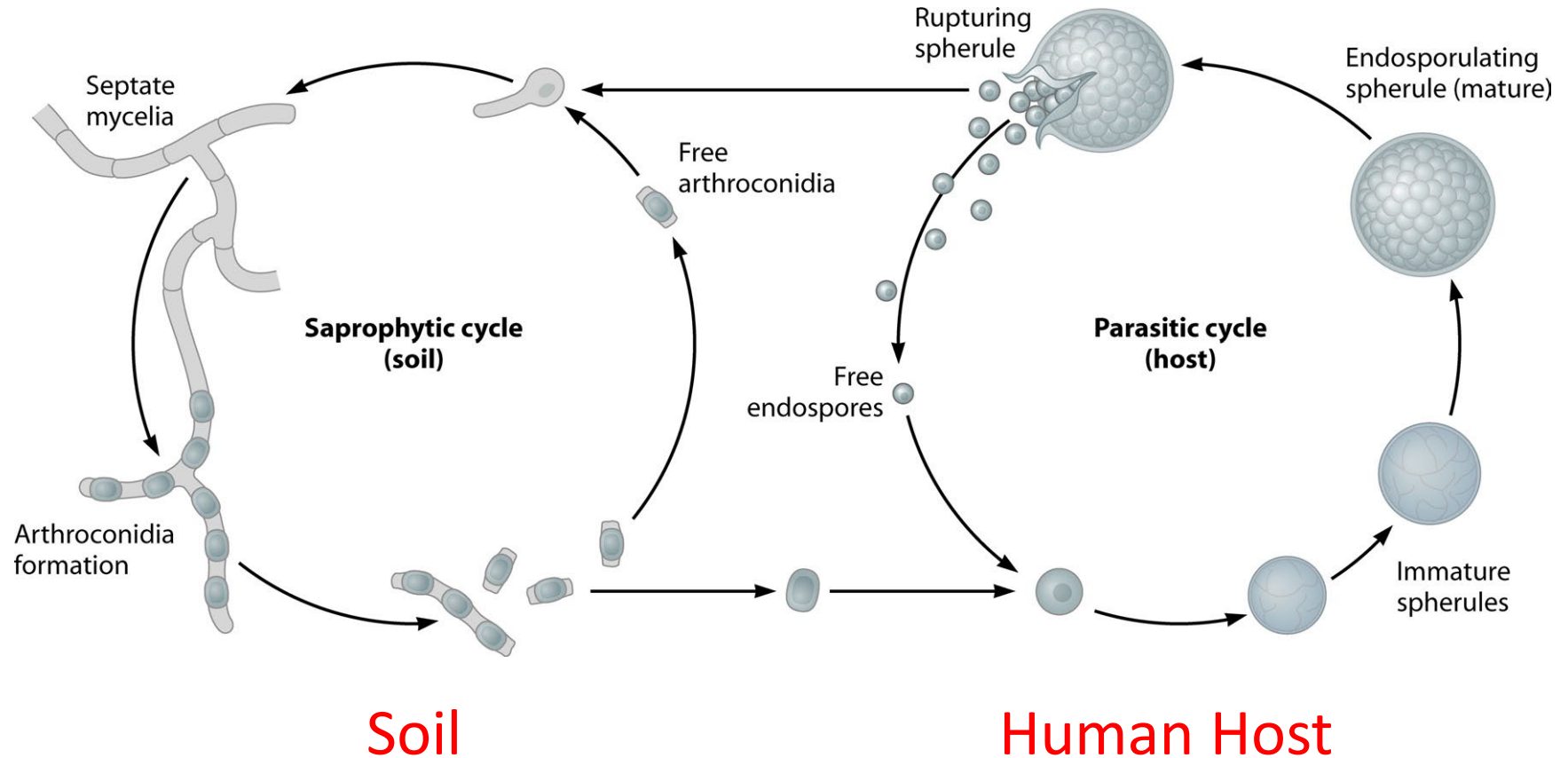
Revisionist Environmental Cycle

Hypothesis testing



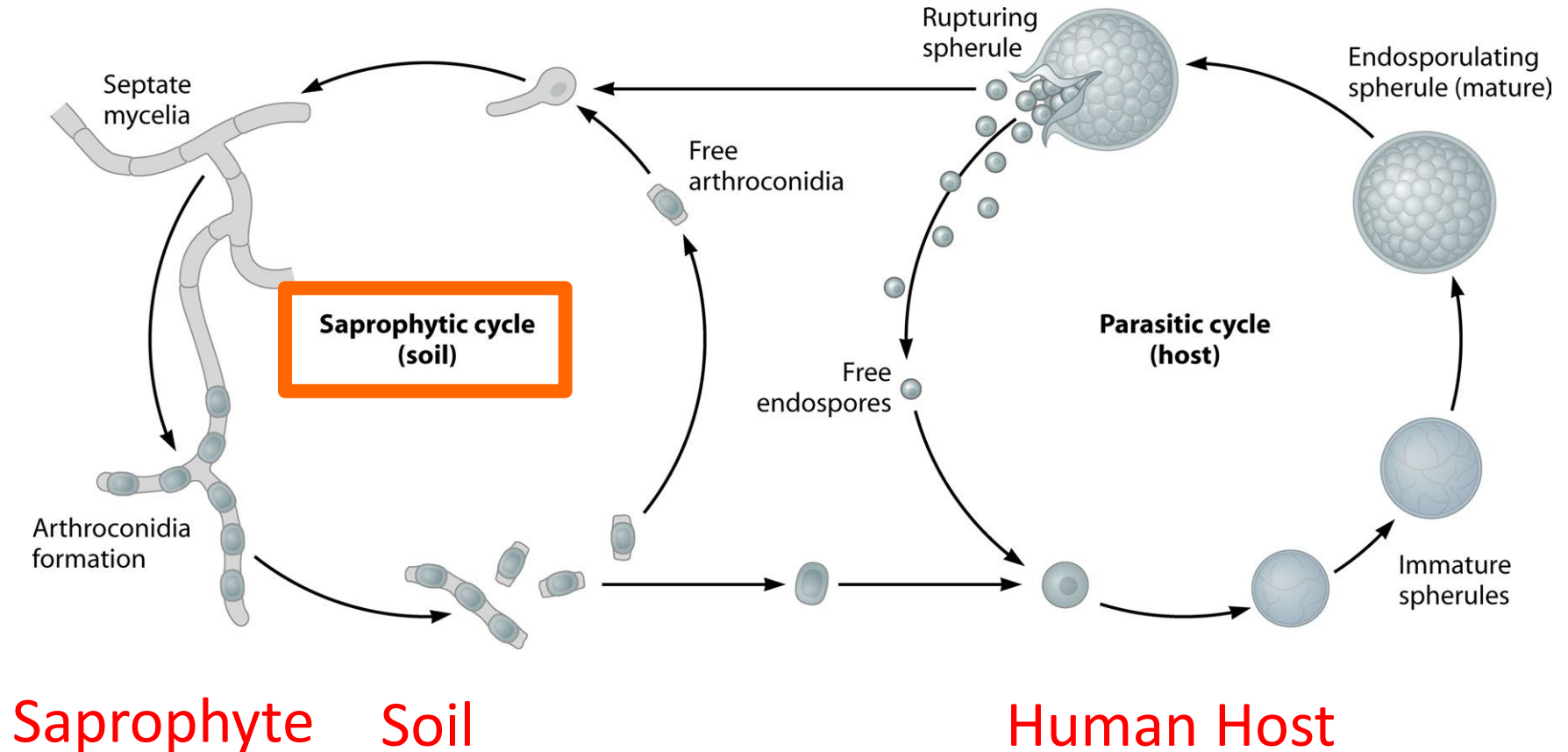
**Recent Advances in Our Understanding of
the Environmental, Epidemiological,
Immunological, and Clinical Dimensions of
Coccidioidomycosis**

Chinh Nguyen, Bridget Marie Barker, Susan Hoover, David
E. Nix, Neil M. Ampel, Jeffrey A. Frelinger, Marc J. Orbach
and John N. Galgiani
Clin. Microbiol. Rev. 2013, 26(3):505. DOI:
10.1128/CMR.00005-13.



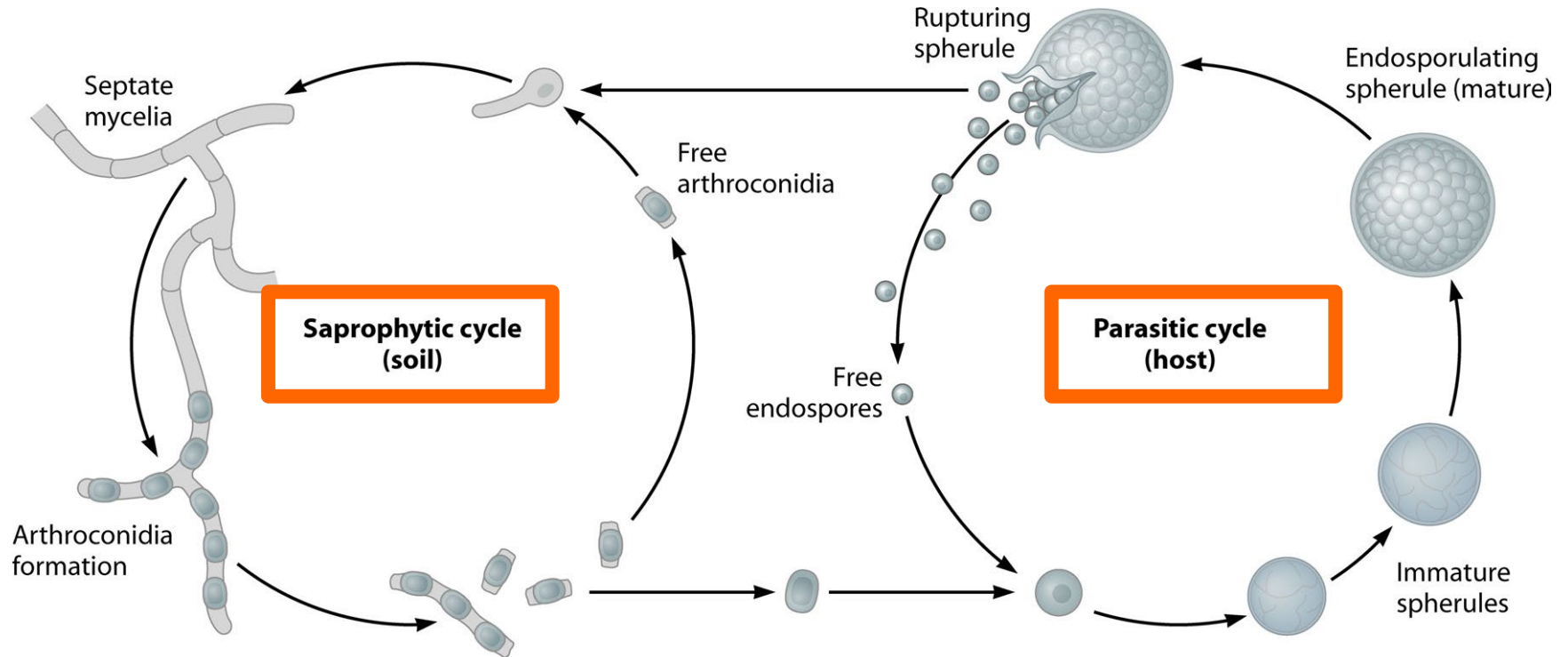
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10.1128/CMR.00005-13.



Saprophyte Soil

Human Host Parasite

Environmental background and significance

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Letter

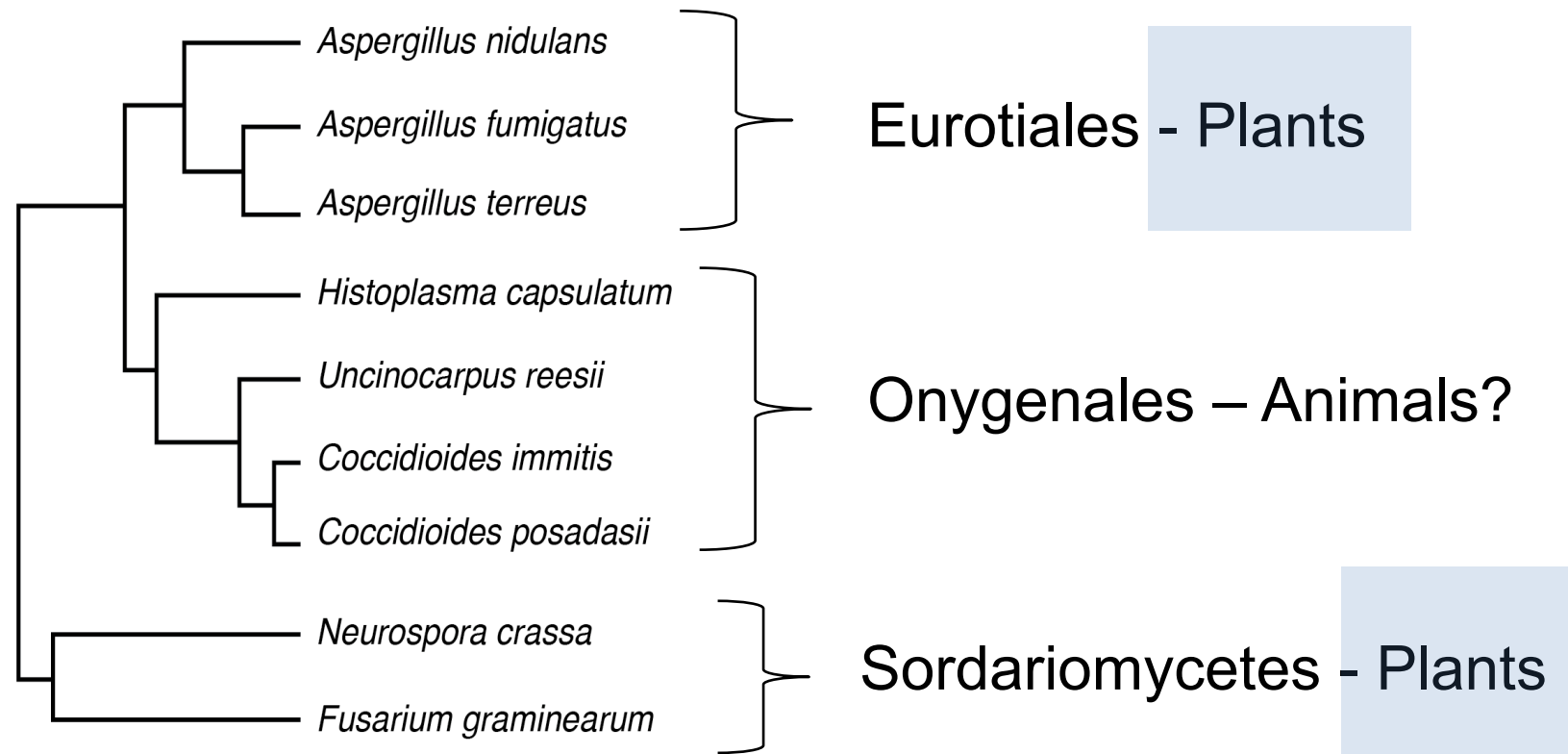
Comparative genomic analyses of the human fungal pathogens *Coccidioides* and their relatives

Thomas J. Sharpton,^{1,11} Jason E. Stajich,¹ Steven D. Rounsley,² Malcolm J. Gardner,³ Jennifer R. Wortman,⁴ Vinita S. Jordar,⁵ Rama Maiti,⁵ Chinnappa D. Kodira,⁶ Daniel E. Neafsey,⁶ Qiandong Zeng,⁶ Chiung-Yu Hung,⁷ Cody McMahan,⁷ Anna Muszewska,⁸ Marcin Grynberg,⁸ M. Alejandra Mandel,² Ellen M. Kellner,² Bridget M. Barker,² John N. Galgiani,⁹ Marc J. Orbach,² Theo N. Kirkland,¹⁰ Garry T. Cole,⁷ Matthew R. Henn,⁶ Bruce W. Birren,⁶ and John W. Taylor¹

1890 1910 1920 1940 1960 1980 2000 2020

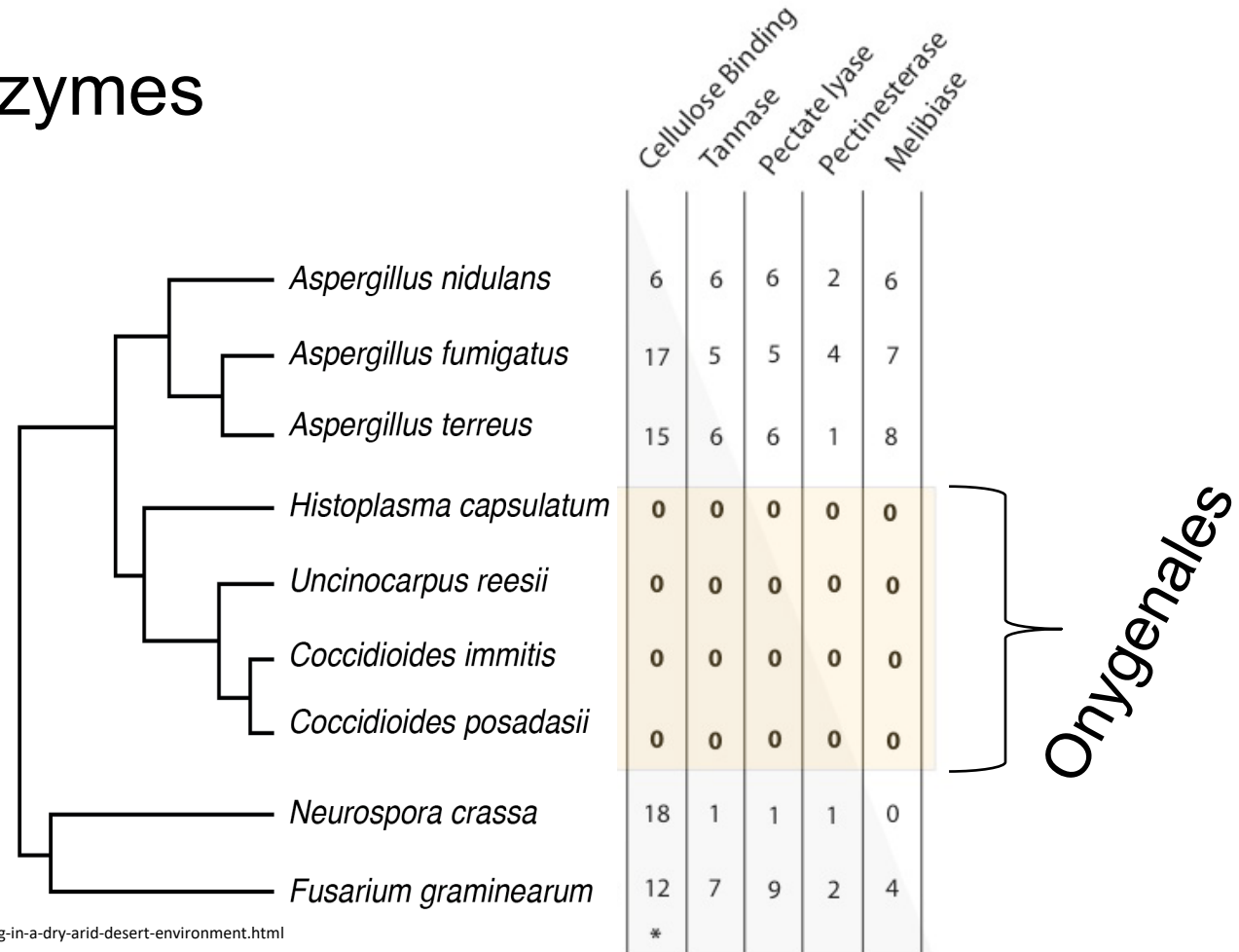


Evolution of Gene Family Size



Gene Family Reductions:

Genes coding enzymes
that digest plants



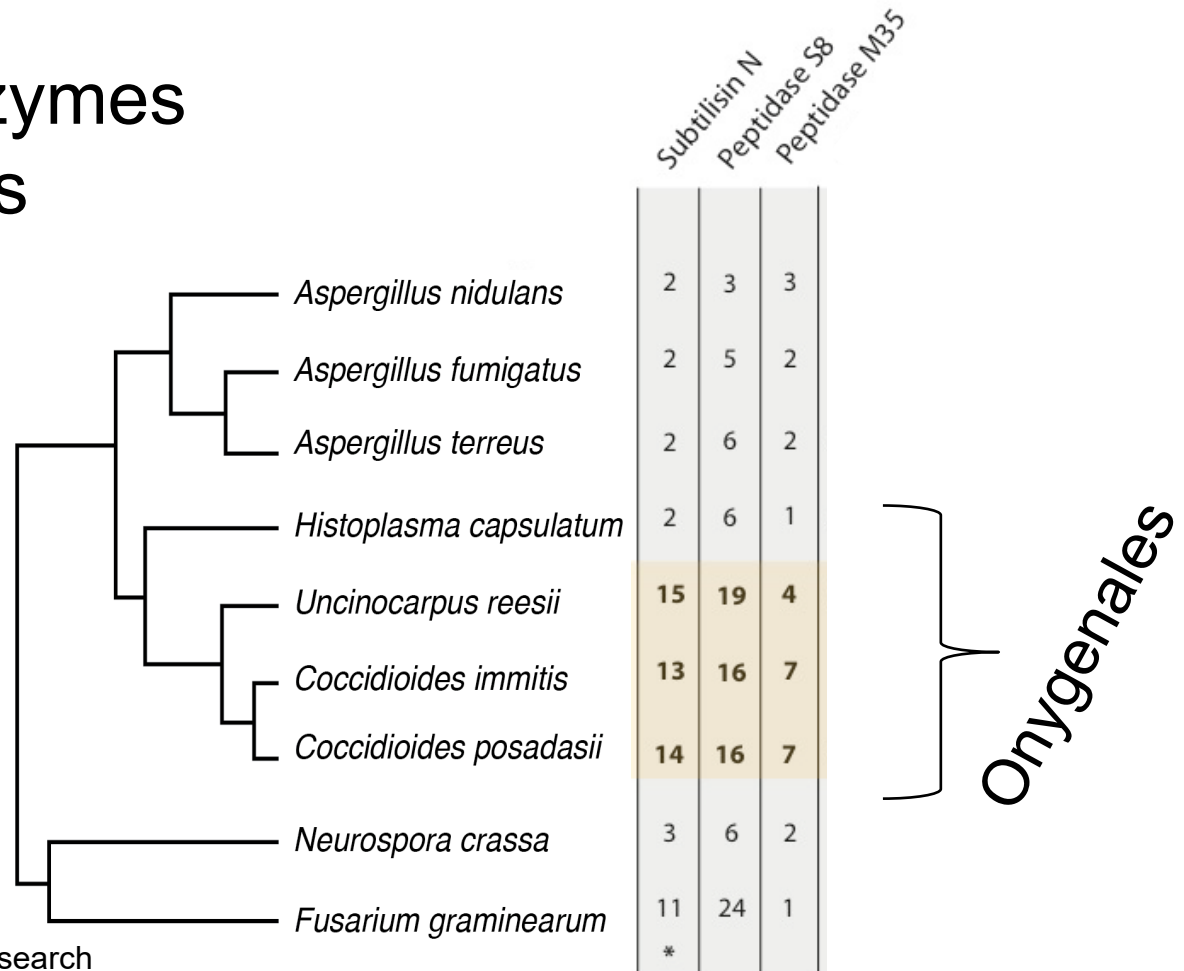
https://www.123rf.com/photo_27279678_dried-out-dead-plants-lying-in-a-dry-arid-desert-environment.html

Gene Family Expansion:

Genes coding enzymes
that digest animals



Perognathus longimembris



Sharpton, Stajich et al. 2009. *Genome Research*

Wet protein in a dry desert



Environmental background and significance



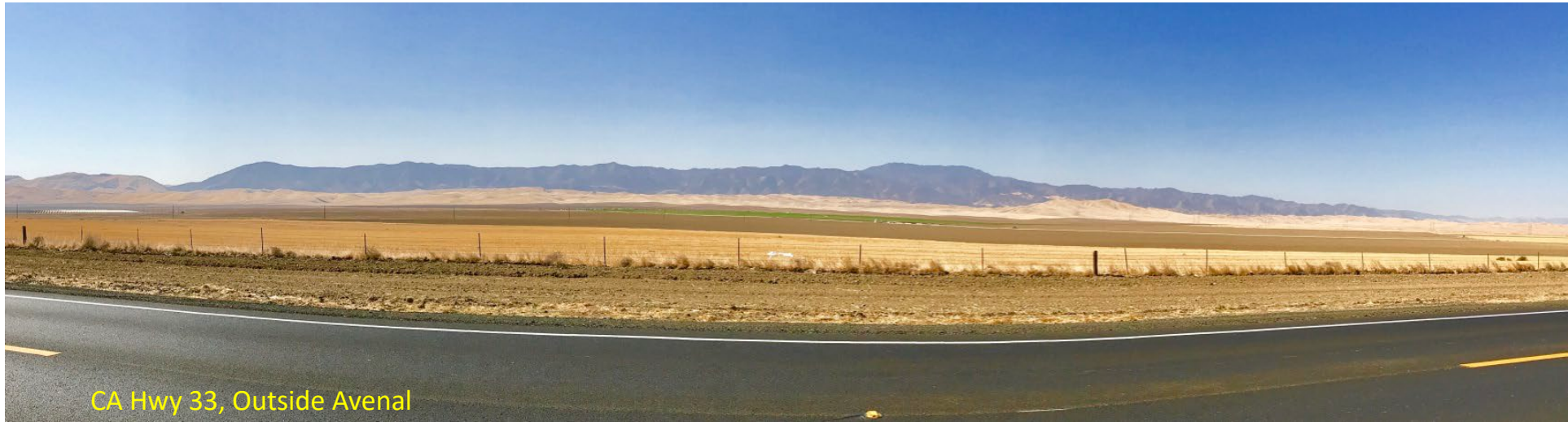
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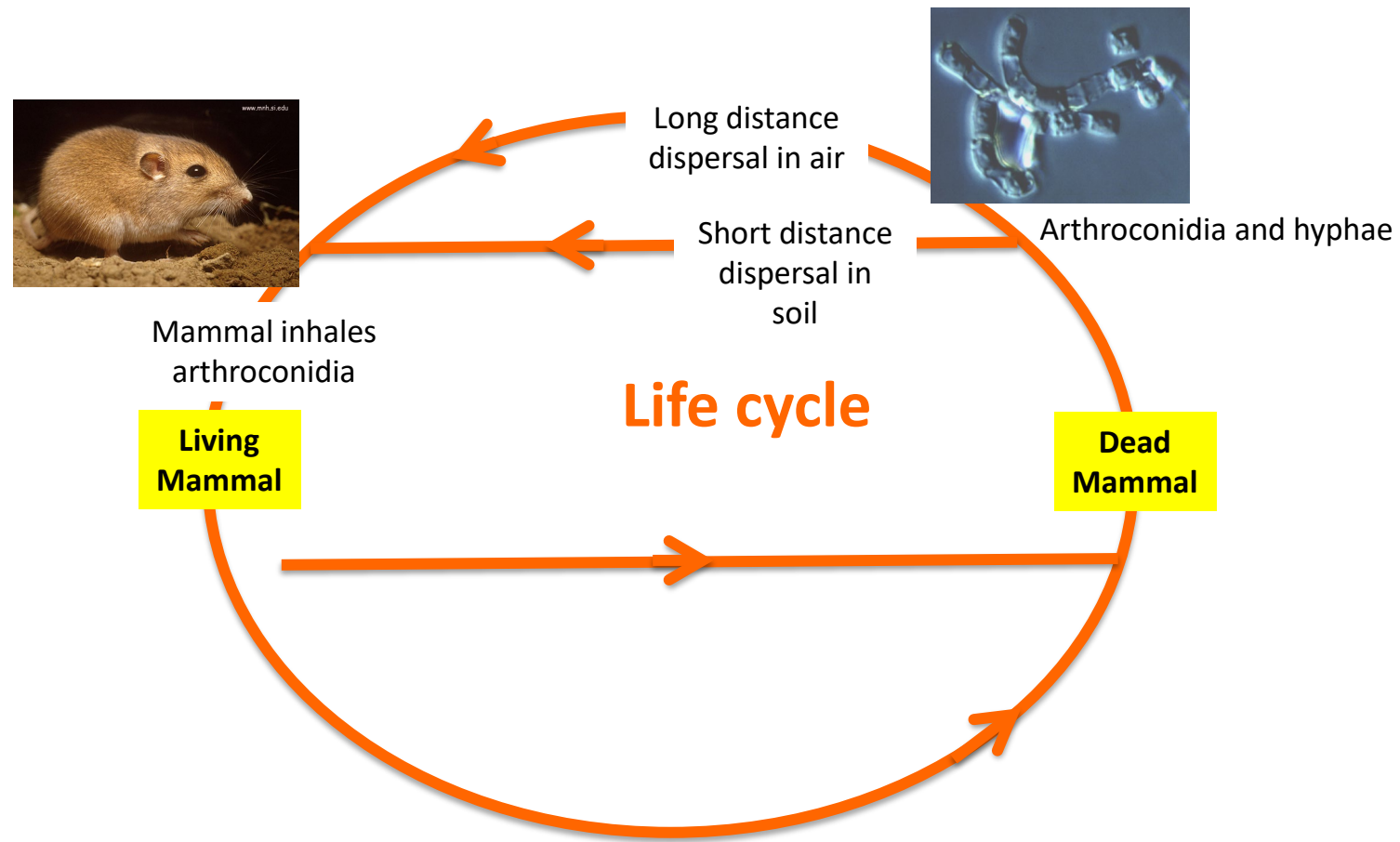
Hypothesis testing

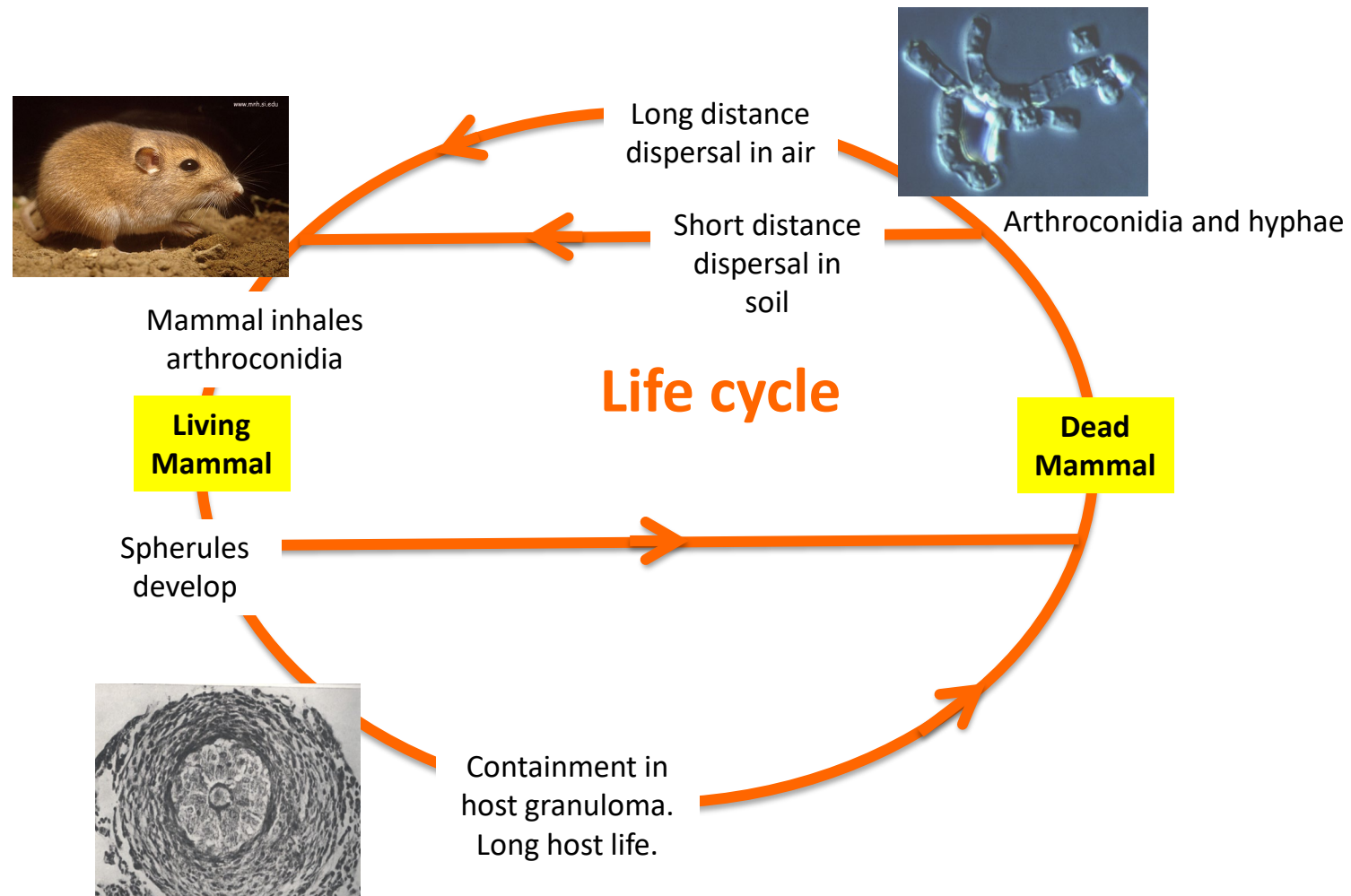


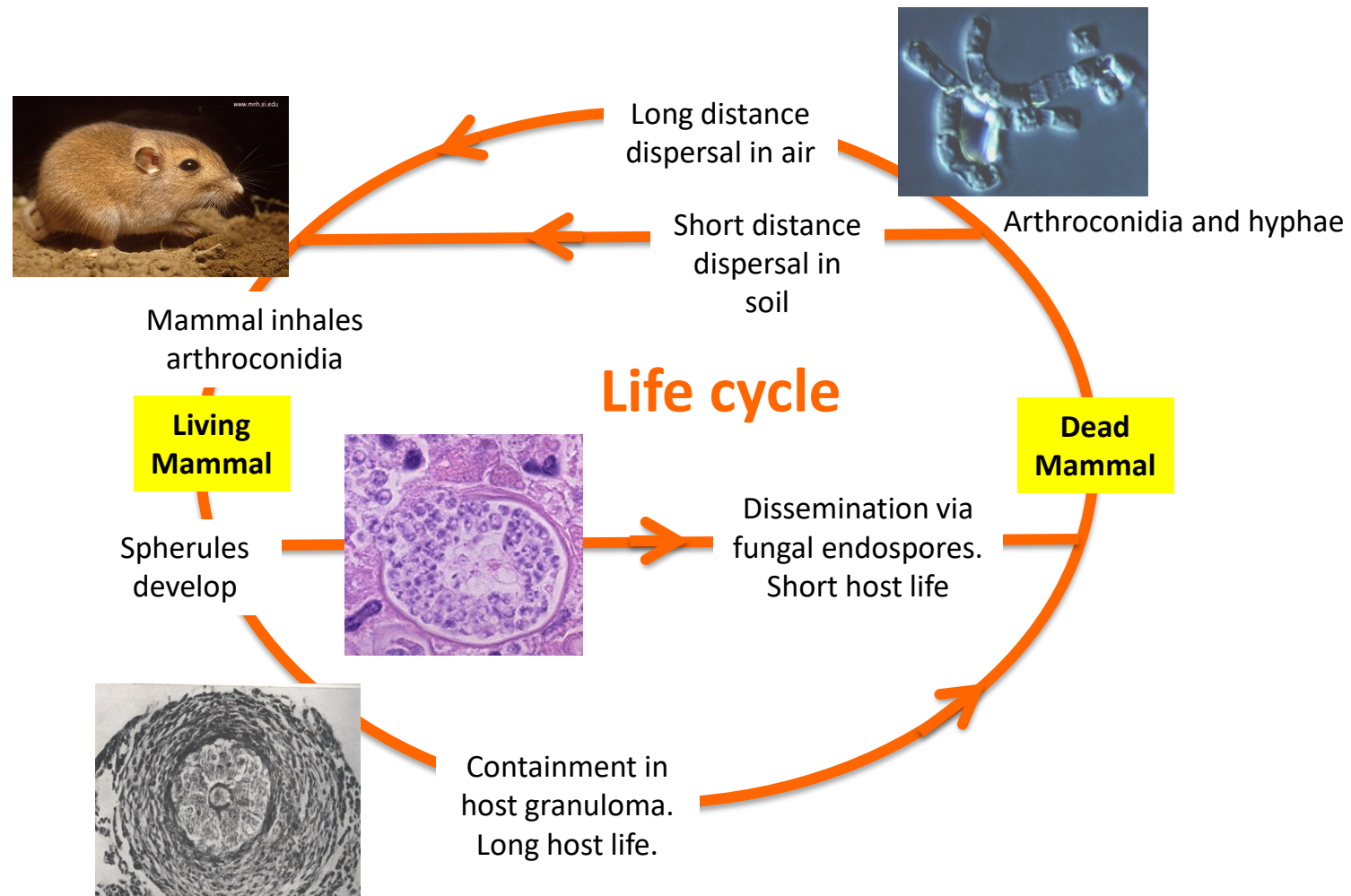
Review Article

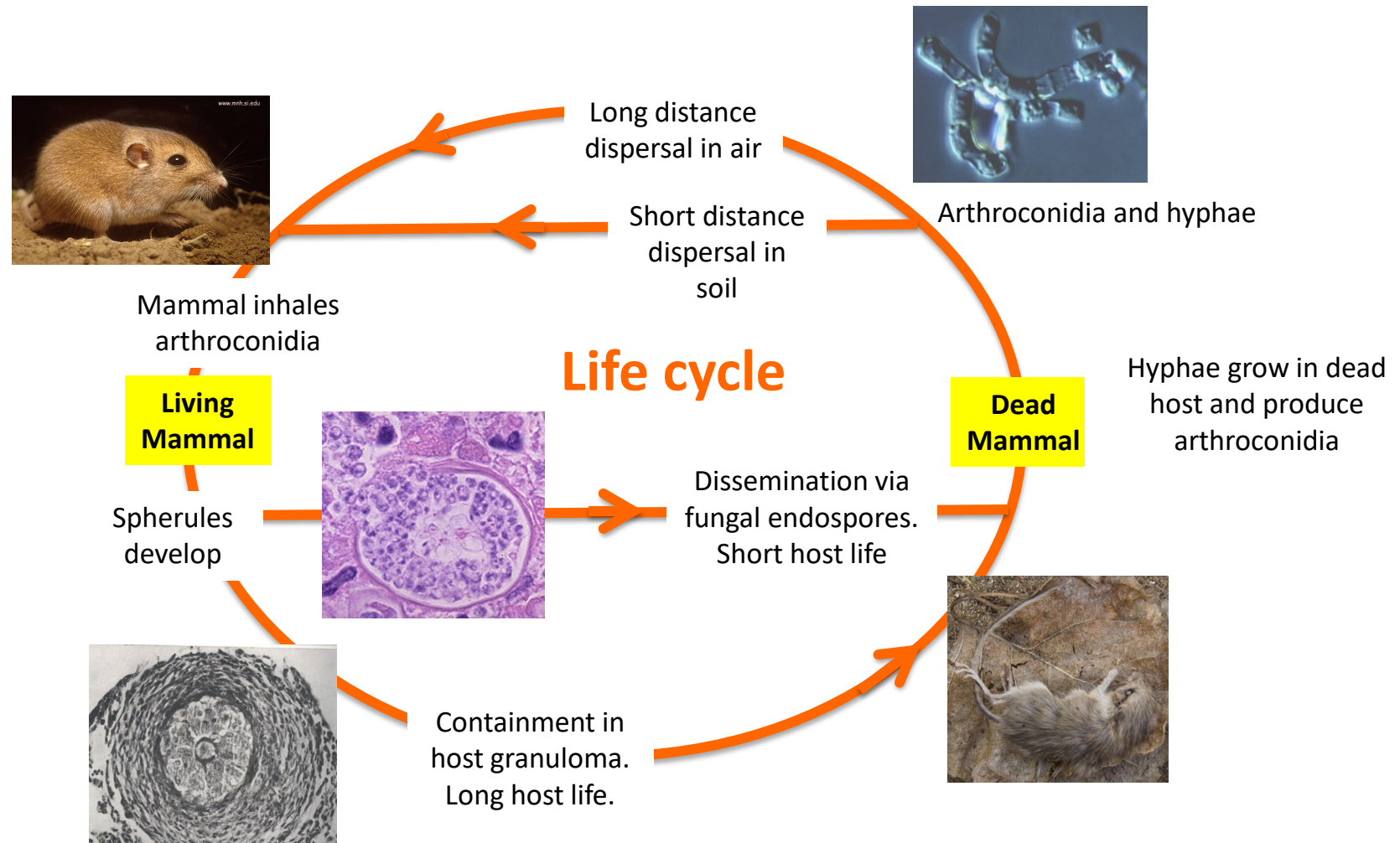
The endozoan, small-mammal reservoir hypothesis and the life cycle of *Coccidioides* species

John W. Taylor^{1,*} and Bridget M. Barker²







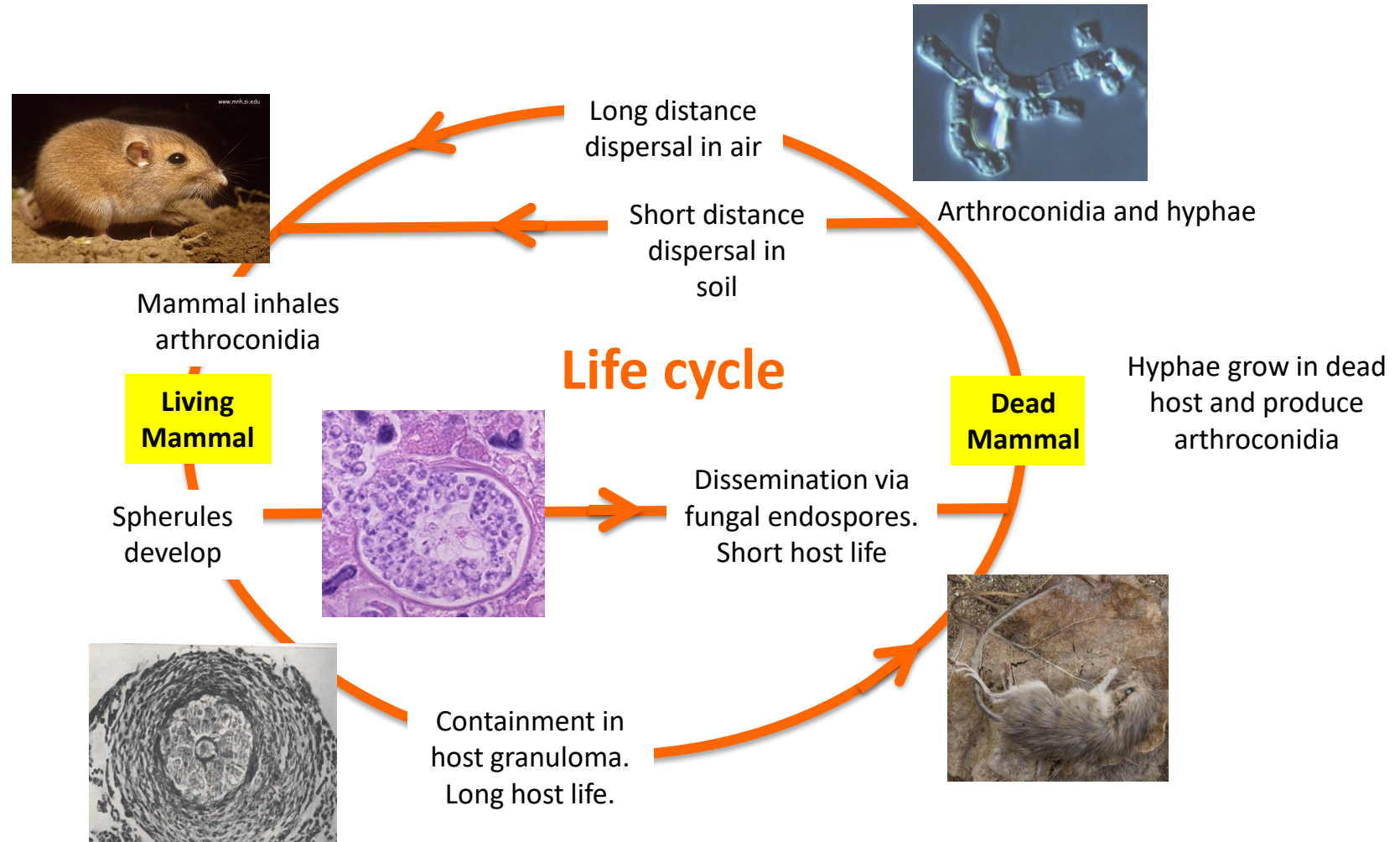


Coccidioides
environmental
cycle.

No saprophyte

No soil

No human host



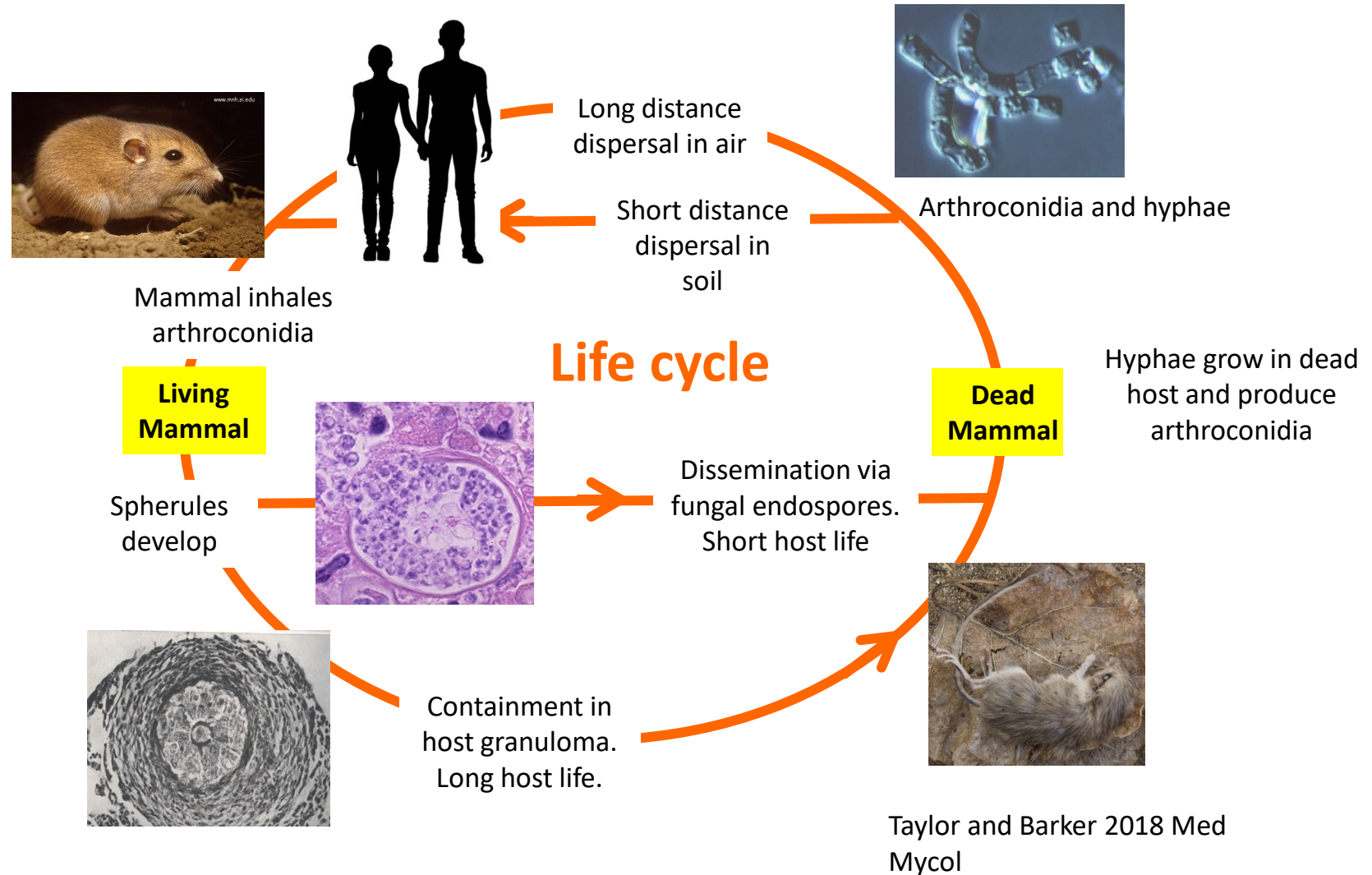
Humans are a dead end for *Coccidioides*

Coccidioides
environmental
cycle.

No saprophyte

No soil

No human host



Environmental background and significance



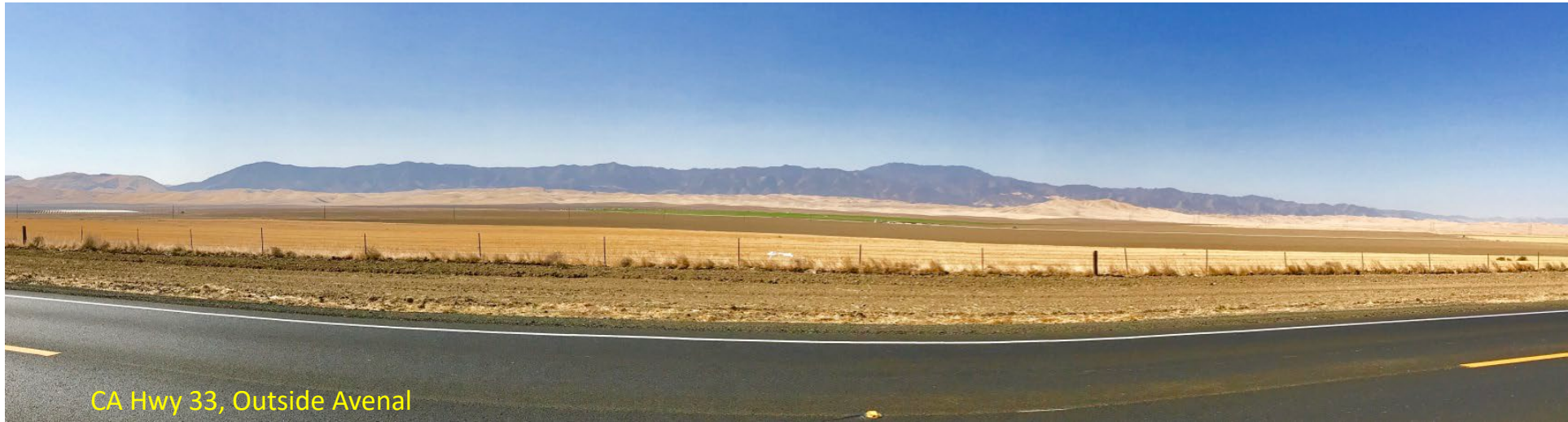
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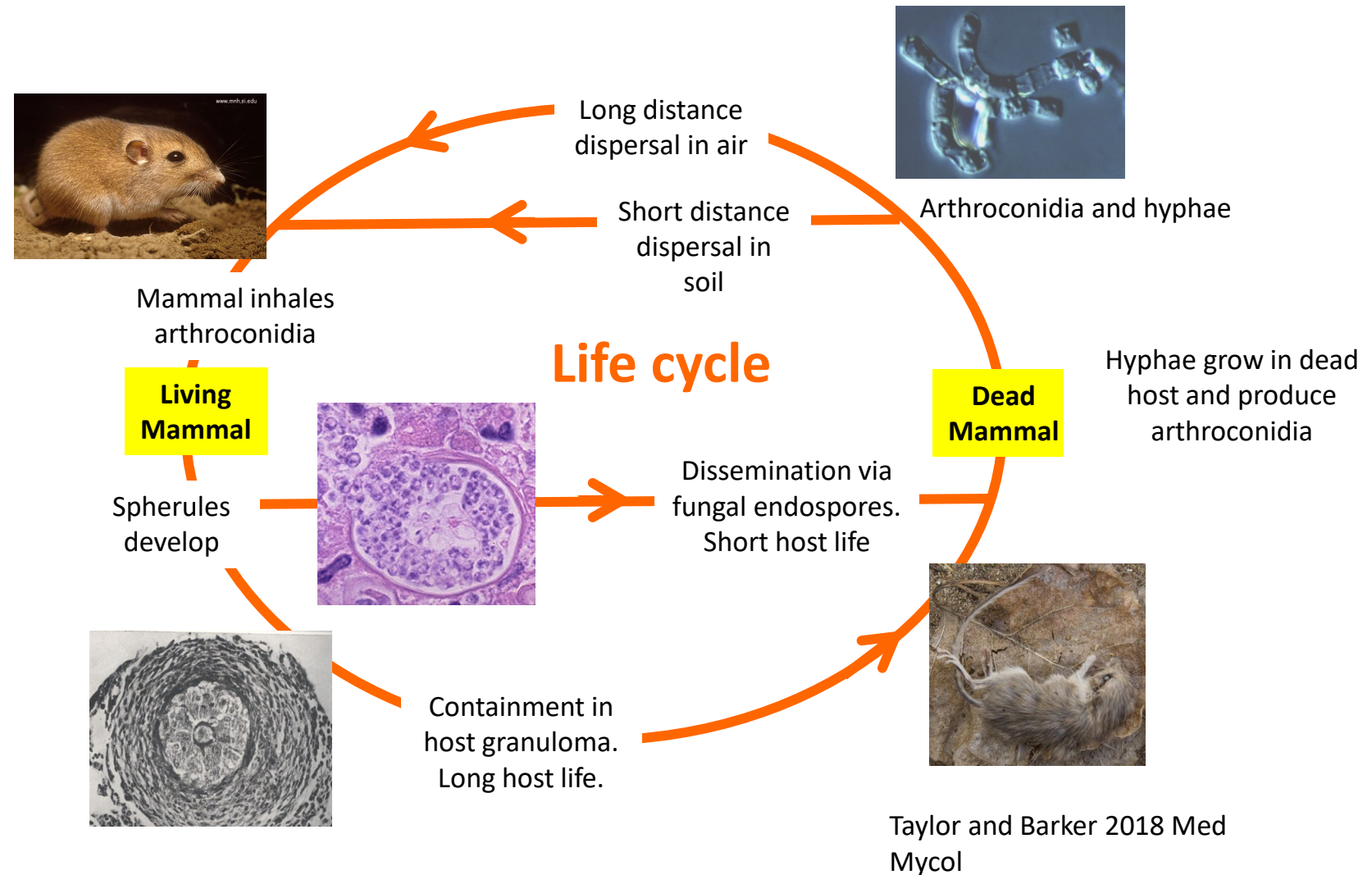
Genomics

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If this cycle is correct, native rodents should harbor *Coccidioides*



Public Health Reports

Vol. 57 • NOVEMBER 13, 1942 • No. 46

Emmons and Ashburn, 1942

1942

THE ISOLATION OF *HAPLOSPORANGIUM PARVUM* N. SP.
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COCCIDIDOMYCOSIS ^{1, 2}

L. L. ASHBURN, Passed Assistant
Public Health Service



	Total trapped	Lesions	Only <i>C. immitis</i> isolated	Only <i>H. parvum</i> isolated	<i>C. immitis</i> and <i>H. parvum</i> isolated	Total animals	
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Kangaroo Rat							
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Catalán-Dibene et al. 2014, Meritxell Riquelme's lab at CICESE in Ensenada, Baja California



Fungal Biology

Volume 118, Issue 3, March 2014, Pages 330-339



Detection of coccidioidal antibodies in serum of a small rodent community in Baja California, Mexico

Jovani Catalán-Dibene ^{a, d, 1}, Suzanne M. Johnson ^b, Ricardo Eaton ^c, Adriana L. Romero-Olivares ^{d, 2}, Raúl C. Baptista-Rosas ^{a, e, 3}, Demosthenes Pappagianis ^b, Meritxell Riquelme ^d  

Location	Native Rodents	<i>Coccidioides</i>	Percentage
Val de las Palmas	40	3	7.5%

Paris Salazar-Hamm et al. 2022 from Don Nativig's lab at the University of New Mexico



frontiers

| Frontiers in **Fungal Biology**

26 September 2022

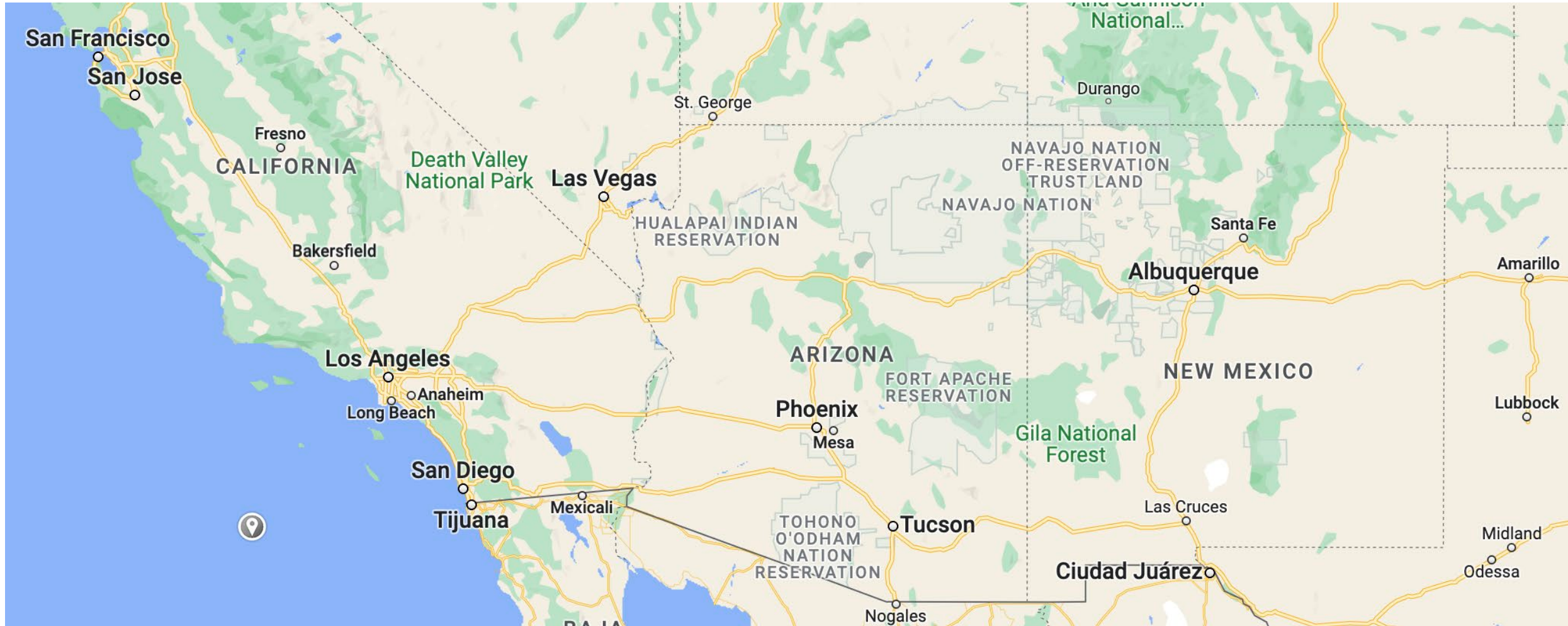
Breathing can be dangerous: Opportunistic fungal pathogens and the diverse community of the small mammal lung mycobiome

Paris S. Salazar-Hamm^{1*}, Kyana N. Montoya¹, Liliam Montoya²,
Kel Cook¹, Schuyler Liphardt¹, John W. Taylor²,
Joseph A. Cook^{1,3} and Donald O. Nativig¹

¹Department of Biology, University of New Mexico, Albuquerque, NM, United States, ²Department of Plant and Microbial Biology, University of California, Berkeley, Berkeley, CA, United States,

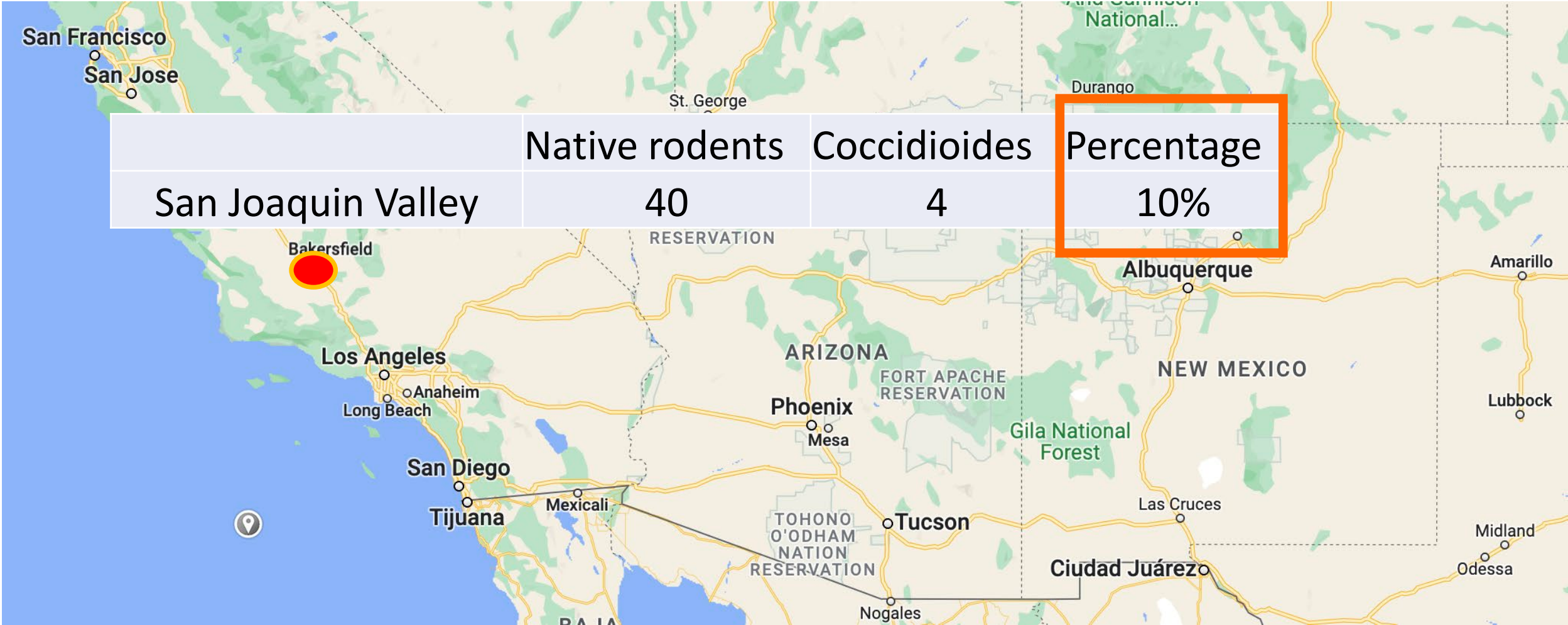
³Museum of Southwestern Biology, University of New Mexico, Albuquerque, NM, United States

Paris Salazar-Hamm et al. 2022 from Don Nativig's lab at the University of New Mexico
Lungs of 200 rodents in NM, AZ, CA, tested for *Coccidioides*.

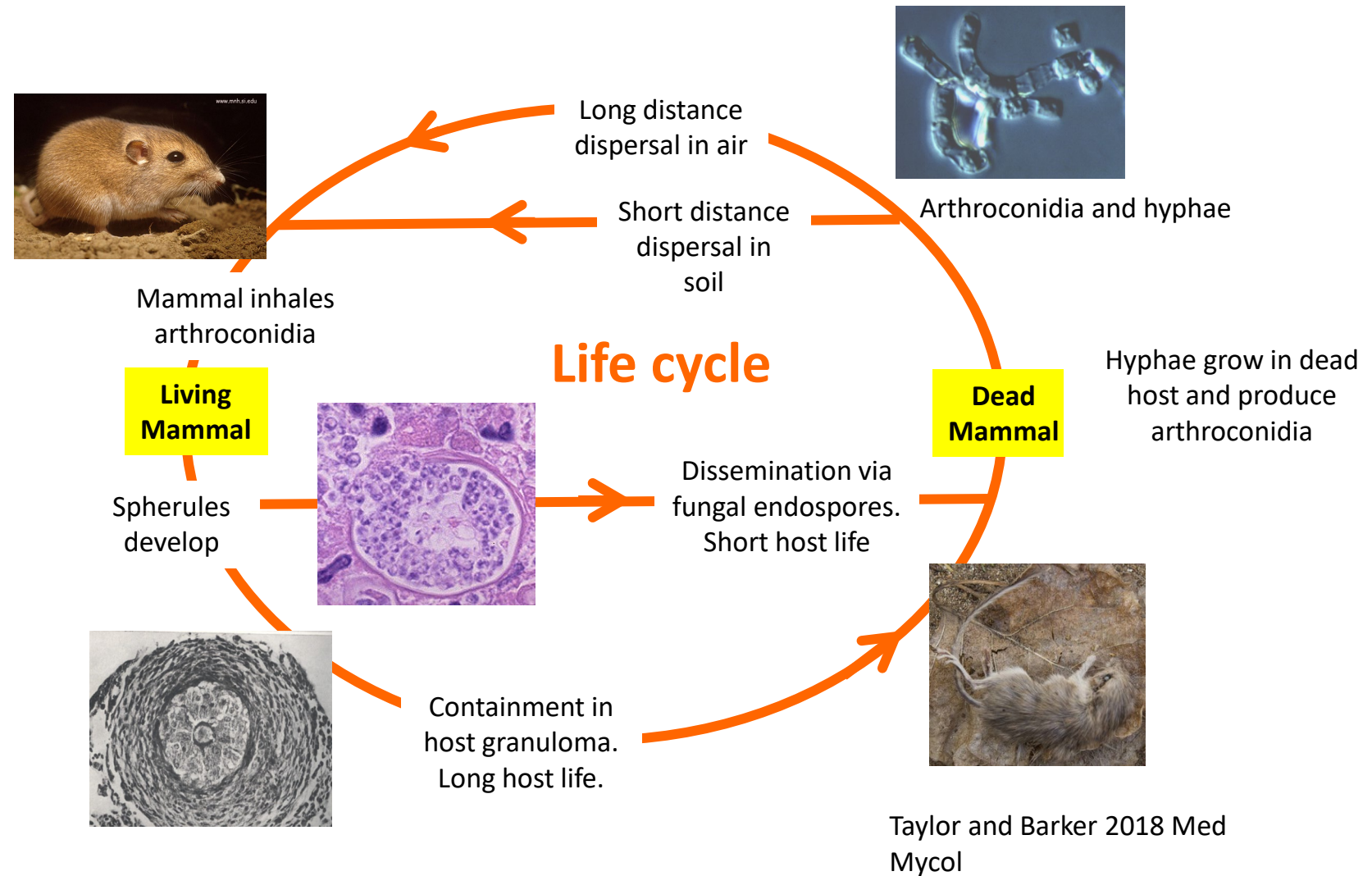


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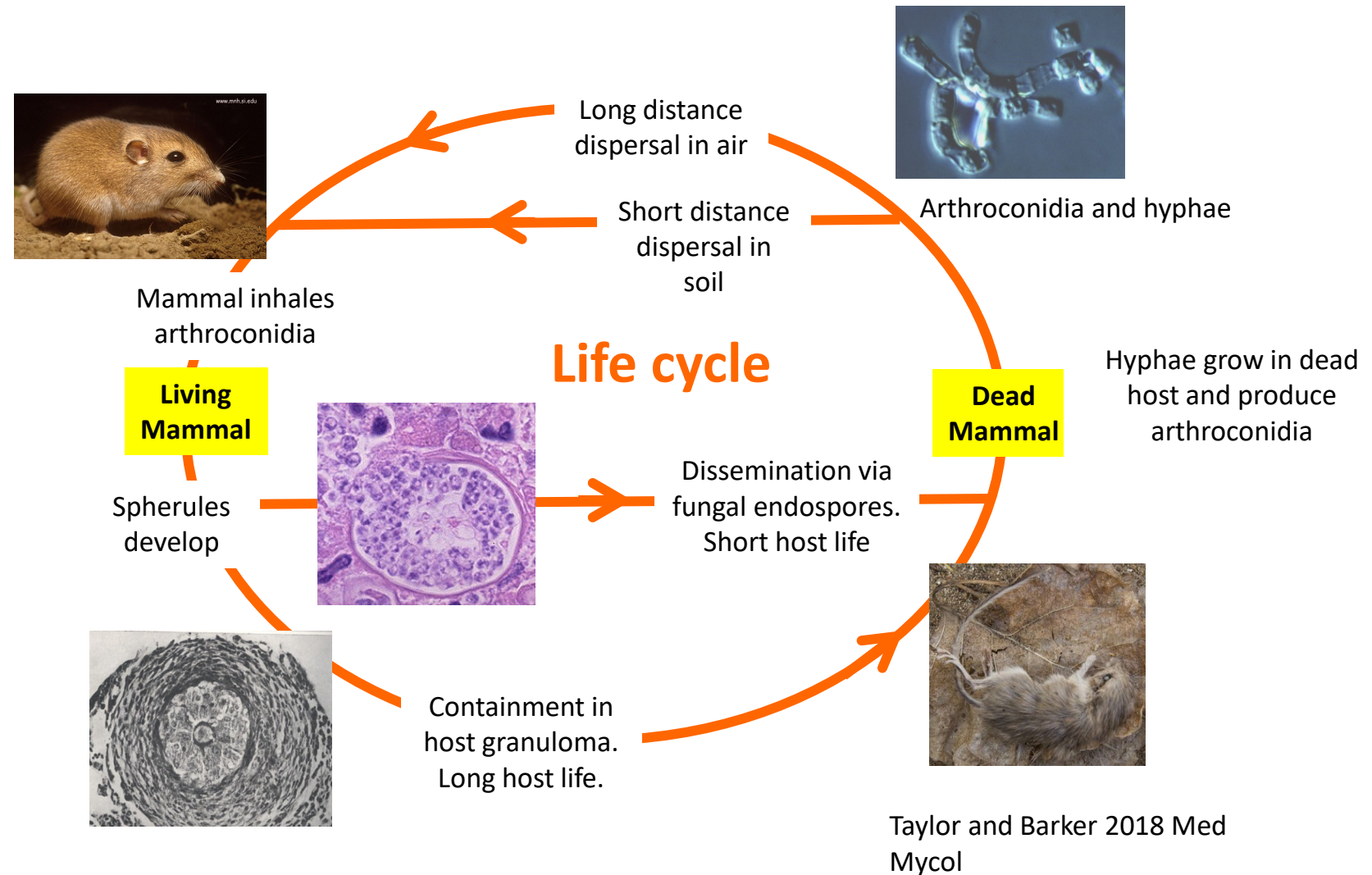
Lungs of 200 rodents in NM, AZ, CA, tested for *Coccidioides*.



Native rodents harbor *Coccidioides*



If this cycle is correct, rodent burrows should contain *Coccidioides*



Baptista-rosas et al. 2012, Meritxell Riquelme's lab at CICESE in Ensenada, Baja California



Fungal Ecology

Volume 5, Issue 2, April 2012, Pages 177-190



Molecular detection of *Coccidioides* spp. from environmental samples in Baja California: linking Valley Fever to soil and climate conditions

Raúl C. Baptista-rosas ^{a, b}, Jovani Catalán-dibene ^b, Adriana L. Romero-olivares ^b, Alejandro Hinojosa ^c, Tereza Cavazos ^d, Meritxell Riquelme ^e  

Location	Burrows	Coccidioides	Percentage
Val de las Palmas	50	17	34%
San Jose de la Zorra	13	3	23%

Kollath et al. 2020 in Bridget Barker's lab at Northern Arizona University

2020

Mycopathologia (2020) 185:145–159
<https://doi.org/10.1007/s11046-019-00391-2>



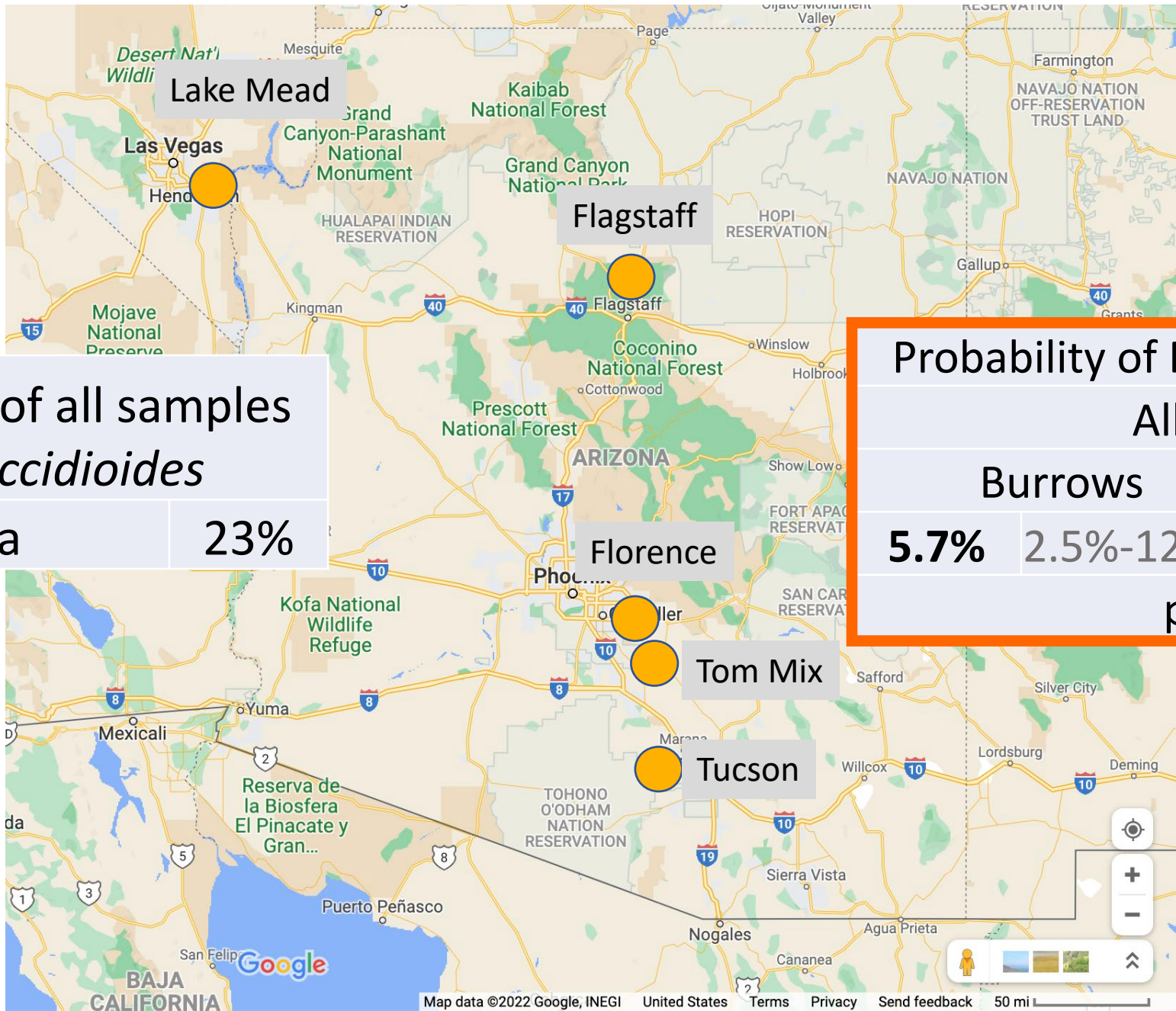
ORIGINAL PAPER

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**

456 soil samples, 5 sites in Arizona

Kollath et al. 2020 in Bridget Barker's lab at Northern Arizona University



Percentage of all samples
with *Coccidioides*

Arizona	23%
---------	-----

Probability of Detecting Coccidioides			
All Five Sites			
Burrows		Outside Burrows	
5.7%	2.5%-12.5%	2.01%	0.5%-6.8%
p = 0.015			

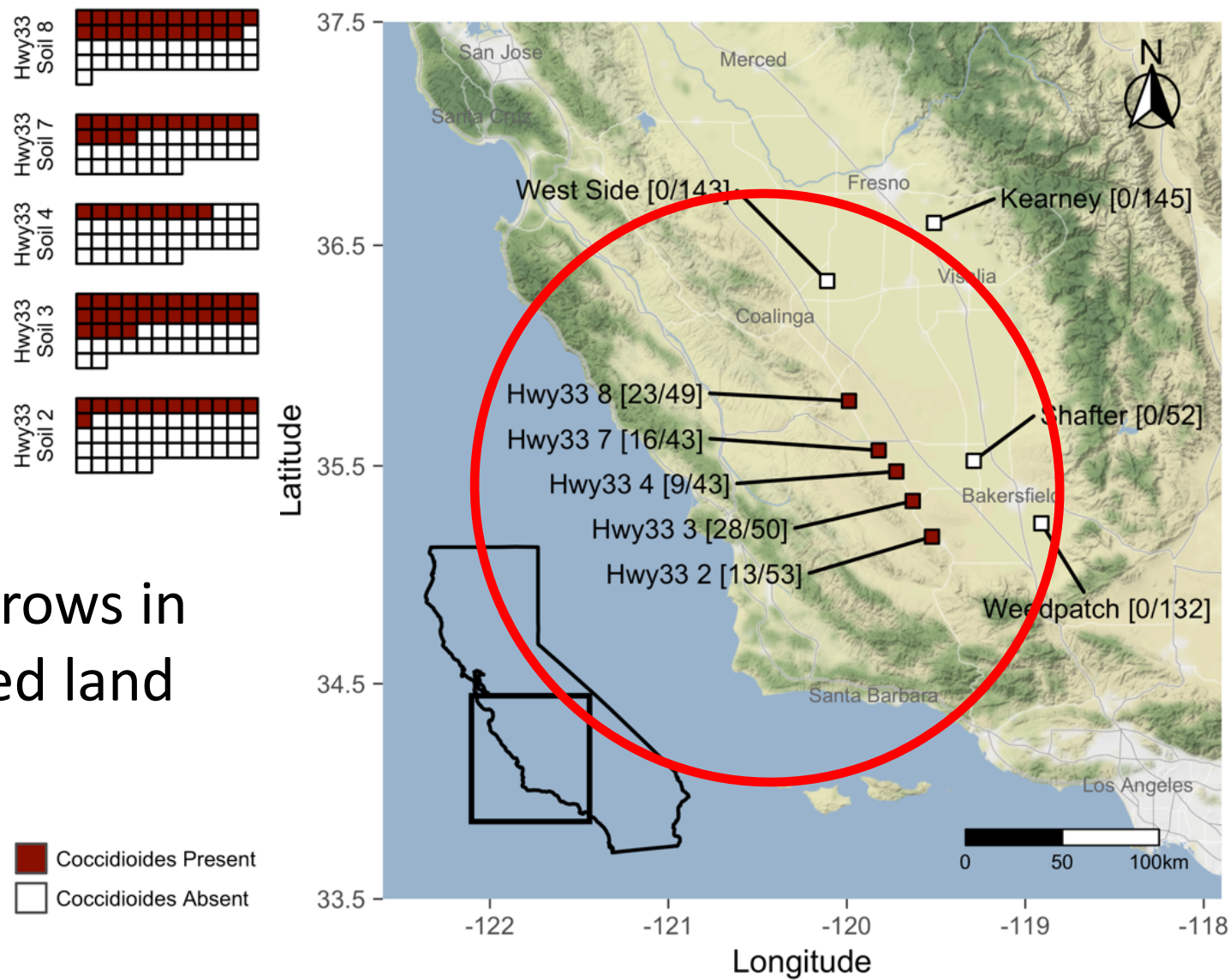
Robert Wagner, Liliam Montoya, Jennifer R. Head, Simon Campo, Justin Remais, John W. Taylor. Manuscript 2023.

Coccidioides in undeveloped and agricultural soils

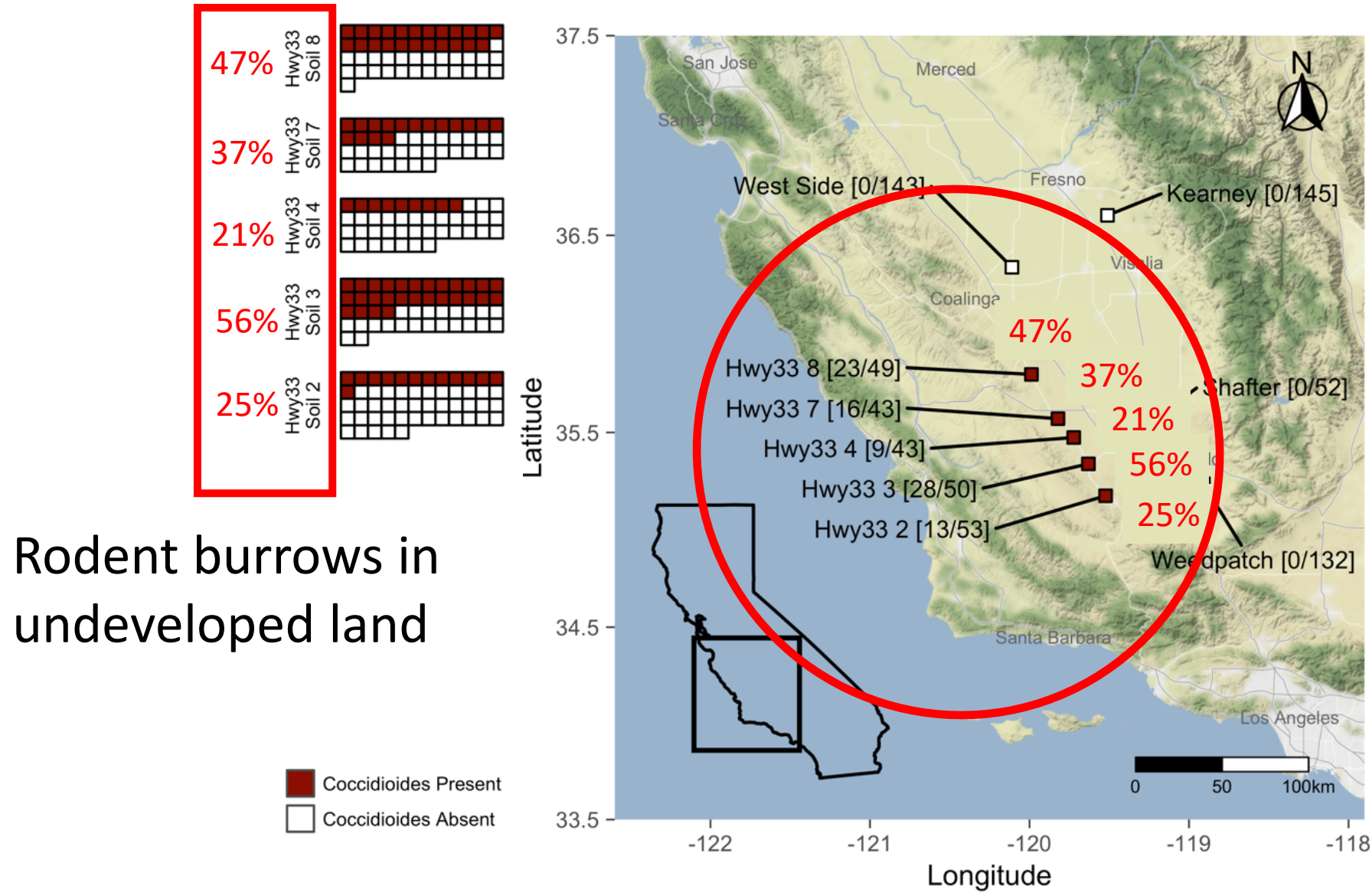
238 soil samples from 5 sites with
monthly sampling over one year

Robert Wagner, Liliam Montoya, Jennifer R. Head, Simon Campo, Justin Remais, John W. Taylor. Manuscript 2023.

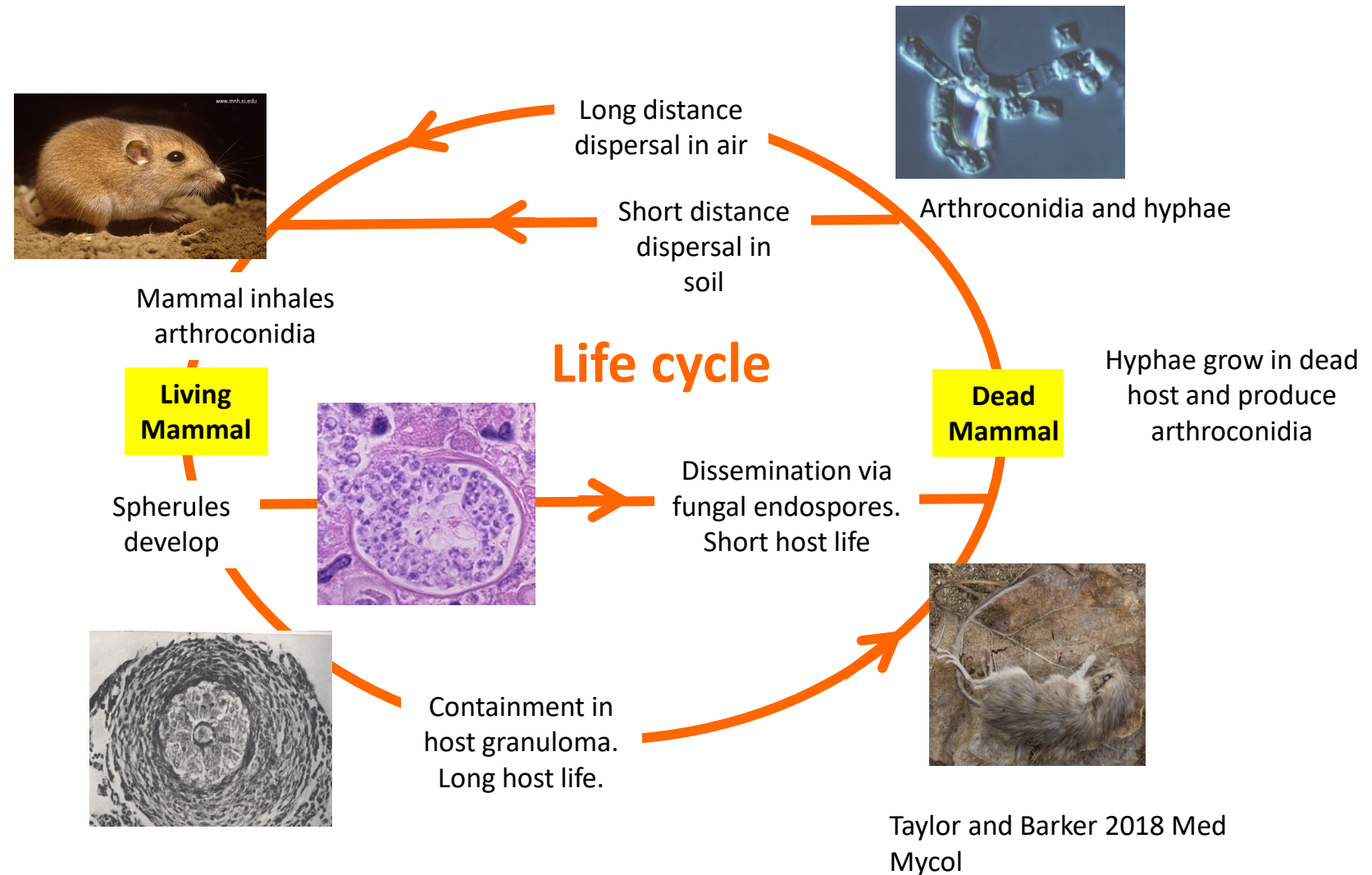
Rodent burrows in undeveloped land



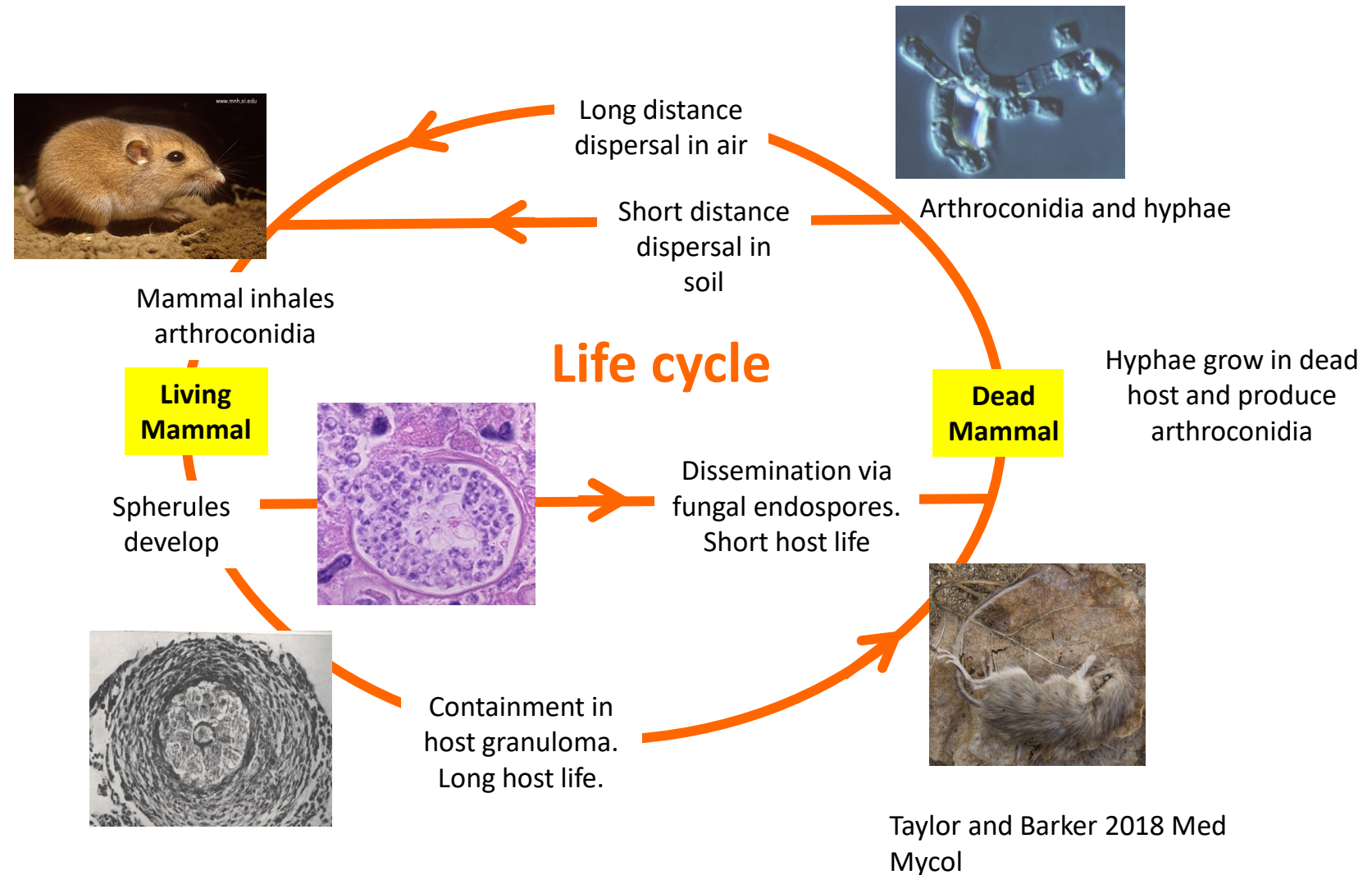
Robert Wagner, Liliam Montoya, Jennifer R. Head, Simon Campo, Justin Remais, John W. Taylor. Manuscript 2023.



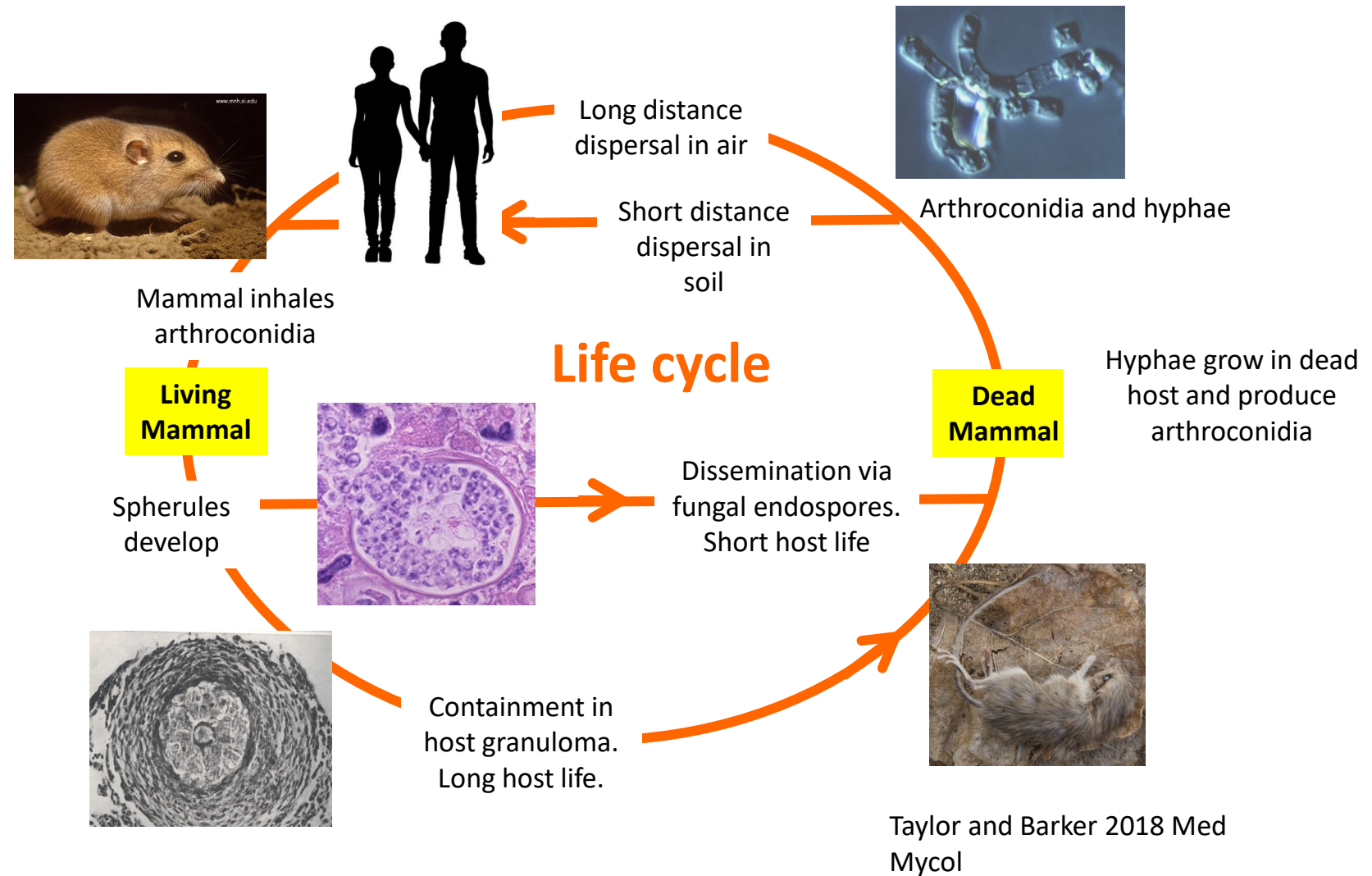
Rodent burrows do contain *Coccidioides*



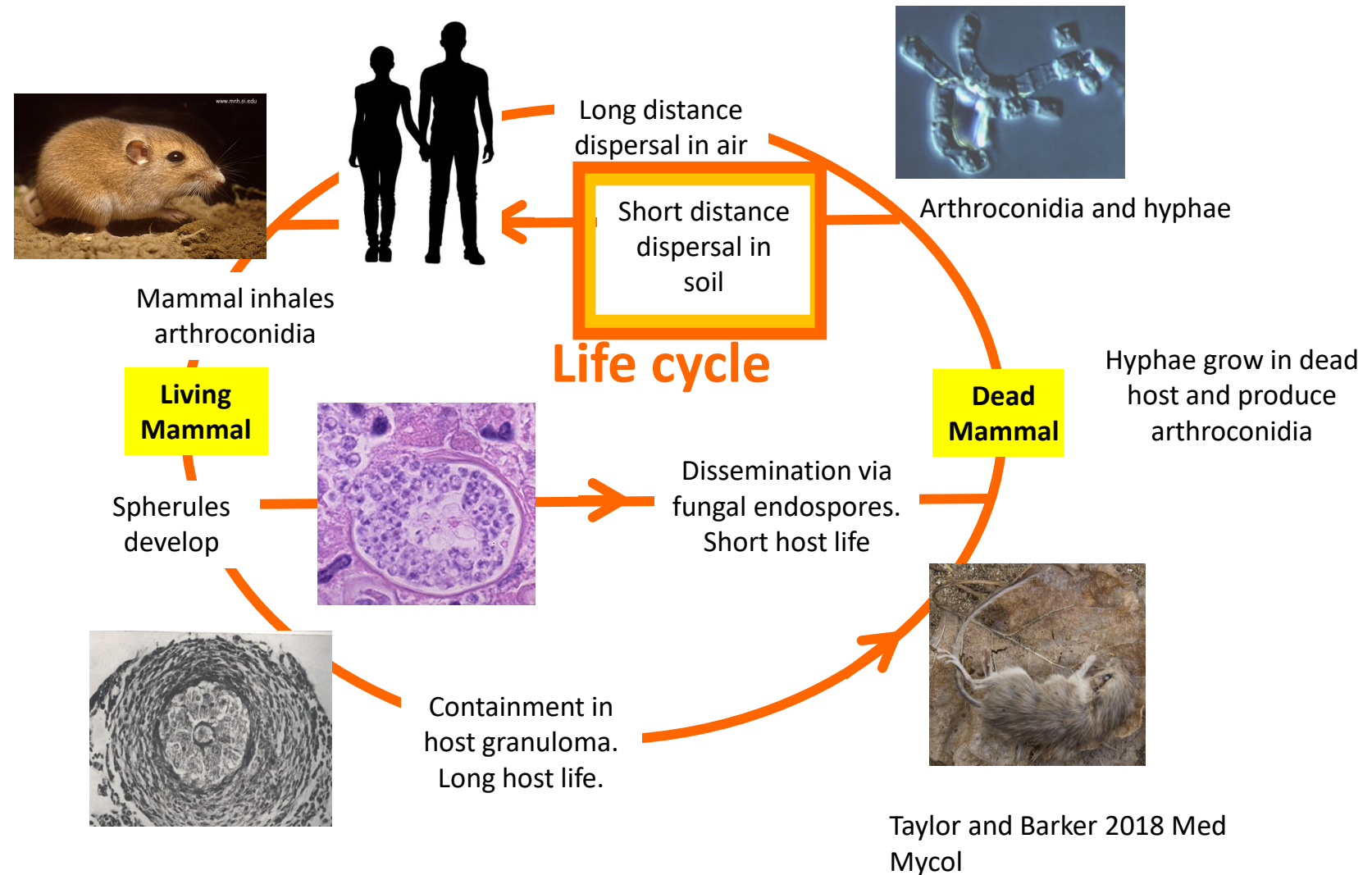
Transmission of *Coccidioides* among rodents



Transmission to humans from the environment



Transmission to humans from the environment



Risk of coccidioidomycosis to workers.

Outbreaks (2 or more cases at the same time and place) reported for:

Highway construction workers – Caltrans loses \$12M lawsuit

Solar Panel installers – Wilkin et al. 2015 EID, Laws et al. 2018 MMWR

Prisoners – Wheeler et al. 2015 EID, Plata v. Brown, SCOTUS, 2010

Prison workers – de Perio et al. 2015 EID

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All outbreaks are on undisturbed land.

**No outbreaks reported for agricultural workers,
~ 400,000 of whom work in the San Joaquin Valley**

**No outbreaks reported for agricultural workers,
~ 400,000 of whom work in the San Joaquin Valley**



[Emerg Infect Dis.](#) 2020 Jul; 26(7): 1430–1437.

PMCID: PMC7323545

doi: [10.3201/eid2607.200024](https://doi.org/10.3201/eid2607.200024)

PMID: [32568046](https://pubmed.ncbi.nlm.nih.gov/32568046/)

Risk for Coccidioidomycosis among Hispanic Farm Workers, California, USA, 2018

Stephen A. McCurdy, Catherine Portillo-Silva, Carol L. Sipan, Heejung Bang, Kirt W. Emery

Self-reported dust exposure	Cases	Controls	Adjusted Odds Ratio
Never or sometime	32	41	1, reference
Halftime or more	78	52	1.9

RESEARCH

Risk for Coccidioidomycosis among Hispanic Farm Workers, California, USA, 2018

Stephen A. McCurdy, Catherine Portillo-Silva, Carol L. Sipan, Heejung Bang, Kirt W. Emery

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Specific Crop	Cases	Controls	Adjusted Odds Ratio
Carrots	14	5	2.9

RESEARCH

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Can Coccidioides be detected in agricultural land?

RESEARCH

Risk for Coccidioidomycosis among Hispanic Farm Workers, California, USA, 2018

Stephen A. McCurdy, Catherine Portillo-Silva, Carol L. Sipan, Heejung Bang, Kirt W. Emery



Article

Valley Fever: Environmental Risk Factors and Exposure Pathways Deduced from Field Measurements in California

Antje Lauer ^{1,*}, Vicken Etyemezian ², George Nikolich ², Carl Kloock ¹, Angel Franco Arzate ¹, Fazalath Sadiq Batcha ¹, Manpreet Kaur ¹, Eduardo Garcia ¹ , Jasleen Mander ¹ and Alyce Kayes Passaglia ¹

5 samples from non-Agricultural land –
13 samples from Agricultural land –



Article

Valley Fever: Environmental Risk Factors and Exposure Pathways Deduced from Field Measurements in California

Antje Lauer ^{1,*}, Vicken Etyemezian ², George Nikolich ², Carl Kloock ¹, Angel Franco Arzate ¹, Fazalath Sadiq Batcha ¹, Manpreet Kaur ¹, Eduardo Garcia ¹ , Jasleen Mander ¹ and Alyce Kayes Passaglia ¹

5 samples from non-Agricultural land – *Coccidioides* detected

13 samples from Agricultural land - Undetected

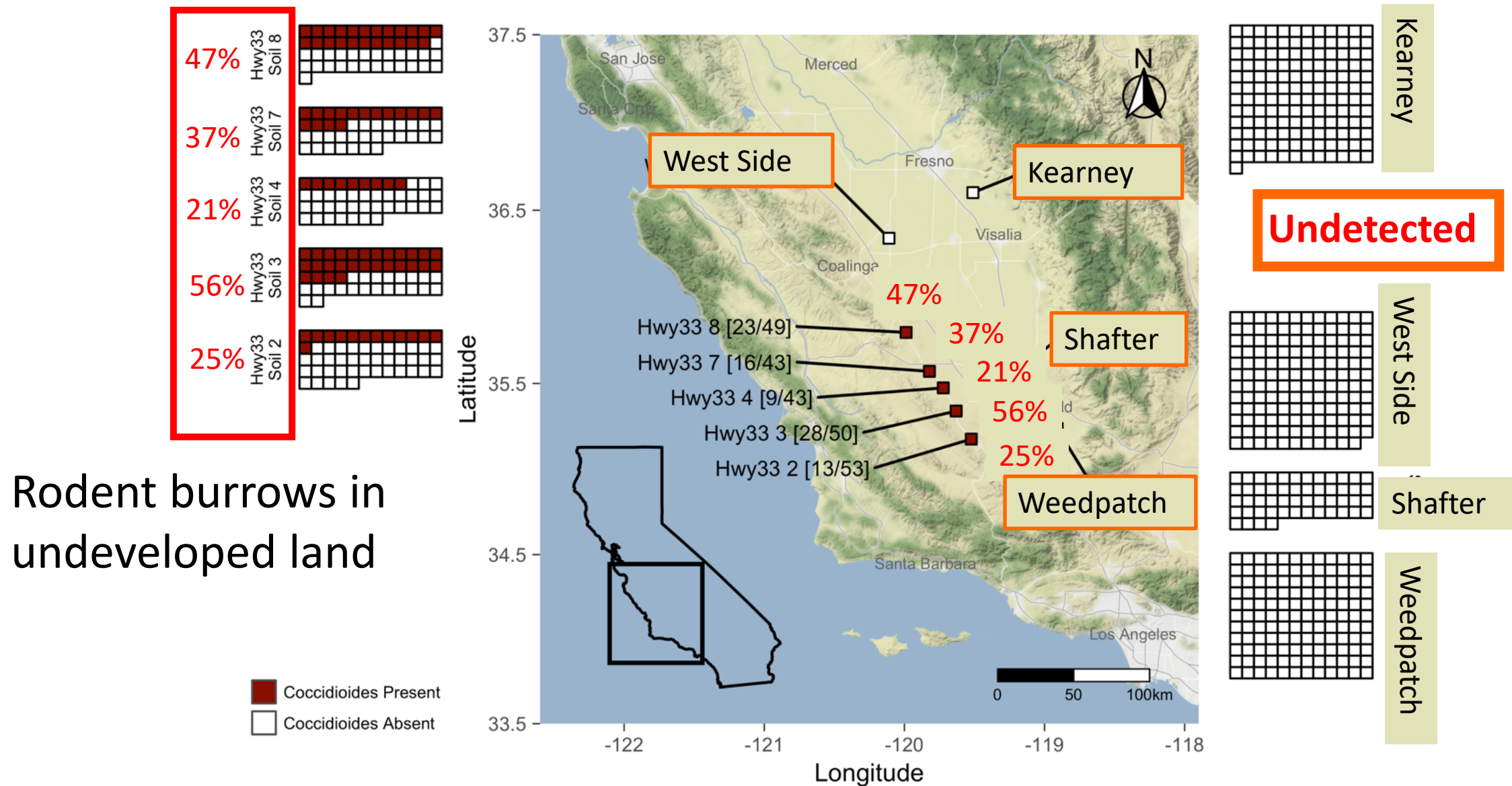
Robert Wagner, Liliam Montoya, Jennifer R. Head, Simon Campo, Justin Remais, John W. Taylor. Manuscript 2023.

Coccidioides in undeveloped and agricultural soils

472 agricultural soil samples collected in summers of 2016, 2017, 2018 and 2021.

238 undisturbed soil samples collected monthly in 2017-2018,

Robert Wagner, Liliam Montoya, Jennifer R. Head, Simon Campo, Justin Remais, John W. Taylor. Manuscript 2022.

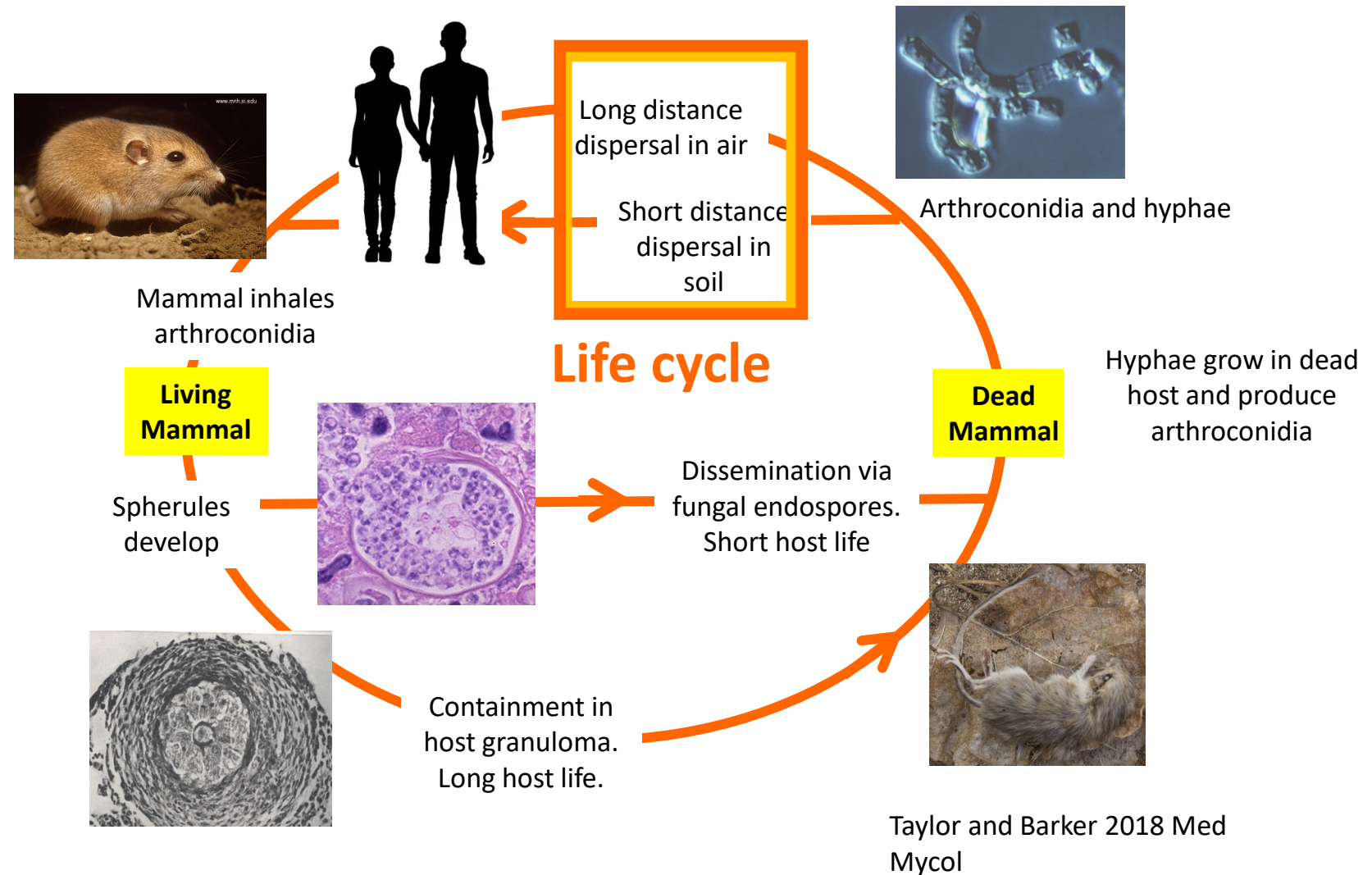


Agricultural workers are at risk for Valley Fever.

Coccidioides undetected in agricultural soils

Another source could be airborne *Coccidioides* spores.

Transmission to humans from the environment



The air mycobiome is decoupled from the soil mycobiome in the California San Joaquin Valley

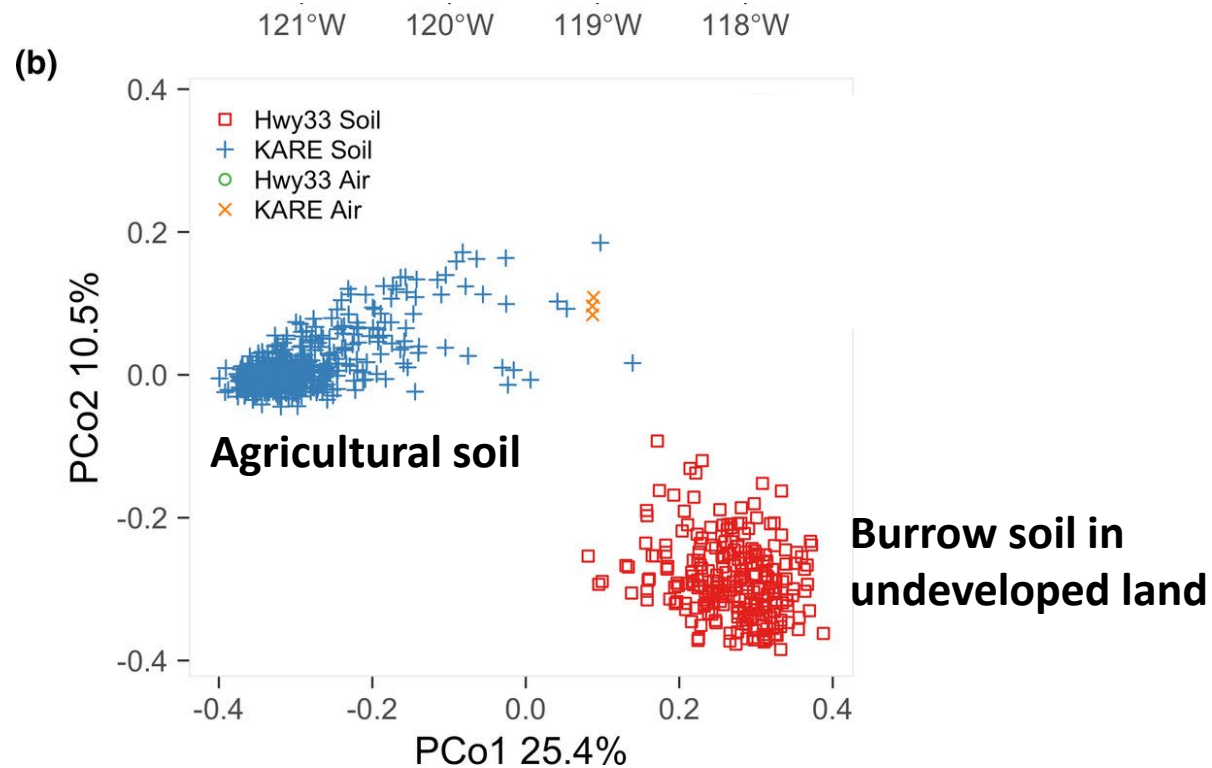
Robert Wagner , Liliam Montoya, Cheng Gao, Jennifer R. Head, Justin Remais, John W. Taylor

First published: 07 August 2022
<https://doi.org/10.1111/mec.16640>

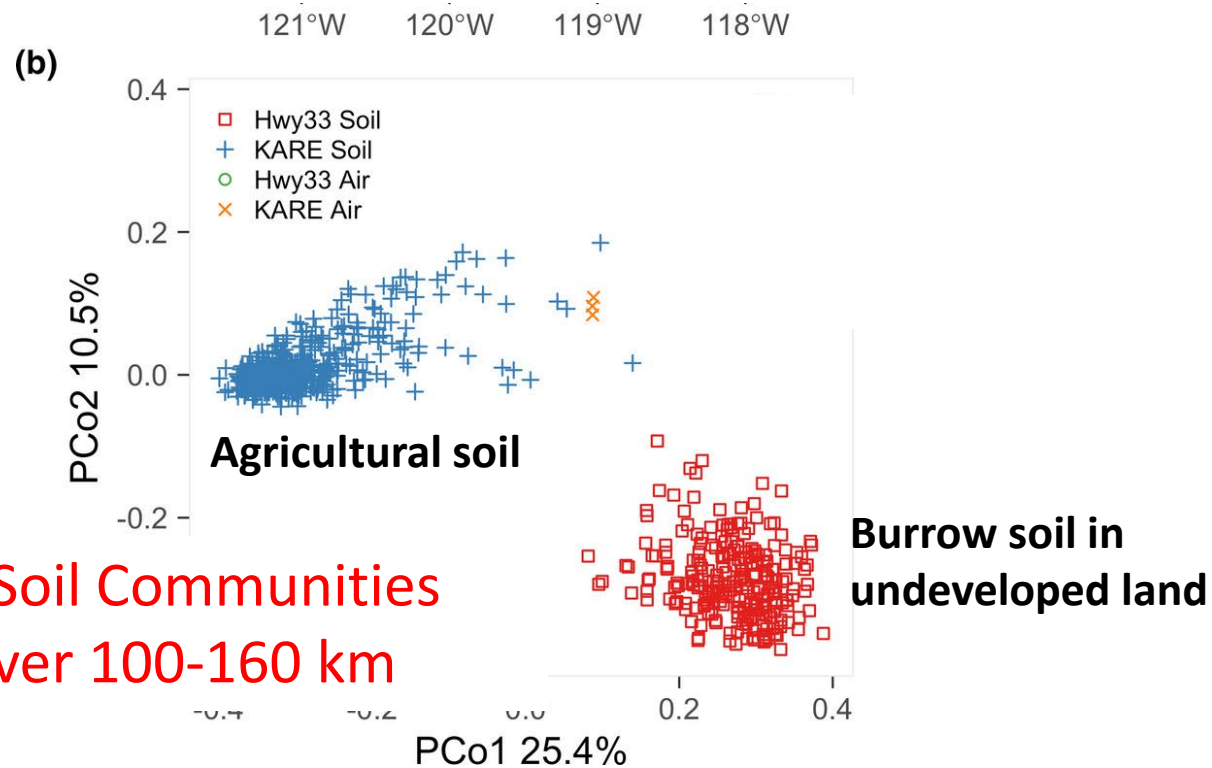
1001 samples

Land	Soil	Air
Undisturbed, 5 sites	238	175
Agricultural, KARE	498	90

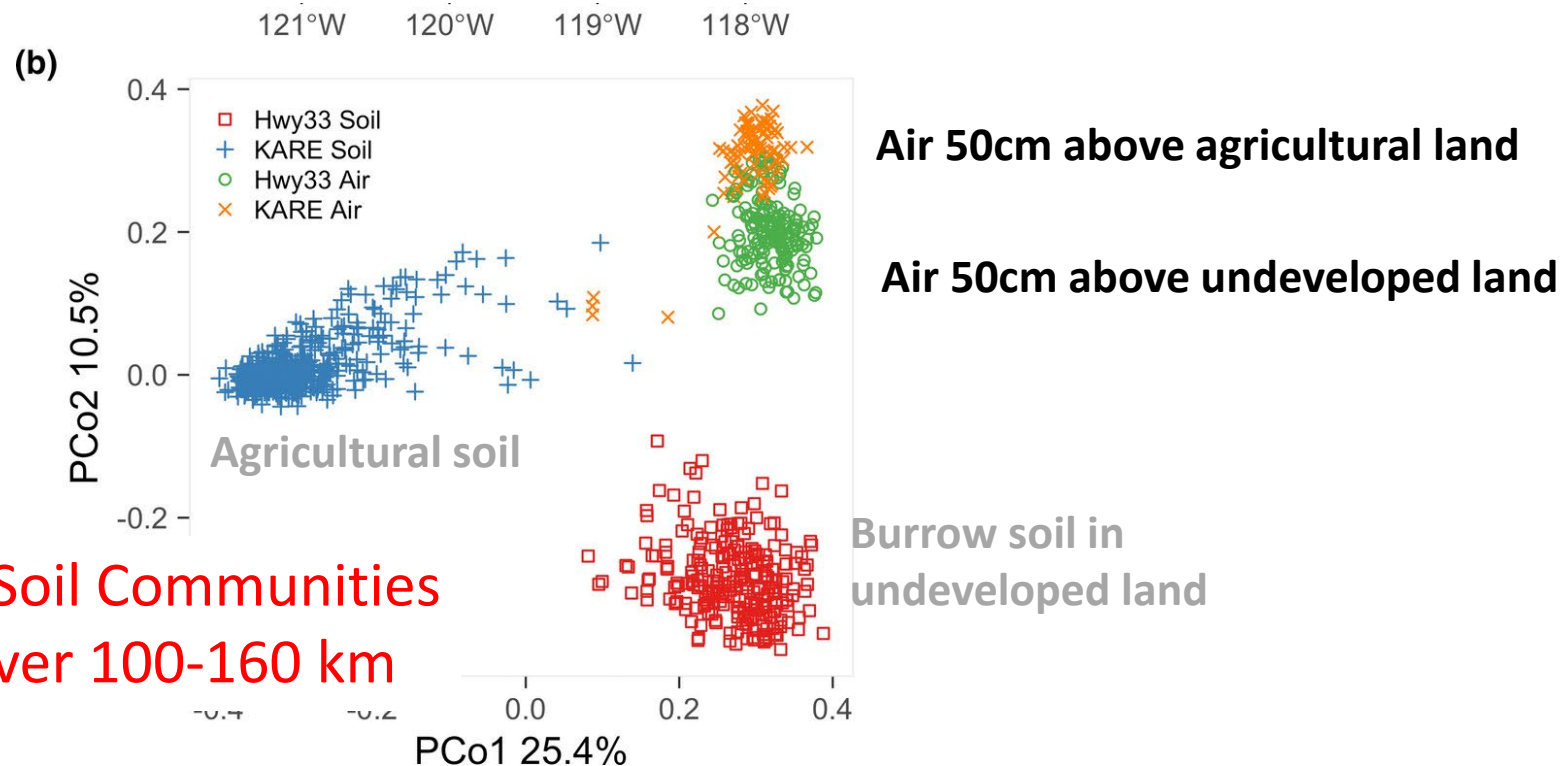
Ordination of Fungal Communities



Ordination of Fungal Communities

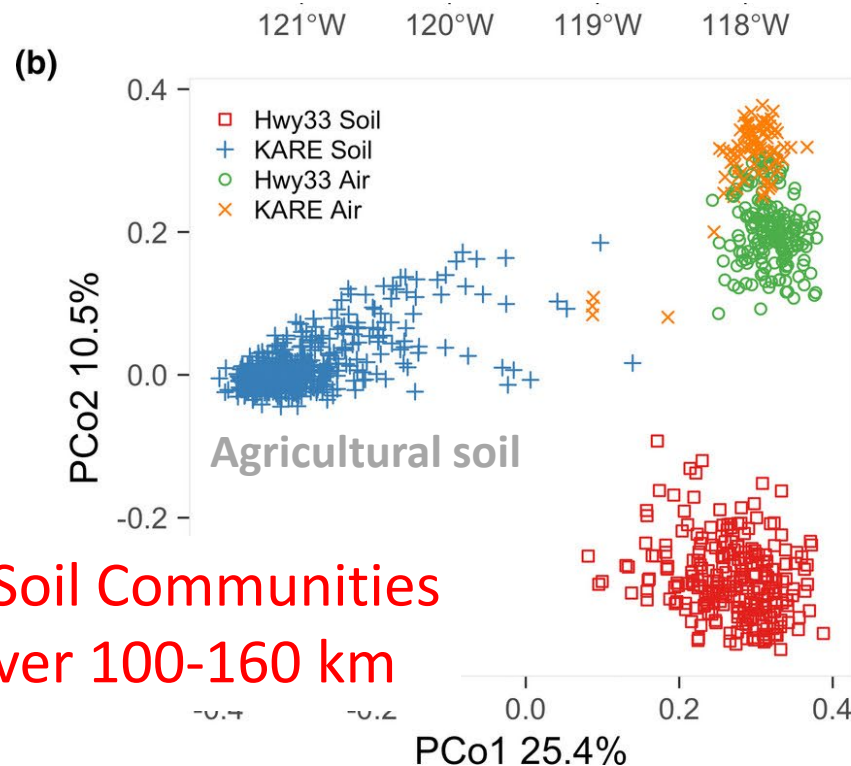


Ordination of Fungal Communities



Fungal Soil Communities
differ over 100-160 km

Ordination of Fungal Communities



Fungal Soil Communities
differ over 100-160 km

Fungal Air Assemblages **do not**
differ over 100-160 km

Air 50cm above agricultural land

Air 50cm above undeveloped land

ir
ir
ir
ir
ir

Do agricultural workers acquire Valley Fever from airborne spores?

Do agricultural workers acquire Valley Fever from airborne spores?

We don't know.

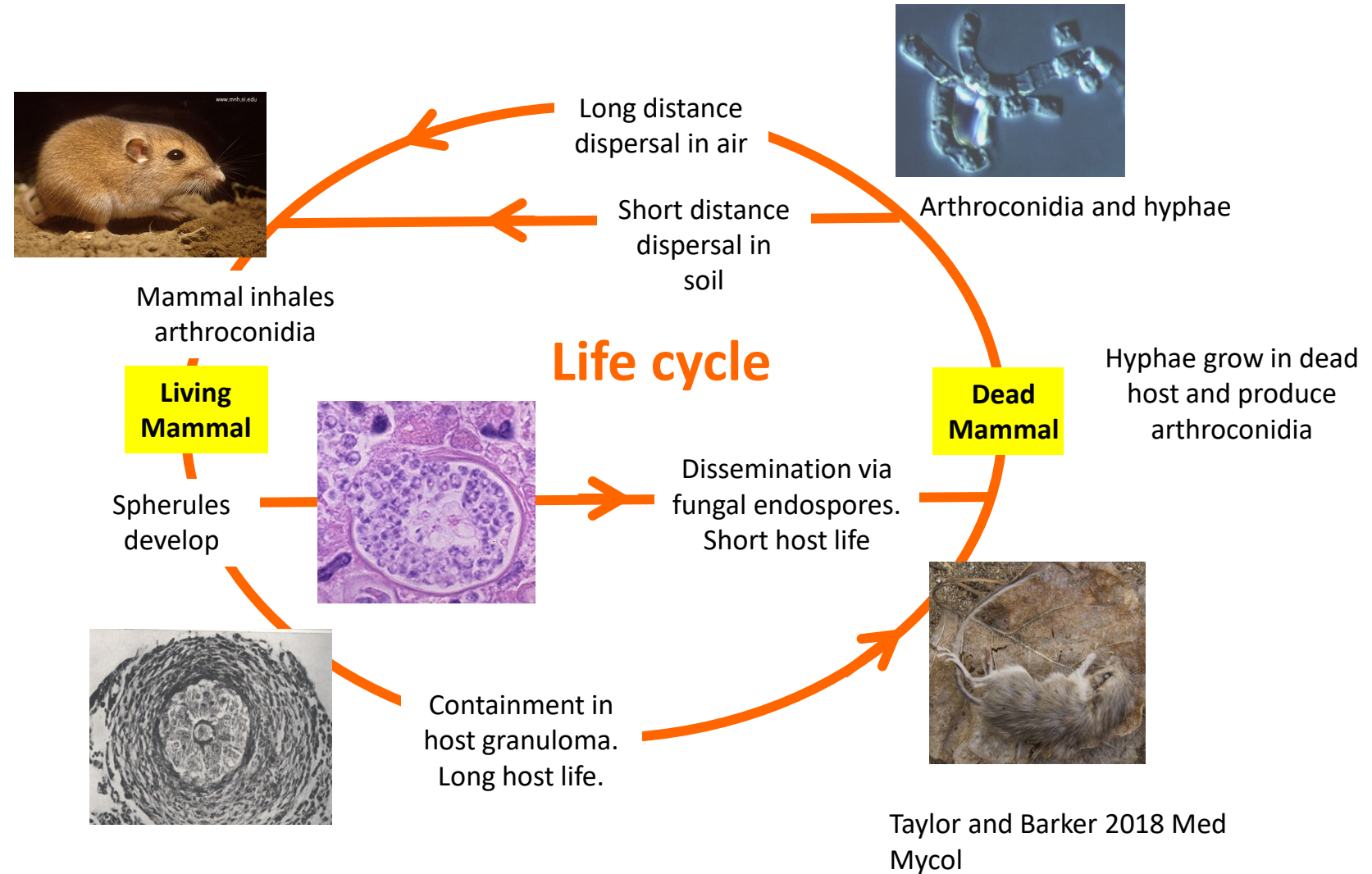
We have not detected *Coccidioides* in passively settled dust samples.

First Grand Challenge:
Effective air sampling for *Coccidioides*.



Second Grand Challenge:

Transmission of *Coccidioides* among native rodents.



Questions?



jtaylor@berkeley.edu

CALIFORNIA

- UC Berkeley
 - Rob Wagner
 - Lily Montoya
 - Justin Remais
 - Jennifer Head-Zhutenneger
- UC San Francisco
Anita Sil
- UC Berkeley
Rachel Brem



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