

ACTINOMYCETES: THE PROBLEM IS YOU?!?

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What Tools are/were Necessary to Study Actino as a driver of CIRS?

Commercially available dust sampling for Actino

 Validated Dominance Index (MAPK) and Prevalence Index (TGFBR)

 NGS –Next Generation Sequencing: After decades of Refining Detection and Differentiation methods NGS a rapid, cost effective method for speciation (illumina.com)

 HPLC (High-Performance Liquid Chromatography) reduces time and can analyze MYCOLIC ACIDS

 "Unsaponifiable Wax" was isolated after prolonged saponification; the alcohol-insoluble saponified wax fraction was termed "MYCOLIC ACID"

 GENIE – Refinement of transcriptomics for specific patterning (trigger) of gene expression immunoreactivity

Skin ACTINO – envirobiomics.com > #21

Serum Actino identification techniques (purple top tube)

Screening for Hiomarkers of Actinobacteria Associated with WaterDamaged Buildings – Part 1

Authors:
Scientist R<sup>2</sup> & Link D<sup>2</sup>

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## **ACTINOMYCETES: THE PROBLEM IS YOU?!?**

Shoemaker, R., et al. Medical Research Archives vell 9 usus 1. Medical Research Archives
RESEARCH ARTICLE

Newer Molecular Methods Bring New Insights into Human- And BuildingHealth Risk Assessments from Water-Damaged Buildings: Defining Exposure
and Reactivity, the Two Sides of Causation of CIRS-WDB Illus

Authors

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ABSTRACT:

Scientific disciplines dependent on accurate analytics invariably evolve due to advances in technical aspects of measurement. In disciplines in which adoptate measurement is not available for applications to public health policy, the impact of new paradigms in measurement can extend for health and the properties of the properties of the properties of the defect of exposure to waterdamaged buildings (WDB) on humin health. What causes the putative illness and what government should do to make buildings as fef our ac, have been impacted by development of

reactivity specific to these bacteria are now revolutionizing (i) both detection and quantitation for nowly recognited pulpageine organisms, and (ii) the approach to the genomic basis of diagnosis and treatment of disease as smallested by differential gene activation. NGS permits quantitation and treatment of the contractive of the co

current recommensations for assessment of exposure-reactivity to lung and memous of remediation based on fungi alone do not support continued use, now that endotoxins and Actinobacteria are found to be the major causes of human illness from exposure to WDB.

Keywords: transcriptomics, molecular hypometabolism, Next-Generation Sequencing Actinobacteria, endotoxins, Gram-negative rods

- Pathogenic Actinomycetes elucidated as a CAUSE of CIRS:
  - "Massive and unique increase in triple positive results compared to all other groups sorted by 3 variables of exposure, MAPK and TGFBR"
- Actino is understood as Driver of MHM:
  - "Given the inhibition of translocases in MHM, there will also be a reduction in transport of ions, solutes, ADP, and pyruvate across the outer mitochondrial membrane (OMM) into the mitochondrial matrix through the VDAC.
  - VDAC closure results from (i) Polycyclic Ethers produced by Actinobacteria, (ii) Beta tubulins; (iii) AZOLE ANTIFUNGALS, particularly intraconazole"

VDAC and Pyruvate

# Metabolism, molecular hypometabolism and inflammation: Complications of proliferative physiology include metabolic acidosis, pulmonary hyportension, T reg cell deficiency, insulin resistance and neuronal injury Raduc Rhomely Rhomely Raduc Rhomely Rho

- "If Pyruvate is not converted to lactate, we expect pyruvate to cross into the mitochondrial matrix to be used for fuel"
- "The pore (VDAC is 2-3 nm in diameter) will permit entry of solutes, ions, ADP and pyruvate through the outer membrane to reach the intermembranous space"
- Finished ATP exit the pore
- NB. Absence of Translocases secondary to MHM, metabolites of Streptomyces and Actino (in particular vanilomycin), and possibly Piericidin A, tubulin, issues with hexokinase and AZOLES result in failure of aerobic respiration (net 33-35 ATP).
- "Azole antifungal medications, unfortunately, are widely used by some involved in the management of illness acquired following exposure to the environment of WDB. This inappropriate use of azoles creates proliferative physiology; it must be recognized for its significant contribution to adverse metabolic outcomes, especially grey matter nuclear atrophy".

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# **ACTINOMYCETES: THE PROBLEM IS YOU?!?**

Proc Natl Acad Sci U 8 A 2015 Dec 29;112(52):E7276-85. doi: 10.1073/pnas.1512867112.Epub 2015 Dec 10.

Antifungal drug itraconazole targets VDAC1 to modulate the AMPK/mTOR signaling axis in endothelial cells

Saran A Head 4 Wei shi 4 Hand Zhao 4 Killi Ldorshow 4 Kalvan Pasunoqia Yue Lhen 4 Zhiyou Deng 4 Kub-lind 11 4 (bono 3up 5 him.) Wenzin Tan, 1 Homas Hartung 4 Jin Zhang 4 Yindmind Zhao 4 Kole 2 (bolombini 4, Jun 2 tu 4 Affiliations expand PMID: 2665341 PMCID: 2016/4703001 DOI: 10.1073/pnas.5152867112 Free PMC article-Abstract

Itraconazole, a clinically used antifungal drug, was found to possess potent antiangiogenic and anticancer activity that is unique among the azole antifungals. Previous mechanistic studies have shown that itraconazole inhibits the mechanistic target of rapamycin (mTOR) signaling pathway, which is known to be a critical regulator of endothelial cell function and angiogenesis. However, the molecular target of itraconazole that mediates this activity has remained unknown. Here we identify the major target of itraconazole in endothelial cells as the mitochondrial protein voltage-dependent anion channel 1 (VDAC1), which regulates mitochondrial metabolism by controlling the passage of ions and small metabolites through the outer mitochondrial membrane. VDAC1 knockdown profoundly inhibits mTOR activity and cell proliferation in human umbilical vein cells (HUVEC), uncovering a previously unknown connection between VDAC1 and mTOR. Inhibition of VDAC1 by itraconazole disrupts mitochondrial metabolism, leading to an increase in the cellular AMP:ATP ratio and activation of the AMP-activated protein kinase (AMPK), an upstream regulator of mTOR. VDAC1-knockout cells are resistant to AMPK activation and mTOR inhibition by itraconazole, demonstrating that VDAC1 is the mediator of this activity. In addition, another known VDAC-targeting compound, erastin, also activates AMPK and inhibits mTOR and proliferation in HUVEC. VDAC1 thus represents a novel upstream regulator of mTOR signaling in endothelial cells and a promising target for the development of angiogenesis inhibitors.

- + **Keywords:** VDAC1; angiogenesis; itraconazole; metabolism; mitochondria.
- + Conflict of interest statement
- Conflict of interest statement: The intellectual properties covering the use of itraconazole and its stereoisomers as angiogenesis inhibitors have been patented by the Johns Hopkins University and licensed to Accelas Pharmaceuticals, Inc., of which J.O.L. is a cofounder and equity holder. The potential conflict of interest has been managed by the Office of Policy Coordination of the Johns Hopkins School of Medicine.

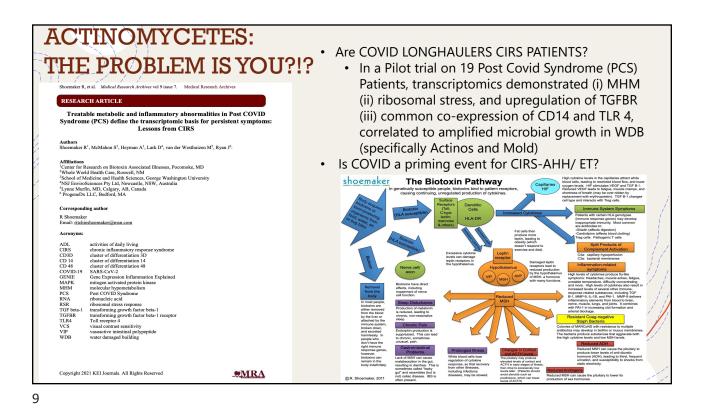
  The results disclosed in this article are not directly related to those intellectual properties.

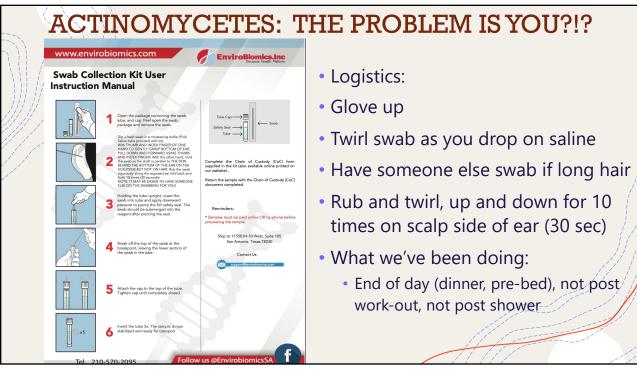
- When Should You Consider to put CIRS-AHH (Chronic Inflammatory Response Syndrome secondary to <u>Actinomycetes Human Habitat</u>) as your DDx?
  - When the patients told you they've already been diagnosed:
- By their Chiropractor with Adrenal Fatigue
- By their Naturopath with Mitochondrial Dysfunction
- By their Medical Doctor with Chronic Fatigue Syndrome

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#### **ACTINOMYCETES: THE PROBLEM IS YOU?!?**

- Diagnosing CIRS secondary to Actinomycetes
  - Contrary to misinformation / miseducation there is a strict diagnostic Criteria for CIRS:
  - Screening: History of WDB, and other biotoxin exposure in NP paperwork, interview and cross examination, VCS, Clustered Symptoms
  - Confirmation with 4 or more confirmatory labs = CIRS: failed VCS (survivingmold.com), HLA, MMP-9, TGFB-1, C4a (non-futhon NJ), alpha- MSH (Labcorp), ACTH/ am cortisol, ADH/ Osmo, anti-gliadin antibodies, low VEGF
  - Envirobiomics.com #6, 7, 8, 9, 13, 14 (different combos for FAB)
  - GENIE Ideal, but potentially less necessary if only FAB exposure is Actinos, more necessary if
    multiple FAB; GENIE is helpful regardless if financially viable, saves money if patient is not
    progressing due to missing ongoing exposure.
  - NQ FDA approved imaging w/ published brain volume patterns specific to CIRS WDB, CIRS PLS, preliminary data on Cortical Atrophy correlating with Endotoxin exposure, 90% of multinuclear atrophy is secondary to CIRS is Actinomycetes or Endotoxin (Shoemaker 2019, Roswell)
  - Actino-Skin #21 envirobiomics.com (it "HERTSMI" too?)
  - Actino Serum in proof of concept





- Questions / Considerations for Dermal Actinomycetes:
  - Puberty?
  - Heat post shower?
  - Work out?
  - Normal fluctuations?
  - Topical oil products /moisturizers?
  - Effects of Prescriptions / Mediciations, Hx of Antibiotics?
  - Immunosuppression / Overwhelmed Immune System / Low MSH?

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### **ACTINOMYCETES: THE PROBLEM IS YOU?!?**

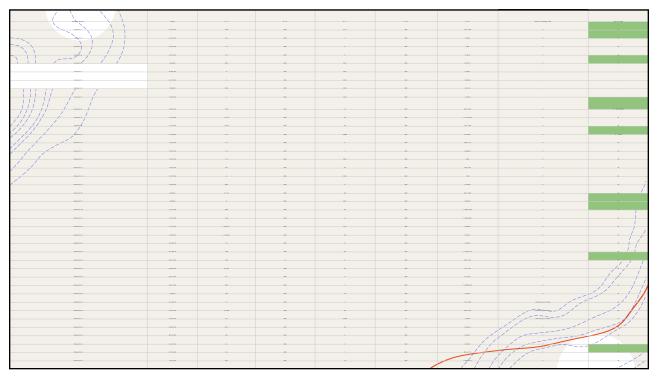


- Actino Serum:
  - · Lavendar top tube, send bubble wrapped
  - Mark "Attn Gianni" and make sure Provider, clinic and patient identification is clear
  - Sample must arrive cool room temp (remember you sending to Texas!)
  - If during hot weather, you can ice pack outside of bubble wrap; must arrive room temp or cool, not frozen!

- 36 confirmed cases of CIRS per strict diagnostic criteria
- 7 of the 36 had new generation Genie reports; all 7 were in Stage II (on Welchol/CSM, but still in exposure), 6 showed typical patten of Actinomycetes activity, but only one had "borderline" TGFBR positive.
- At least one Actinomycetes Swiffer collected in their primary residence
- Follow –up Actino skin (envirobiomics.com>shop ># 21) swabs collected
- 5 of the 36 patients drawn for Actino plasma vesicles to verify possibility of detection via NGS technology
- Natural Body wash applied with daily showers (60 seconds of lather and wait) and post Actino skin swab conducted on two patients

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Rationt Name	House Testing Y/N	Date	Level/Location	Actino DI/PI	C.T.	cx	CS	CA	P.A.
Patiest 1, 2, 2, 4	Y	11/2021	Garden Level	12/25	772	667	28	п	197
		11/2021	Upstairs	16/83	44,928	10,435	4,928	9,275	38,841
Patient S	/	12/5/21	Top Floor	1,0/27.1	4,013	en en	248	1,010	38,569
7 11 / /	/	-	Main Floor	06/42	1,512	1,309	ND ND	1,381	1,725
			Basement	0.6/1.1	1,190	1,929	969	221	1,138
		3/14/21	Main Floor	08403	17,237	ND	ND	21,863	455,871
Patient G	Υ	12/30/20	Whole House	12510	4,729	ND ND	ND	525	11,783
-111111111111111111111111111111111111		8/16/21	Whole House	0.9/14.8	13,077	11,851	2,452	ND	117,899
		6/14/22	Whole House	0.5/7.9	6,661	ND	ND	ND	8,807
9 applies 7, B	Y	10/15/21	Old House	12/197	17,495	2,320	967	19,429	102,750
		6/6/22	New House	2.0/179.2	20,278	387	820	23,696	24(151
Patient 9	Y	6/11/21	Whole House	05/29	839	ND ND	ND	1,007	4,229
0/1/		5/28/02	Whole House	1.1/168	9,502	576	ND	1,056	34,841
believe 10/	Y	7/5/22	Whole House	20/0.0	9,950	6,219	ND	10,157	45,432
Patient 11, 12, 13, 14	Y	6/16/22	Main Floor	0.7/4.6	17,867	1,643	2,255	46,664	18,214
/			Basement	06/3.4	7,763	ND ND	ND	34,931	12,671
Select 15	Y	7/1/22	Whole House	22/1720	33,807	1,614	ND	ND	94,053
Patient 16	Y	4/14/22	1st and 2nd Floors	08/44	532	ND	ND	1,374	1,772 /
			Basement	04/04	1,244	ND	ND	ND ND	ND /
atient 17	Y	8/16/21	Whole House	13/103	811	1,092	292	ND	4,350
stient 18, 19, 20	Y	1,26/21	Whole House	24/9.0	4,921	ND	83	USI	0,656
atient 21	Y	6/7/22	Whole House	13/118	8,209	1,123	ND	31,926	912 / /
atient 22, 23	Y	7/22/22	RV	12/89.0	23,448	12,505	ND	43,769	569,515
stient 24	Y	12/7/21	Whole House	1400	8,992	66,734	ND	1,934	19,107
Pasient 25	Y	4/25/22	Upstains	05/03	2,370	7,196	ND	ND	2370
		4/25/02	Main Floor	0.2/1.1	3,422	3,190	ND	647	/ /m /
		4/25/02	Sasement	03/29	1,015	20,127	ND	ND	w// / /
atient 26, 27	Y	8/16/22	Whole House	1.955.9	54,505	ND	2,103	1717	105,205
atient 28	Y	8/18/22	Whole House	22/35.7	143,314	8,301	3,502	lan /	Asan /
Patient 32	Y	4/9/22	Cabin	18/55.5	40,322	1,258	52.MS	79,206	146,100
		5/21/02	Cabin	19545	47,144	22,923	/51,200	109.437	120,62
Patient 33	Y	3/27/22	Whole House	18/21.0	118,729	ND /	M220		71,688
Patient 34	Y	5/21/21	Condo	0.0/49.4	1,467	1115	ND		46,273
Patient 35, 36	Y	3/28/22	Whole House	0.9/14.5	5,830	229	1 24	280	11,715
		8/5/22	Whole House	14425	30971	101 1	//288	1000	The /



ACI	INO	MYC	ETES	: Plası	na Ve	sicles				
Patient Name	Date	Test Method	С. Т.	C. X.	C. S.	C. A.	P. A.			
Patient 1	7/28/22	3A	3	ND	ND	ND	535			
Patient 5	8/4/22	3A	1469	ND	132	552	1107			
Patient 7	8/16/22	3A	1244	ND	122	329	1252			
Patient 8	8/16/22	3A	1178	ND	ND	279	831			
Patient 33	8/1/22	3A	841	ND	ND	283	1717			

	Patient Name	Date	Test Method	С. Т.	C. X.	C. S.	C. A.	P. A.
	Patient 1	7/28/22	3A Plasma	3	ND	ND	ND	535
/' /		6/12/22	Actino Skin	228	ND	272	ND	103,340
	Garden Level	11/2021	1.2/2.5	773	667	28	71	397
	Upstairs	11/2021	1.6/8.3	44,928	10,435	4,928	9,275	38,841

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Patient 5	8/4/22	3A Plasma	1469	ND	132	552	1107
	6/4/22	Actino Skin	ND	ND	ND	ND	65,197
	8/20/22	Actino Skin	9	ND	ND	ND	77,881
	9/9/22	Actino Skin	ND	ND	ND	ND	93,020
	9/17/22	Actino Skin	7	ND	ND	ND	26,846
	10/8/22	Actino Skin	1	ND	ND	ND	17,969
Top Floor	12/3/21	1.0/37.1	4,013	631	248	3,010	38,569
Main Floor	-	0.6/4.2	1,512	1,309	ND	1,381	3,725
Basement	-	0.6/1.1	1,190	3,909	969	221	1,138
Main Floor	3/14/21	0.8/40.3	17,237	ND	ND	21,883	455,871

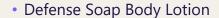
==		) )	2.4	10.14	ND	100	200	4050	
1	Patient 7	/8/16/22	3A	1244	ND	122	329	1252	
		/ 7/12/22	Actino Skin	1,337	ND	33	ND	1,173,166	
	Øld Høuse	10/15/21	1.2/19.7	17,495	2,320	967	19,429	102,750	
	New House	6/6/22	2.8/179.2	20,278	387	820	23,696	24,151	,
	Patient 8	8/16/22	3A	1178	ND	ND	279	831	
			Actino Skin	1,287	1,287	23	ND	120,194	
	Old House	10/15/21	1.2/19.7	17,495	2,320	967	19,429	102,750	
	New House	6/6/22	2.8/179.2	20,278	387	820	23,696	24,151	

Patient 33	8/1/22	3A	841	ND	ND	283	1717
	9/27/22	Actino Skin	41	ND	3	ND	29,095
Whole House	3/27/22	1.8/31.0	118,729	ND	26,229	ND	78,688

Antimicrobial Agents being studied for Actino eradication:

Coal Tar Shampoo

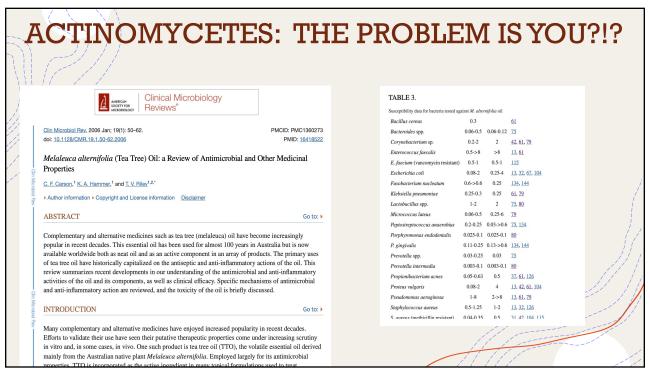
- Hopkington Pharmacy
  - Proprietary Compound







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Patient 5	6/4/22	ND	ND	ND	ND	65,197
Patient 5	8/20/22	9	ND	ND	ND	77,881
Patient 5	9/9/22	ND	ND	ND	ND	93,020
Patient 5	9/17/22	7	ND	ND	ND	26,846
Patient 5	10/8/22	1	ND	ND	ND	17,969

Patient 32	6/23/22	871	ND	20	ND	69,344
						/
Patient 32	8/15/22	26	ND	2	ND	43,587

## **ACTINOMYCETES: THE PROBLEM IS YOU?!?**

- Actinomycetes require both oil and water to amplify
- The literature suggests pathogenic Actinos get their start in WDB
- Can Humans vector Actinos into a clean, new non-WDB home?
- Do we need to address Dermal Actinomycetes to address pathogenic Actinomycetes reservoirs in building that trigger activation/reactivation of CIRS?
- Do we need to address Dermal Actinomycetes as a "seeding" source so our patients maintain their sanity and their weekends (otherwise spent cleaning)?
- Do we need to evaluate for topical skin products ("feeding" the Actino)?
- Is there a role for a short term no-fat, low fat diet?
- · Can we change dermal biome into non-pathogenic biome that lasts?

# **ACTINOMYCETES: THE ANSWER IS THANK YOU!!**

- THANK YOU DR. SHOEMAKER!!!
  - Thanks to Gianni Rossi and Envirobiomics.com
  - Thank you to Alicia Orr research assistant with Deb potential
  - Gabby Lamb Medical Assistant
  - Thank you to my staff and provider team (Genevieve and Dana)
  - Thank you to the patients for never giving up and following through, your lives are profoundly meaningful and worth fighting for!