

Dr Freya Harrison

School of Life Sciences, University of Warwick

@friendlymicrobe

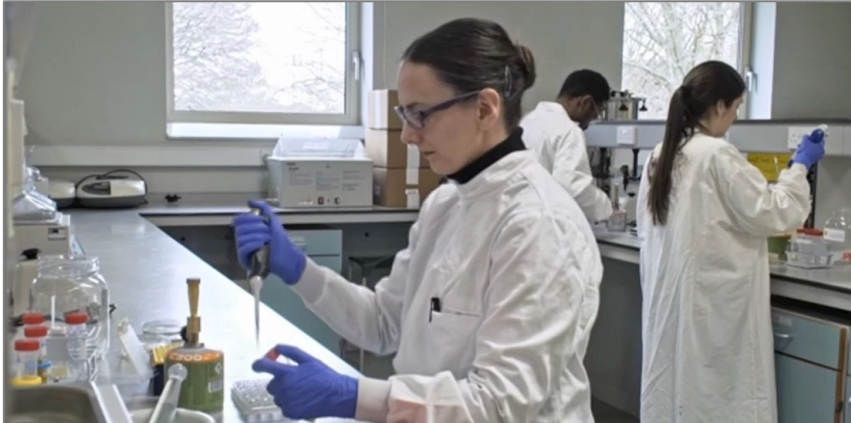


British Library: Cotton MS Vitellius C III, Sloane MS 1975, Royal MS 12, D XVIII

Working as part of a STEM-Arts consortium
to research the historical use of natural products as antimicrobials

From this...

...to this



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ISRCTN10773579 <https://doi.org/10.1186/ISRCTN10773579>

Assessment of the safety of a 'medieval antibiotic' used to treat infected diabetic ulcers on the skin of healthy non-diabetic volunteers

Condition category	Prospective/Retrospective
Infections and Infestations	Prospectively registered
Date applied	Overall trial status
05/01/2021	Ongoing
Date assigned	Recruitment status
08/01/2021	No longer recruiting
Last edited	
22/10/2021	

DE GRUYTER

Chris Jones, Conor Kostick, Klaus Oschema (Eds.)

MAKING THE MEDIEVAL RELEVANT

HOW MEDIEVAL STUDIES CONTRIBUTE TO IMPROVING OUR UNDERSTANDING OF THE PRESENT

DAS MITTELALTER BEIHEFTE

Contents

Chris Jones, Conor Kostick, and Klaus Oschema
Why Should we Care about the Middle Ages? Putting the Case for the Relevance of Studying Medieval Europe — 1

Science

Tobias Kluge and Maximilian Schuh
Providing Reliable Data? Combining Scientific and Historical Perspectives on Flooding Events in Medieval and Early Modern Nuremberg (1400–1800) — 31

Conor Kostick and Francis Ludlow
Medieval History, Explosive Volcanism, and the Geoengineering Debate — 45

Jörg Feuchter
The Middle Ages in the Genetics Lab — 99

Freya Harrison and Erin Connelly
Could Medieval Medicine Help the Fight Against Antimicrobial Resistance? — 113

Education

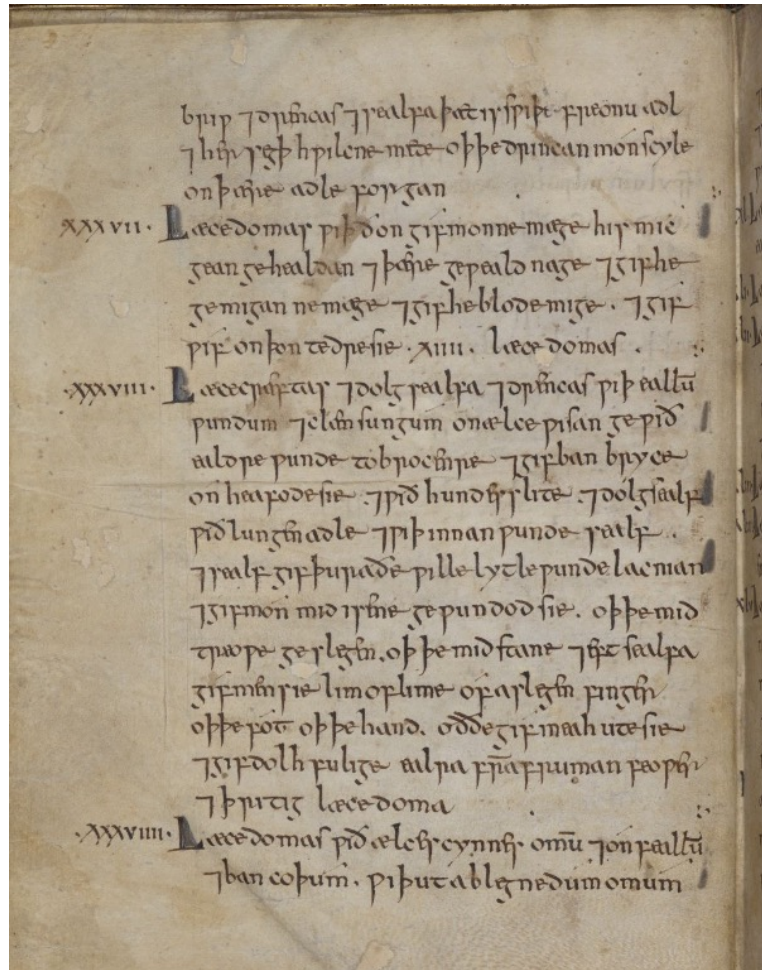
Julien Demade
The Contemporary Detegitimization of (Medieval) History – and of the Traditional University Curriculum as a Whole — 135

Chris Jones and Madi Williams
Pacific Perspectives: Why study Europe's Middle Ages in Aotearoa New Zealand? — 151

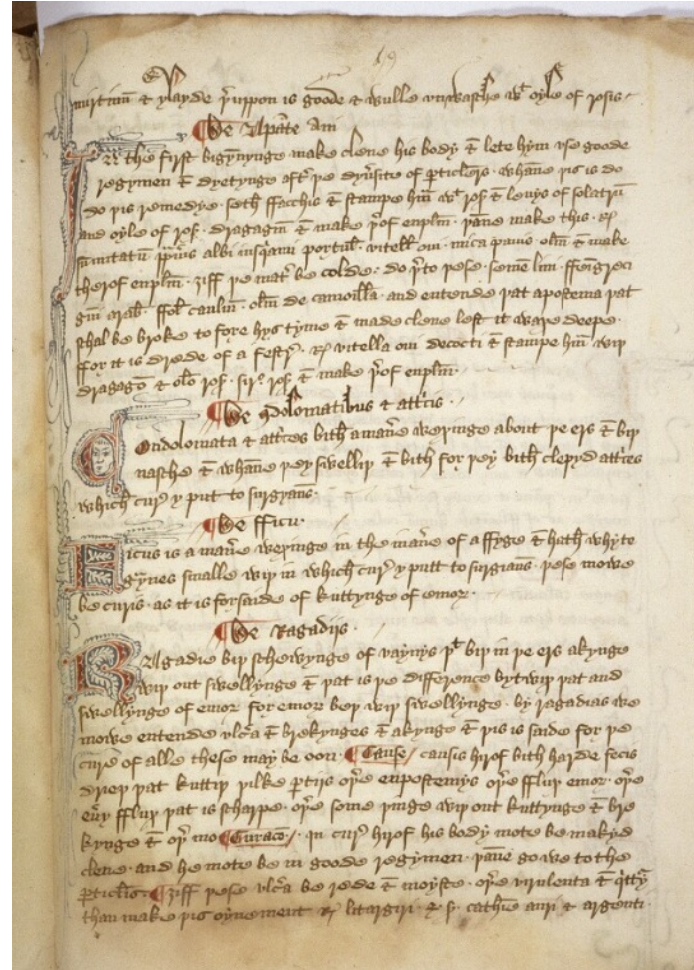
Laura Grazia Di Stefano
How to be a Time Traveller: Exploring Venice with a Fifteenth-Century Pilgrimage Guide — 171

Looking back to move forward

Bald's Leechbook – Old English, 10th century
British Library Royal MS 12 D XVII



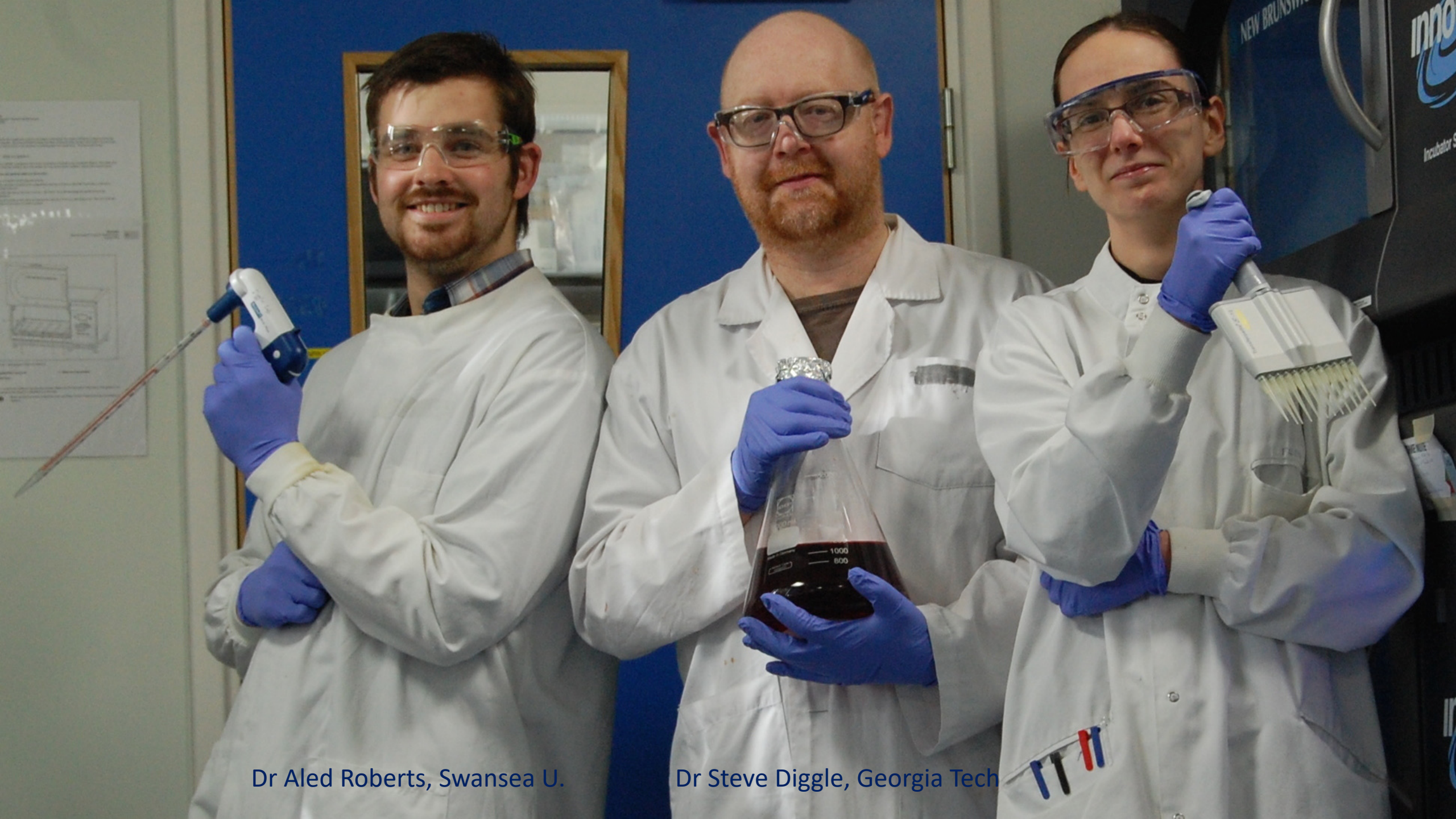
Lylle of Medicynes – Middle English, 15th century
Bodleian Library MS Ashmole 1505



Dr Christina Lee, U. Nottingham



Dr Erin Connelly
PhD U. Nottingham → UKRI FLF U. Warwick



Dr Aled Roberts, Swansea U.

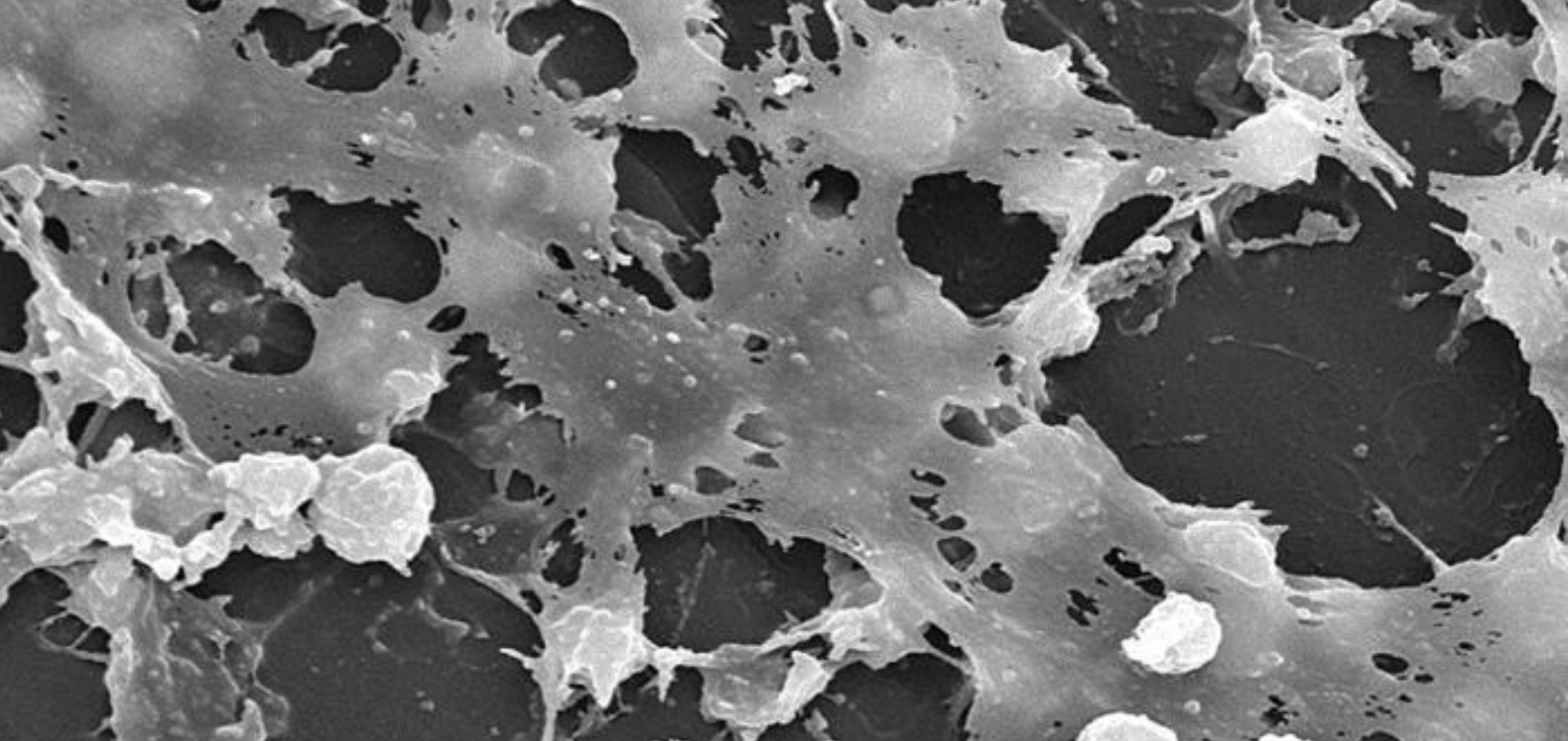
Dr Steve Diggle, Georgia Tech

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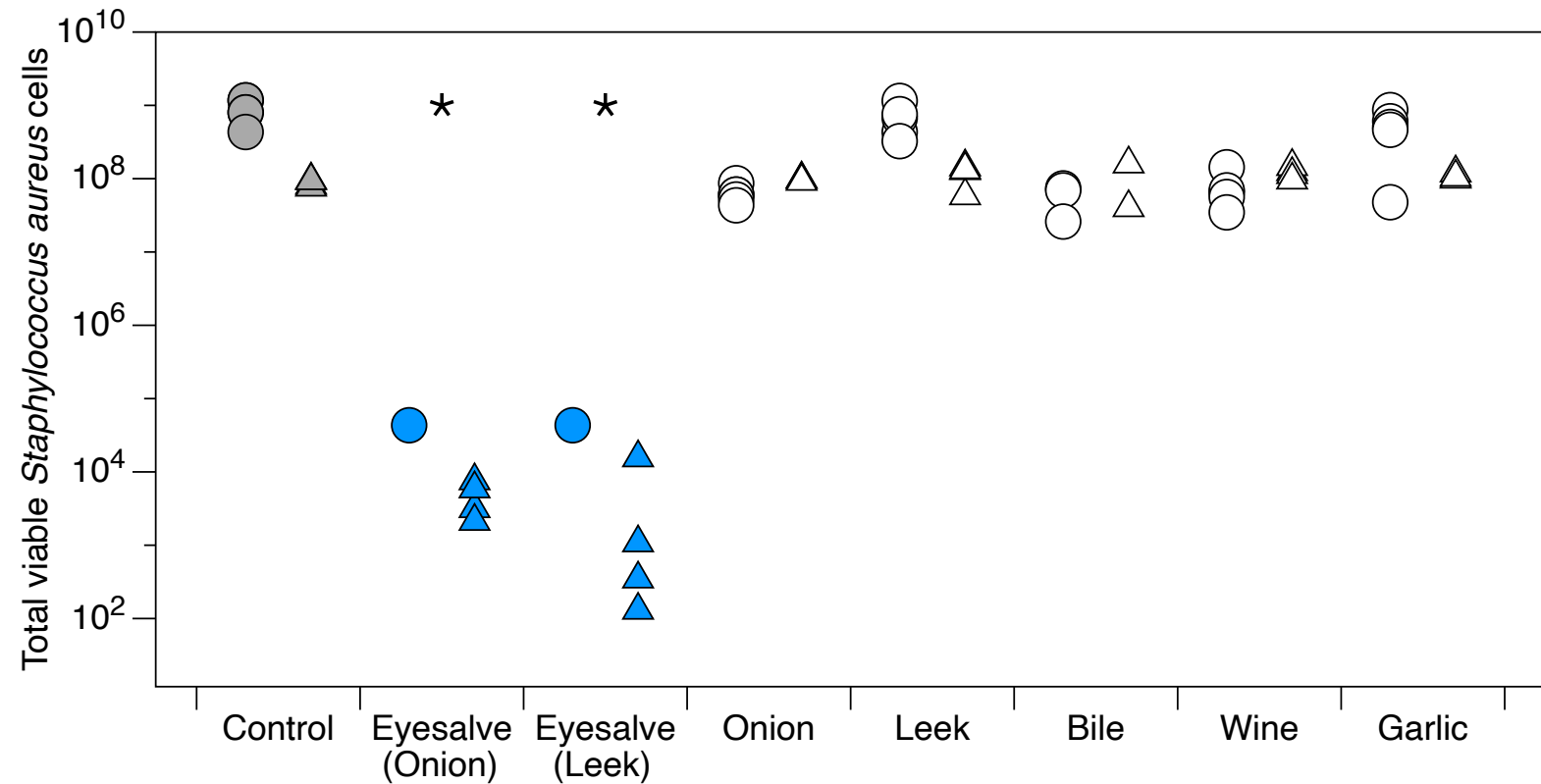
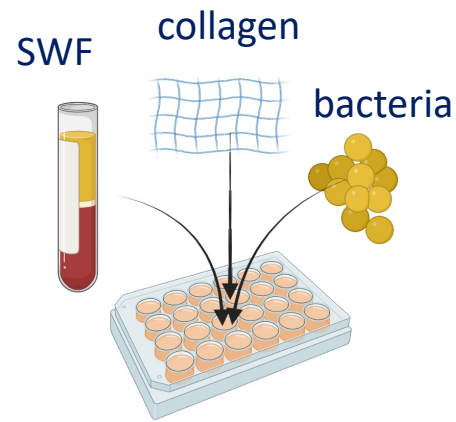
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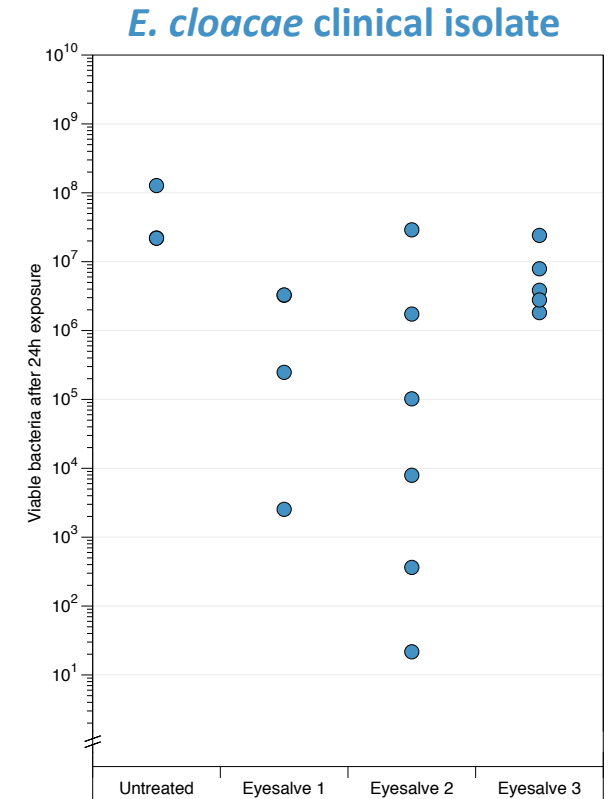
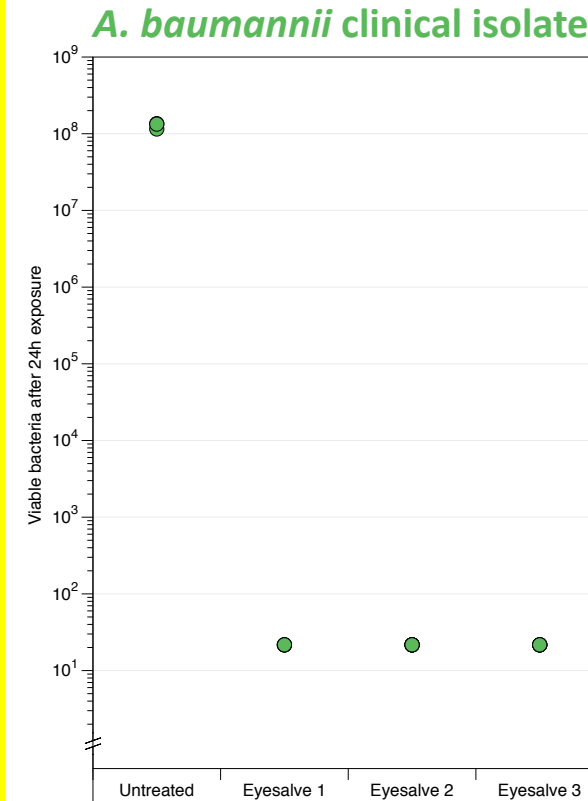
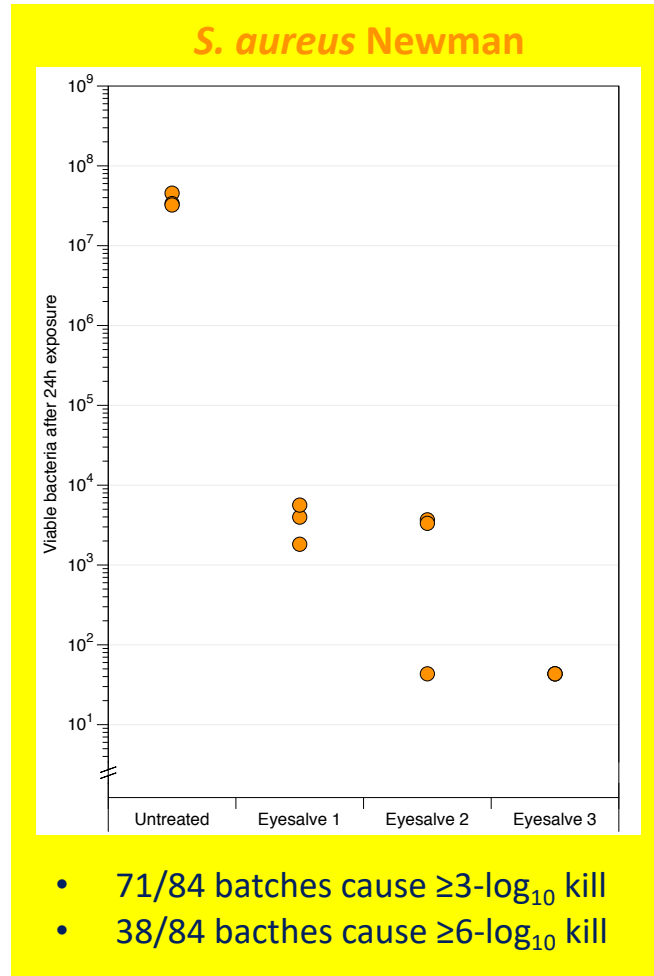
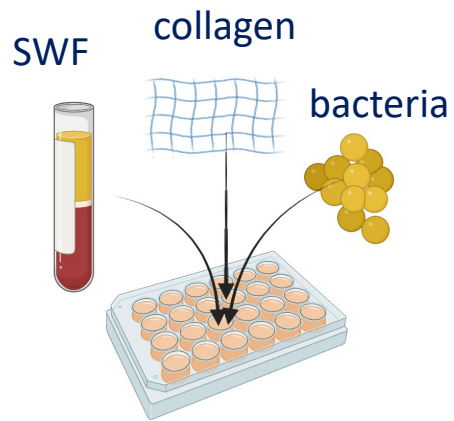
Our first results: Bald's eyesalve kills *S. aureus* in a wound biofilm model



Our work: Harrison et al. 2015. *mBio* 6:e01129-15

Wound model: Werthén et al. 2010. *APMIS* 118:156

Further tests in a synthetic wound biofilm model

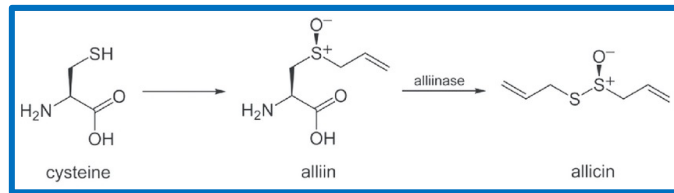


Our work: Furner-Pardoe et al. 2020. *Scientific Reports* 10:12687
SWF/SCW: Werthén et al. 2010. *APMIS* 118:156



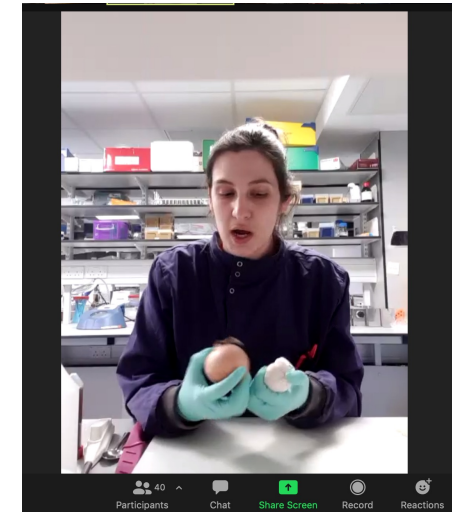
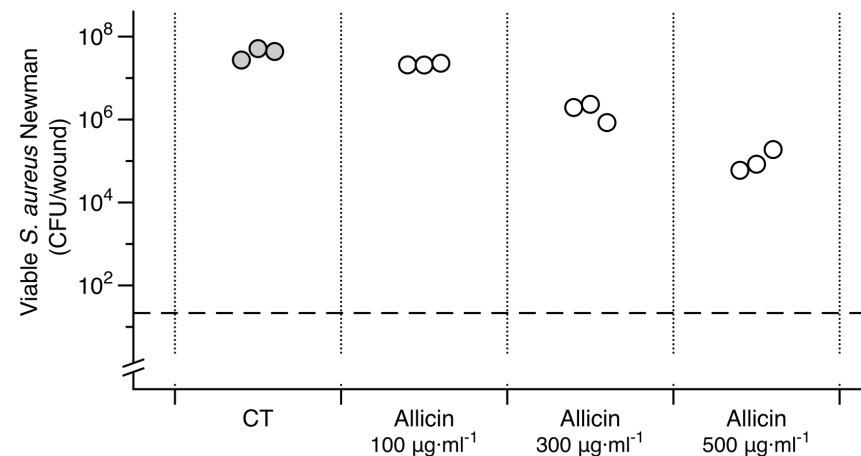
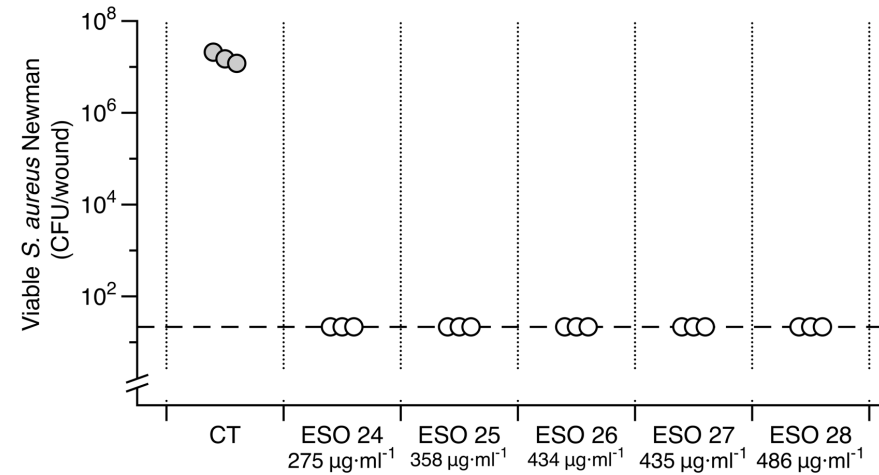
Dr Blessing Anonye
PDRA at Warwick → Lectureship at U. Central Lancashire

Antibiofilm activity requires >1 active molecule



- Explains most bactericidal activity in planktonic culture
- Is not a good drug candidate

But allicin cannot explain activity of Bald's eyesalve in SCW biofilm...



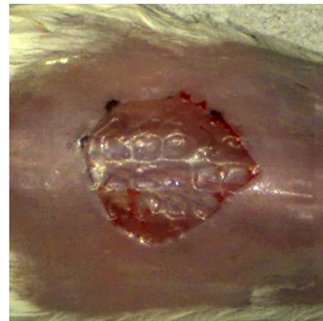
Dr Jess Furner-Pardoe
MRC DTP at Warwick → UKHSA

Furner-Pardoe et al. 2020.
Scientific Reports 10:12687

Does it work on a “real” biofilm in host tissue?

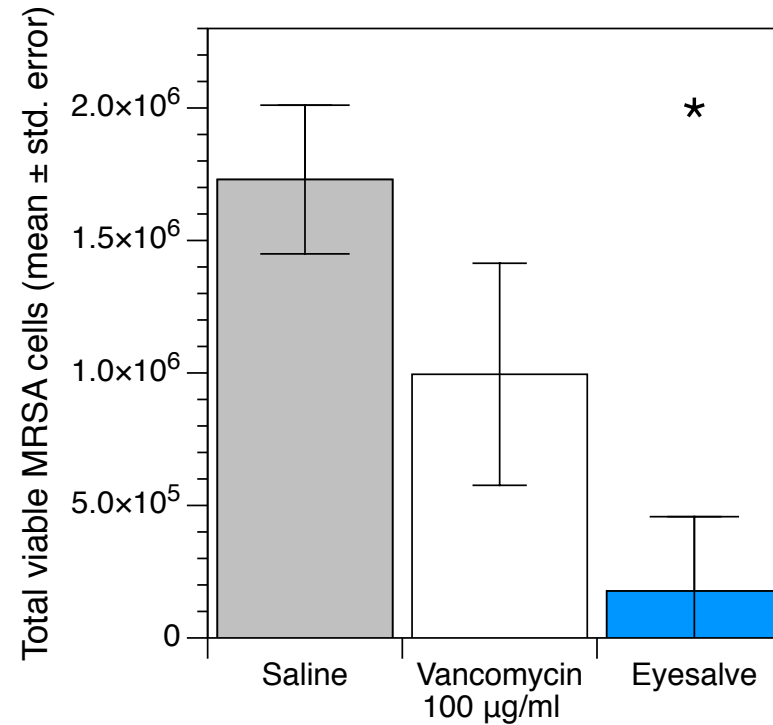


Dr Kendra Rumbaugh, Rebecca Gabriliska @ Texas Tech.



Surgical wound +
OpSite dressing

Biopsy tissue from mice with MRSA wound infection, exposed to Bald's eyesalve / vancomycin / saline for 4 hours



And crucially... is it safe?



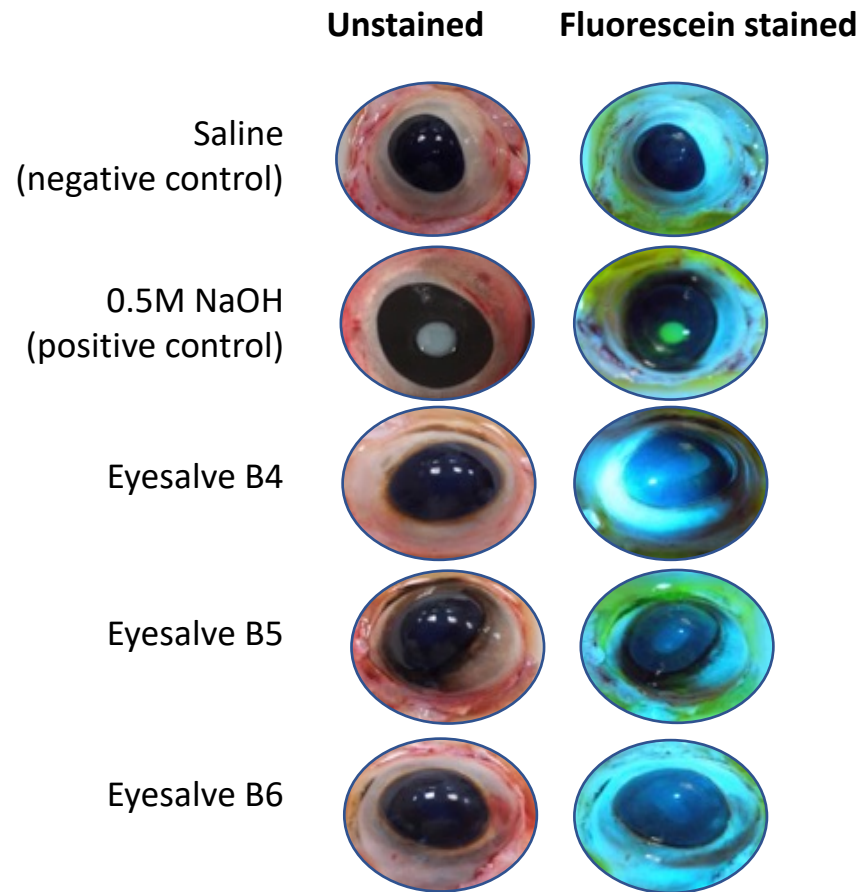
Prof. Lori Snyder & Team,
Kingston Univ. London



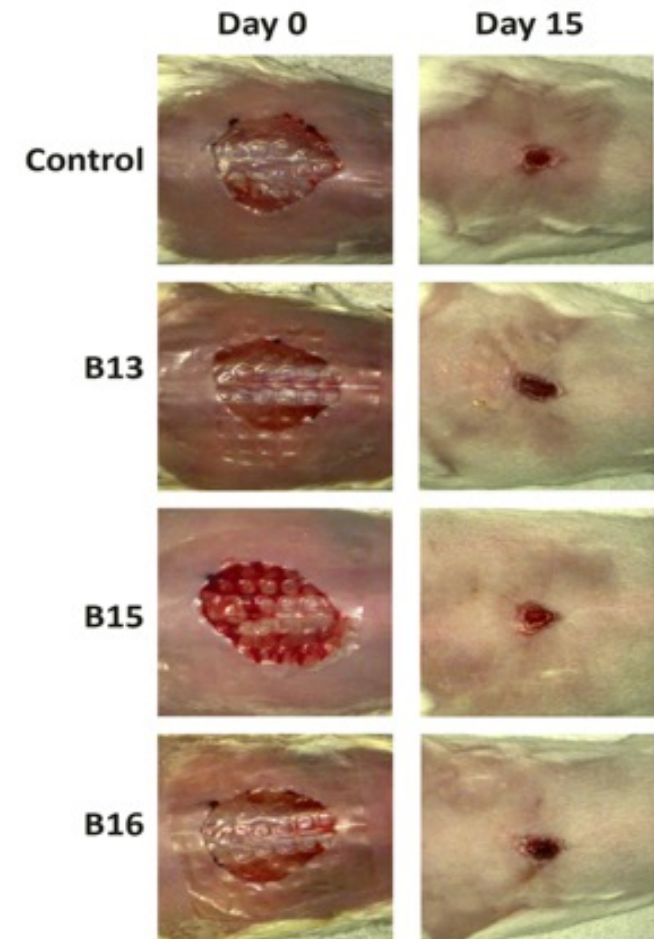
Dr Kendra Rumbaugh
Texas Tech

Anonye et al. 2020.
Scientific Reports 10:17513

Bovine Corneal Opacity & Permeability Assay



Mouse wound closure



And crucially... is it safe?

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Assessment of the safety of a 'medieval antibiotic' used to treat infected diabetic ulcers on the skin of healthy non-diabetic volunteers

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05/01/2021

Registration date

08/01/2021

Last edited

24/11/2022

Recruitment status

No longer recruiting

Overall study status

Completed

Condition category

Infections and Infestations



Prof. Julie Bruce
U. Warwick



Dr Blessing Oyedemi
U. Warwick

Bruce et al. 2022
Scientific Reports 12:19656.

What next?

Chronic wound infections



Diabetic ulcer infection

5.3M people with diabetes worldwide by 2025
10% will get an infected foot/leg ulcer

Venous leg ulcers

2.7M people in Europe

Pressure sores

3.7M people in Europe

+ Burns, SSIs, trauma wounds...

- Osteomyelitis, sepsis, death
- Topical/systemic antibiotics + physical treatments
- Extensive antibiotic resistance
- 35% increase in cost of care vs. acute wound
- Annual cost to NHS is **£3.2Bn**

- Desperate need for new agents to prevent/treat chronic wound infection
- Does Bald's eyesalve include a natural product cocktail we could formulate into an advanced wound dressing?

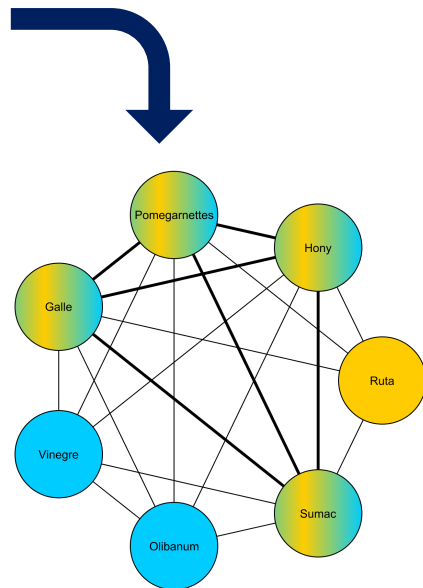
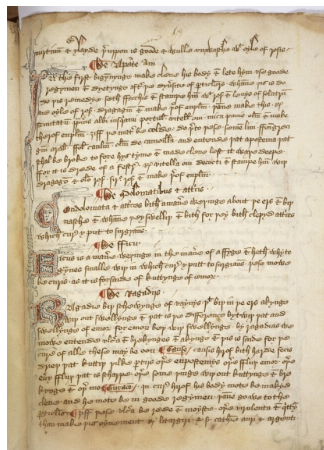


Tosin Orababa
PhD - U. Warwick

Where else has this led?

- A broader look at potential “ancientbiotics” from historical medical books
- For humanities colleagues: support for re-evaluating medical texts, work on medical practice and knowledge transmission
- For STEM colleagues: jump-starting the discovery pipeline for natural products with clinical potential

Quantitative research: datamining



Dr Erin Connelly, U. Warwick
Dr Charo Del Genio, U. Coventry
Connelly et al. 2020. *mBio* 11:e03136-19

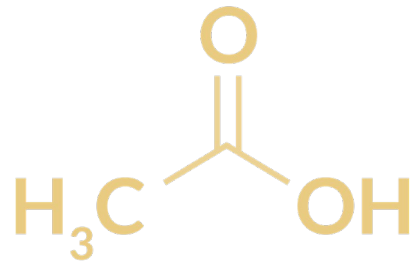
Qualitative research: how were particular ingredients used?



Dr Christina Lee, U. Nottingham
Dr Erin Connelly, U. Warwick
Harrison et al. 2022. *Access Microbiology* 4:000336

Latest work: honey & vinegar

- There is a long history of combining vinegar and honey to treat infection – seen in our datamining and in texts from around the world, across a long span of history.
- Traditional use evolved into current evidence-based clinical use of acetic acid or medical-grade honeys to treat wounds infected with bacterial biofilm.
- BUT no research into combined acetic acid + honey therapy has been published!



+



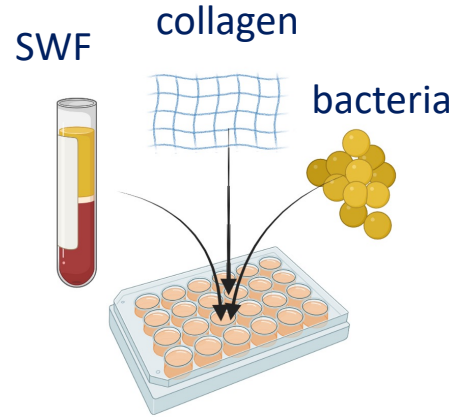
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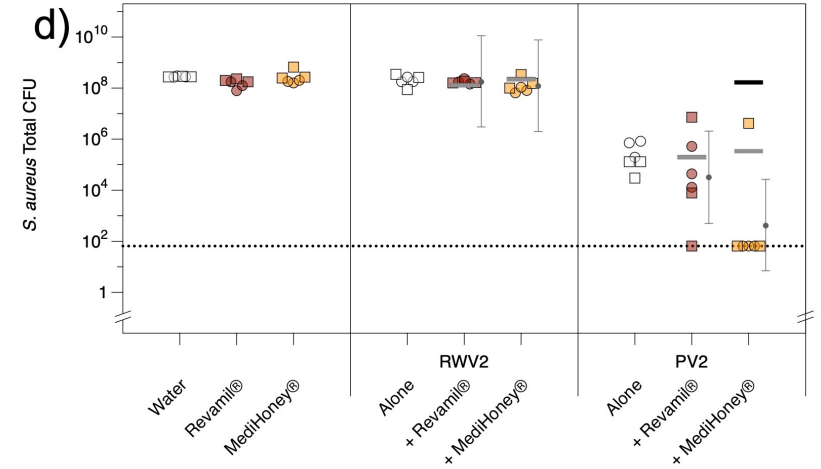
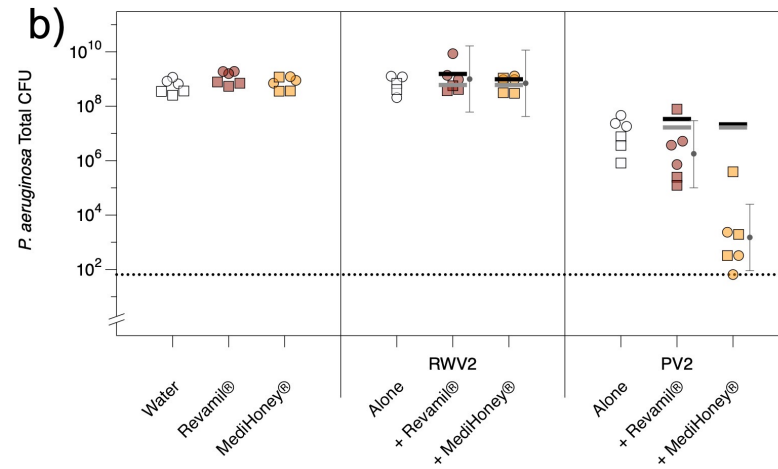
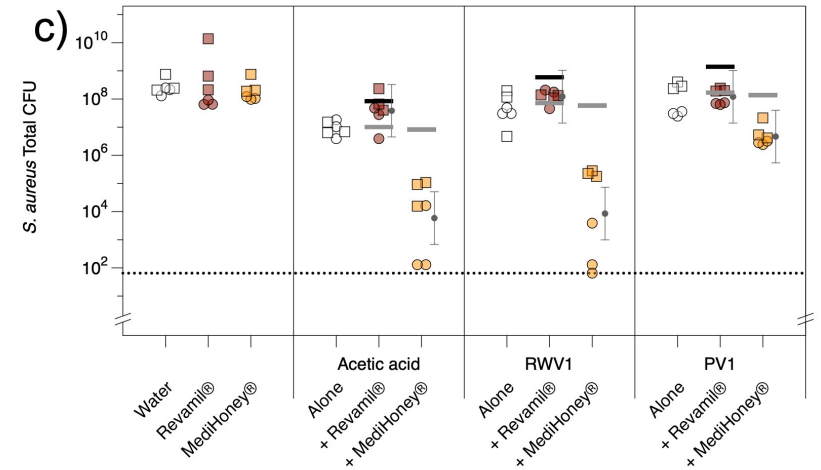
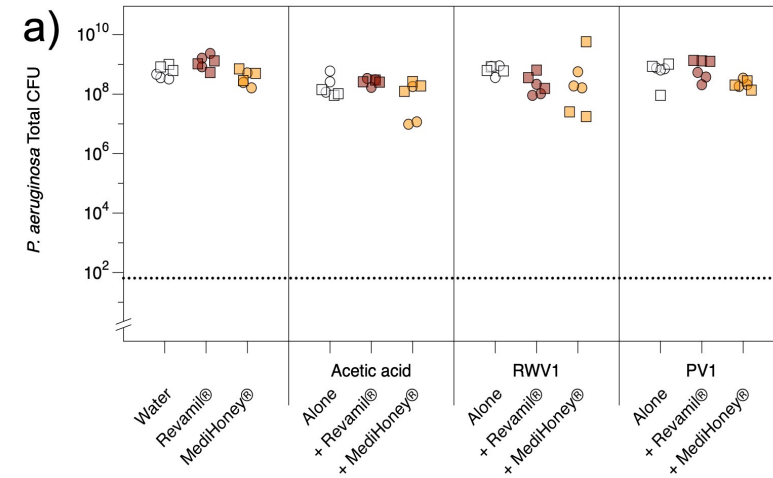
Latest work: honey & vinegar

Anisa Blower
MBio, U. Warwick → PhD, NIAB

Dr Erin Connelly, Dr Chris de Wolf
U. Warwick



- *P. aeruginosa* or *S. aureus*
- Treat with sub-bactericidal doses of honey, acetic acid or vinegar
- Alone or combined
- Red wine vinegar or pomegranate vinegar
- Two commercial honey preparations approved for NHS use
- The concentration of acetic acid is consistent across the pure acetic acid and the vinegars



How can we work effectively across disciplines?



Fiona Tung / The Varsity

Different aims in studying historical remedies

- A pathway to thinking about how medieval physicians practiced
- Does this preparation have any biological activity?
- While these parallel aims are interlinked, they are different
- This has led to some difficulties in trying to communicate to different audiences

Speaking different languages

- Historians of medicine want to explore the social-medical context & capture variations in interpretation
- But scientists want a clear protocol, even though there may not be a “correct” interpretation of a recipe

Knowledge of how work is done in different fields

- “Does your employer know you’re working with dangerous bacteria?”
- “Can’t this be done by a scientist with a good dictionary?”

Gatekeeping attitudes


Difficulties in accessing funding

- Too interdisciplinary – fall between the cracks
- (In)appropriate reviewers

How can we work effectively across disciplines?

Very simply: don't stop talking to each other!

- Ask lots of questions
- Be prepared to take your turn at being the dumbest person in the room
- Treat everyone as partners & co-creators, not suppliers of a service
- Support each other to keep going
- Get creative with seeking funding sources

Patterns  OPEN ACCESS


Perspective
A case study of the Ancientbiotics collaboration

Erin Connelly,^{1,*} Christina Lee,² Jessica Furner-Pardoe,^{1,3} Charo I. del Genio,⁴ and Freya Harrison¹

¹School of Life Sciences, Gibbet Hill Campus, University of Warwick, Coventry CV4 7AL, UK
²School of English, University Park, University of Nottingham, Nottingham NG7 2RD, UK
³Warwick Medical School, Gibbet Hill Campus, University of Warwick, Coventry CV4 7AL, UK
⁴Centre for Fluid and Complex Systems, Coventry University, Coventry CV1 5FB, UK

*Correspondence: erin.connelly@warwick.ac.uk
<https://doi.org/10.1016/j.patter.2022.100632>


THE BIGGER PICTURE Collaborations that cross traditional boundaries between disciplines in STEM and the arts and humanities open up exciting research possibilities. In our team's case, we combined expertise in historical manuscripts, data science, and microbiology to explore the structure and potential efficacy of historical medical recipes. Such an approach can highlight patterns or questions that a single-disciplinary approach is likely to miss. But learning to speak each other's disciplinary languages is not always easy, and misunderstandings can impede work. Here, we present our own experiences as a case study of how we have learned from each other to ask new questions of our source material and the problems we have had to solve along the way.

 **Development/Pre-production:** Data science output has been rolled out/validated across multiple domains/problems

The rewards can be significant and surprising


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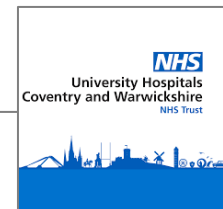
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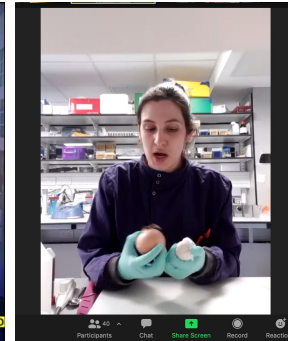
MICROBIOLOGY

Sweet and sour synergy: exploring the antibacterial and antibiofilm activity of acetic acid and vinegar combined with medical-grade honeys

Freya Harrison^{1,*}, Anisa Blower¹, Christopher de Wolf^{1,2} and Erin Connelly^{1,*}



A brilliant topic for outreach/engagement



Dialogue is better than monologue!

- Many conversations with members of the public or colleague suggesting different material based on traditional remedies in their families/countries
- Discussions about animal experiments (3Rs is something I personally feel strongly about)
- Engagement with people who may benefit from new antimicrobials, & possibly be involved in trials
- The talk we did for the WI is a prime example of the last point – they were key to our Phase I trial

Educational outreach – science & history

Teachers got in touch to discuss and report back on practical science lessons they had planned and delivered

- collecting plant materials and testing for activity
- making and testing Bald's eyesalve against bacteria using disk diffusion assays.

Teachers & students got in touch to discuss science fair projects and CREST Award projects inspired by our work (UK/USA/Europe)

We worked with The Science Viking, a freelance deliverer of history and science curriculum enrichment activities, to develop demos for use in school events and at the Big Bang Fair

Working with education professionals ensures you are providing useful content.



Thanks: the Ancientbiotics consortium

Manuscripts



Christina
Lee

Erin
Connelly



Caroline
Petit

Manuela
Marai

Microbes & Safety Tests



Blessing
Anonye

Julie
Bruce

Steve
Diggle

Rebecca
Gabrijska



Aled
Roberts

Kendra
Rumbaugh

Lori
Snyder

Anisa
Blower

Molecules



Jess
Furner-Pardoe

Tosin
Orababa



Chris
de Wolf

Maths



Charo
Del Genio

Academics, Post-docs and PGRs: Sheyda Azimi, Valentine Nweke, Colman Ó Cathail, Blessing Oyedemi, Callum Parsons, Afshan Rafiq, Esther Sweeney, Faith Ukachuckwu, Meera Unnikrishnan, Dave Barrett, Ricky Cain, Christophe Corre, Dong-Hyun Kim, Cath Ortori, Warwick Antimicrobial Screening Facility

UG students: Anisa Blower, Navneet Jandu, Lauren Johnson, Jenny Littler, Gemma Lunn, Conor Macnab, Jason Millington, Mabel Olonisaye-Collins, Shajini Subhaskaran, Thorulf Vargsen, Kate Willett



Plus crowdfunding from 66 members of the public!