Revisiting stilbene clinical trial data in the era of microbiome research reveals a new antibiotic class

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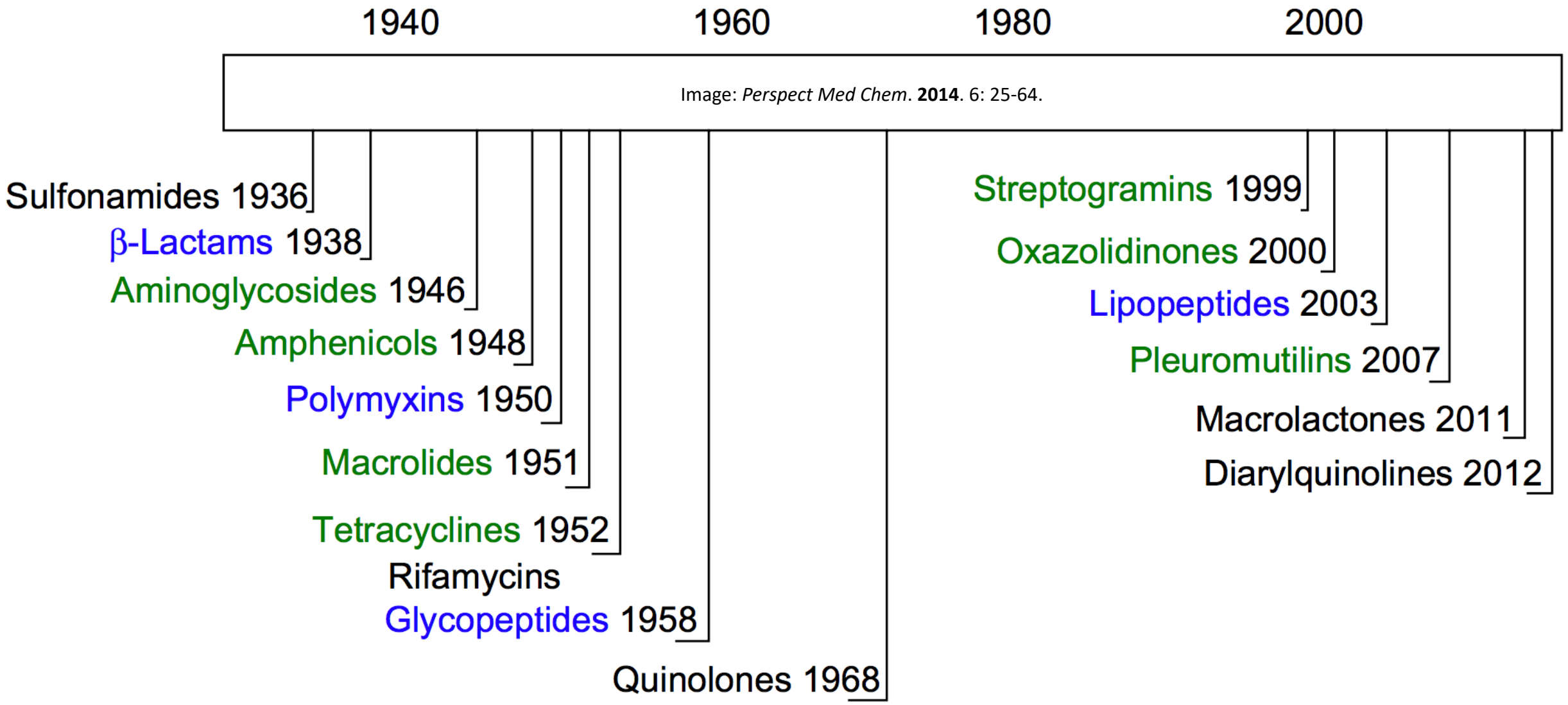
Mucosinix Pharm

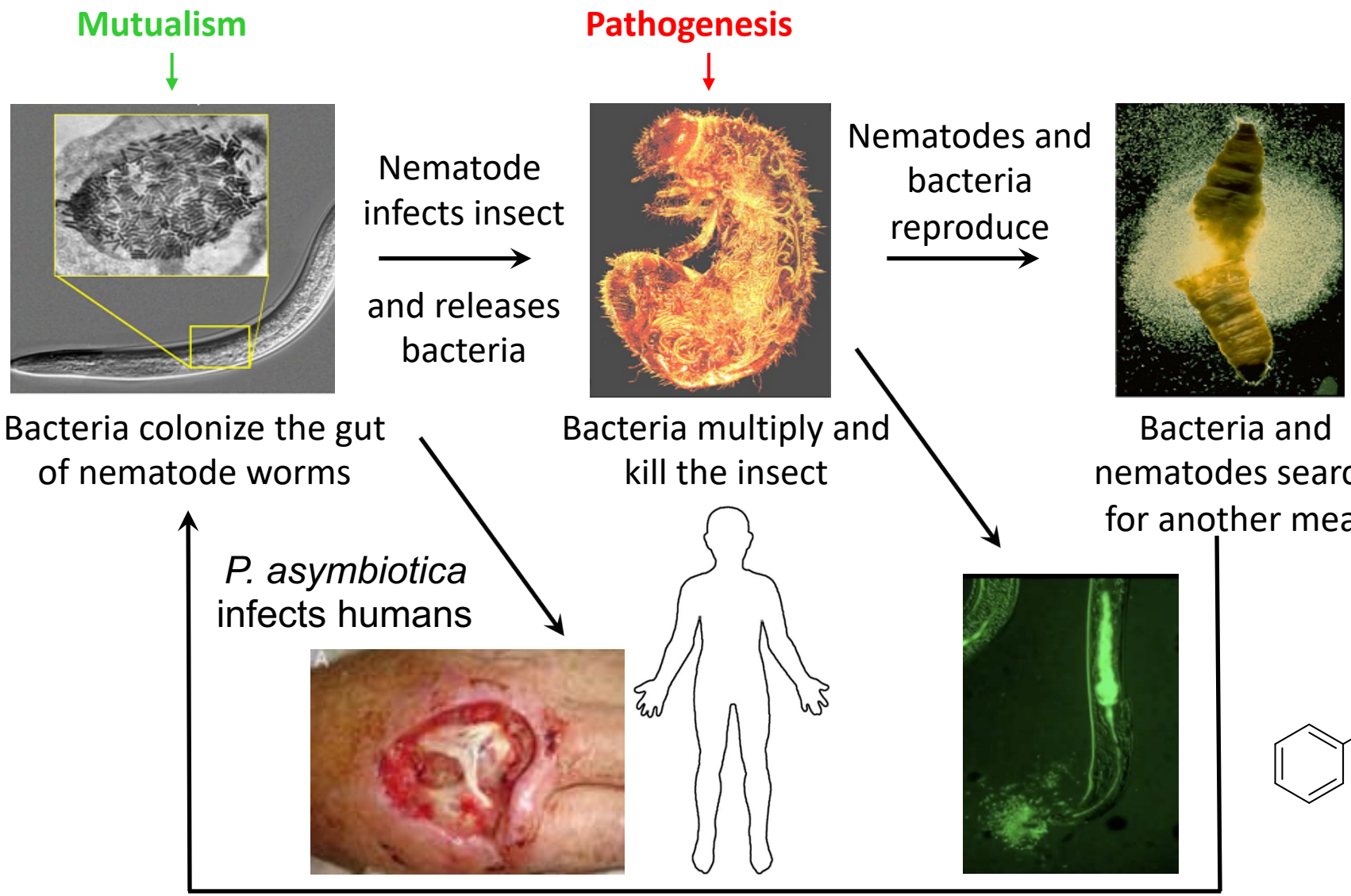
Antibiotic classes are limited and drug resistance is climbing



- **Antibiotic resistance is a major health crisis**

- **ribosome inhibitors; cell wall inhibitors**

Photorhabdus EVOLVED antimicrobials to protect their food source

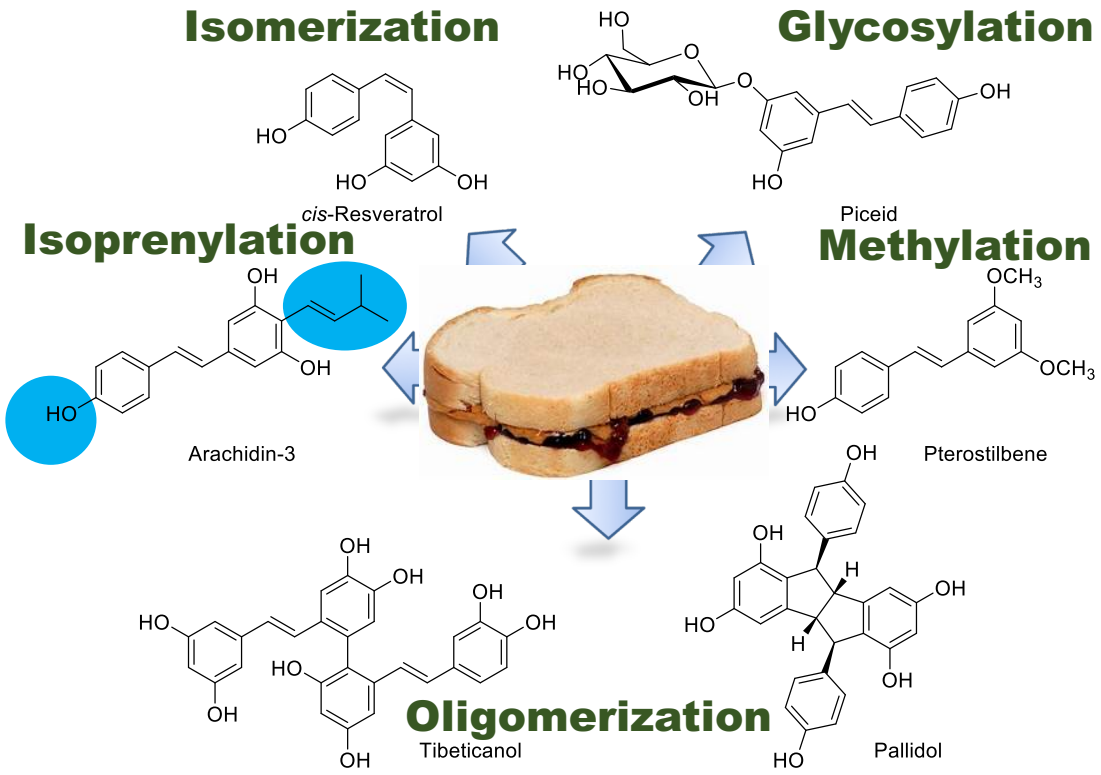


Somvanshi, V.S. et al. *Science* **2012**, *337*, 88-93.

Waterfield, N. **2009**. *Annu. Rev. Micro*. 63: 557.

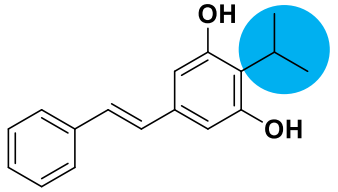
Stilbenes are polyketides widely distributed in dietary plants

Plant Stilbene Diversification



- Stilbene supplements can alleviate IBD symptoms

Bacterial stilbene (substrate)



- **Tapinarof**

ANTIBIOTICS IN MICROBIAL ECOLOGY
Isolation and Structure Assignment of Several New Antibacterial Compounds from the Insect-Symbiotic Bacteria *Xenorhabdus* spp.

VALERIE J. PAUL, SALLY FRAUTSCHY, WILLIAM FENICAL, and KENNETH H. NEALSON

APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Dec. 1995, p. 4329–4333 Vol. 61, No. 12
0099-2240/95/$04.00+0
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Identification of Two Pigments and a Hydroxystilbene Antibiotic from *Photorhabdus luminescens*

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PNAS

An antibiotic produced by an insect-pathogenic bacterium suppresses host defenses through phenoloxidase inhibition

Ioannis Eleftherianos*, Sam Boundy*, Susan A. Joyce*, Shazia Aslam*, James W. Marshall†, Russell J. Cox‡, Thomas J. Simpson‡, David J. Clarke*, Richard H. ffrench-Constant‡, and Stuart E. Reynolds*§

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Communications

VIP Biosynthesis

Bacterial Biosynthesis of a Multipotent Stilbene**

Susan A. Joyce, Alexander O. Brachmann, Itamar Glazer, Lea Lango, David J. Clarke, and Helge B. Bode**

ORIGINAL ARTICLE

Efficacy and safety of topical WBI-1001 in patients with mild to moderate psoriasis: results from a randomized double-blind placebo-controlled, phase II trial

R. Bissonnette,[†,*] C. Bolduc,[†] C. Maari,[†] S. Nigen,[†] J.M. Webster,[‡] L. Tang,[‡] M. Lyle[‡]

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CHEMMEDCHEM COMMUNICATIONS

ChemPubSoc Europe

DOI: 10.1002/cmdc.201300057

From a Multipotent Stilbene to Soluble Epoxide Hydrolase Inhibitors with Antiproliferative Properties

Estel.la Buscató,[a] Dominik Büttner,[a] Astrid Brüggerhoff,[a] Franca-Maria Klingler,[a] Julia Weber,[a] Bastian Scholz,[b] Aleksandra Živković,[a] Rolf Marschalek,[b] Holger Stark,[a] Dieter Steinhilber,[a] Helge B. Bode,[c] and Ewgenij Proschak*[a]

ORIGINAL ARTICLE

See related commentary on pg 2050

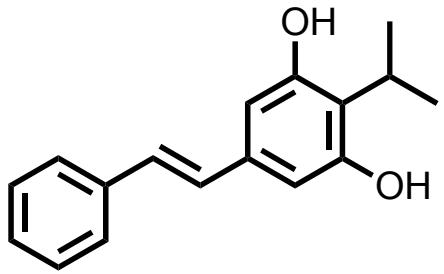
Tapinarof Is a Natural AhR Agonist that Resolves Skin Inflammation in Mice and Humans

Susan H. Smith[1,7,*], Channa Jayawickreme[2,7,*], David J. Rickard[2,*], Edwige Nicodeme[3,*], Thi Bui[1,*], Cathy Simmons[2,*], Christine M. Coquery[1,*], Jessica Neil[1,*], William M. Pryor[1,*], David Mayhew[3,*], Deepak K. Rajpal[2,*], Katrina Creech[2,*], Sylvia Furst[2,*], James Lee[1,*], Dalei Wu[2,*], Fraydoon Rastinejad[2,*], Timothy M. Willson[2,*], Fabrice Viviani[2,*], David C. Morris[1,*], John T. Moore[2,*] and Javier Cote-Sierra[1,*]

- Clinical efficacy for psoriasis & atopic dermatitis (GSK)
- Activates AhR (nm) and Nrf2 to promote clinical efficacy

Duotap: A Novel Antibiotic with a New Indication

- **Antibiotic market for MRSA antibiotics (1.3 billion market by 2026)**



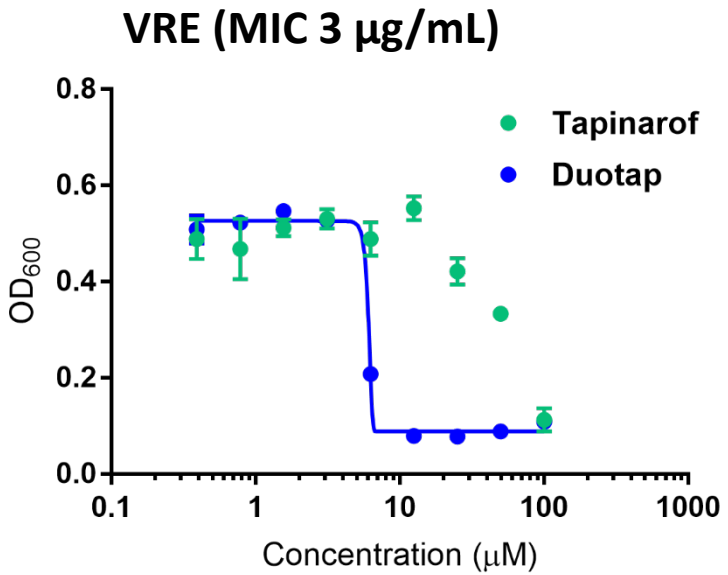
GSK recently sold **Tapinarof** to Dermavant Sciences for **$330 million**

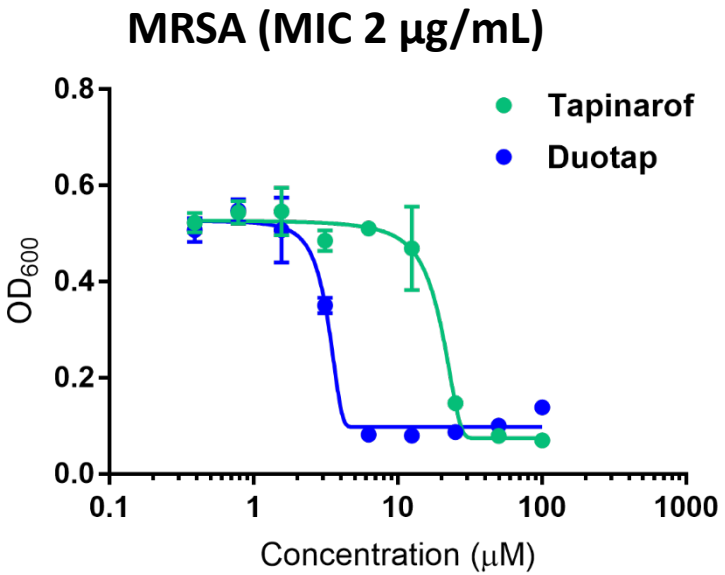
MUX-001 Drug Lead ("Duotap")

Using evolution as a guide, we discovered **MUX-001**, a **novel stilbene** drug lead for **MRSA**

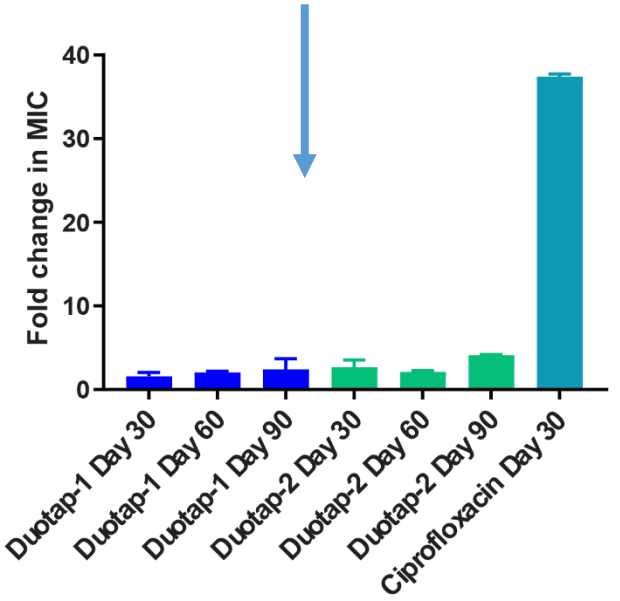
Duotap is effective against drug resistant bacteria

MUX-001
Drug Lead
(Duotap)





- **New class effective against multidrug resistant organisms (Cell wall biosynthesis inhibitor)**
- **MRSA does not develop resistance to MUX-001**



Tyler Goddard & Hyun Bong Park

Use of Proceeds/IP

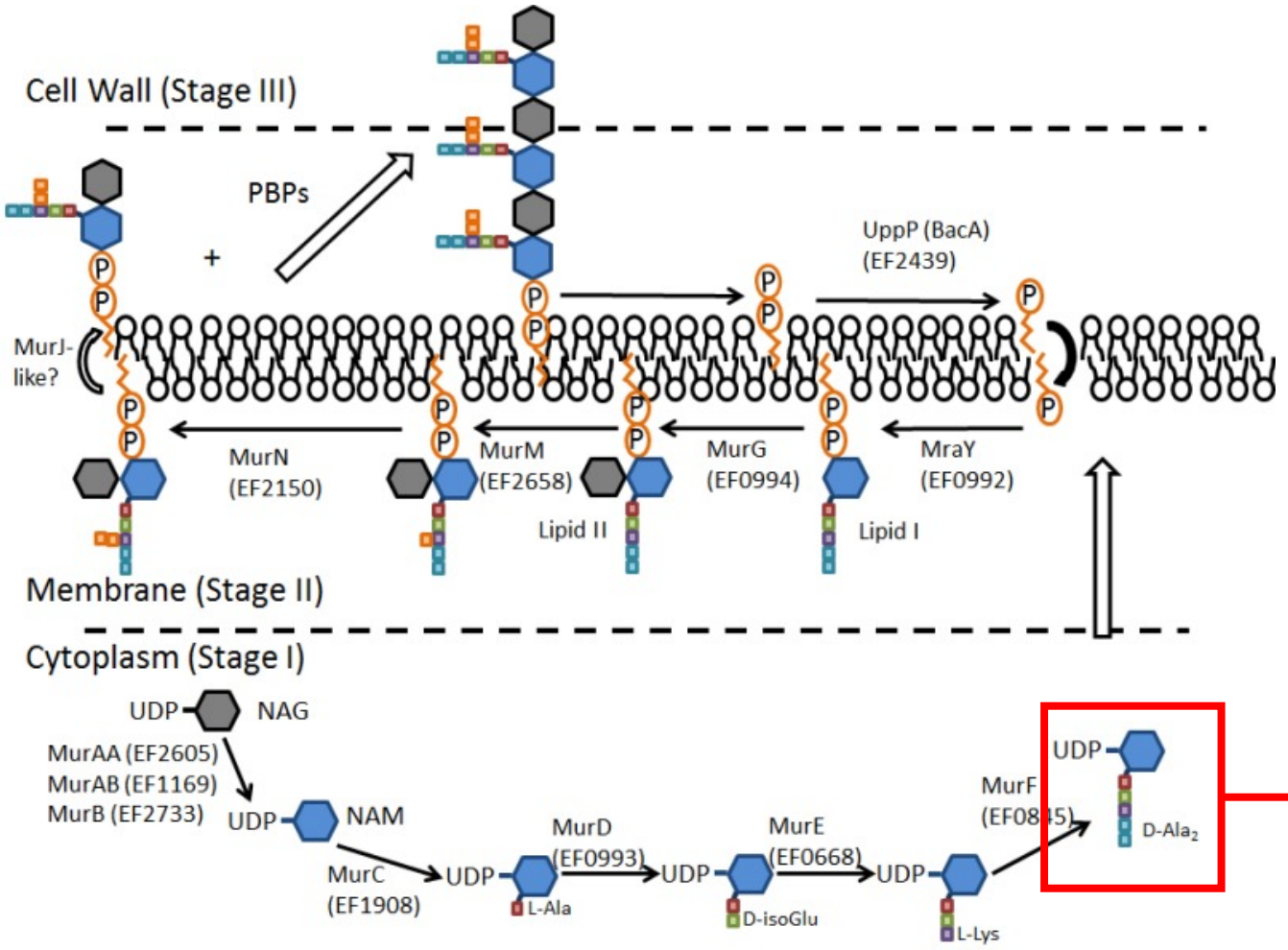
2 year proposal: $300K

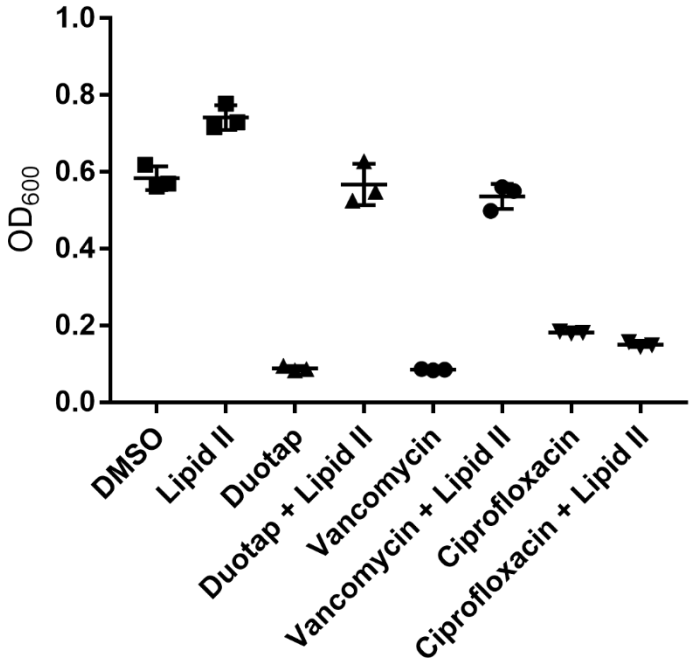
1. **MRSA skin infection models to evaluate antibiotic activity *in vivo* (CRO)**
2. **Biocatalytic SAR work on lead scaffold**

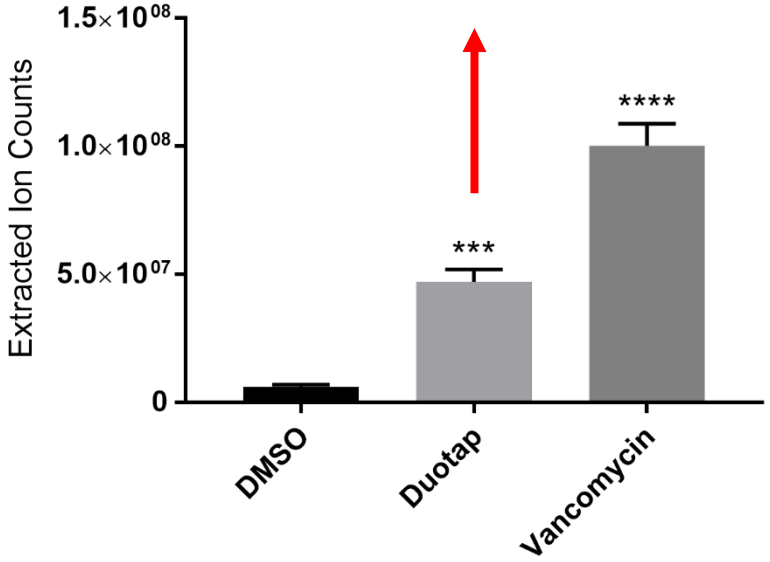
IP: Provisional patent filed for compositions of matter and methods of use.

1. **Biocatalytic pipeline to generate Mux analogs (new compositions of matter)**
2. **Use as an anti-infective against MDR pathogens (provisional in place)**

Duotap inhibits cell wall biosynthesis







Tyler Goddard & Hyun Bong Park

Image: Hancock, L.E., Murray, B.E., Sillanpaa, J. *Enterococcal Cell Wall Components and Structures.*