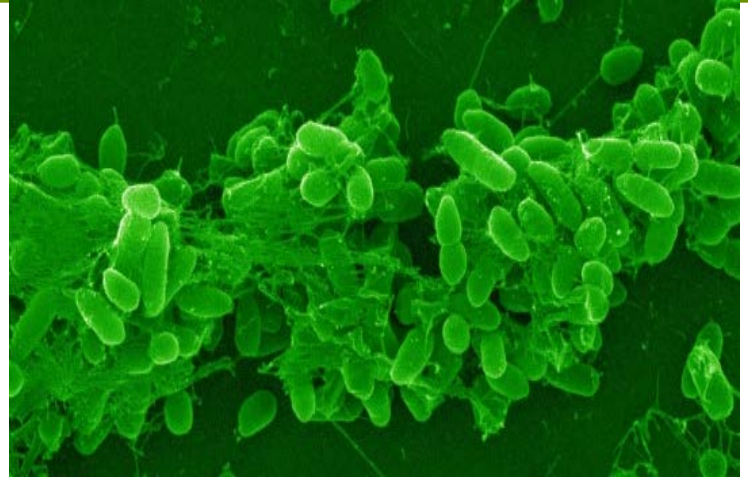

Strategies of Biofilm Disruption

WU Yuqian
Supervised by Prof. Margaret Ip
20151215
Department of Microbiology
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Department of **Microbiology**

香港中文大學
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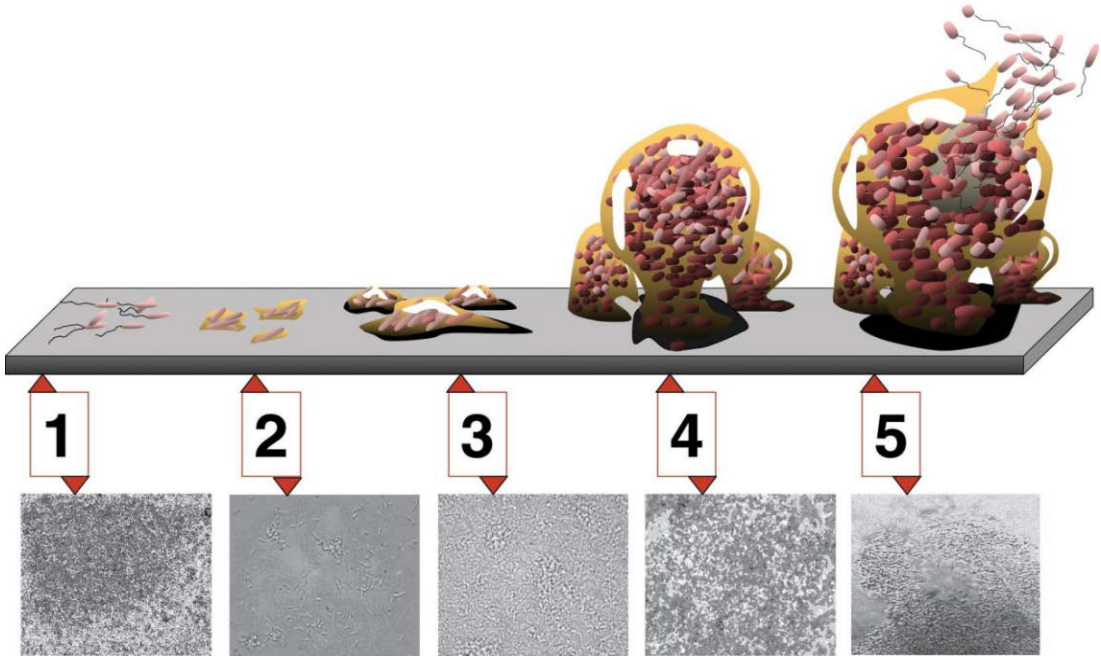
Outline

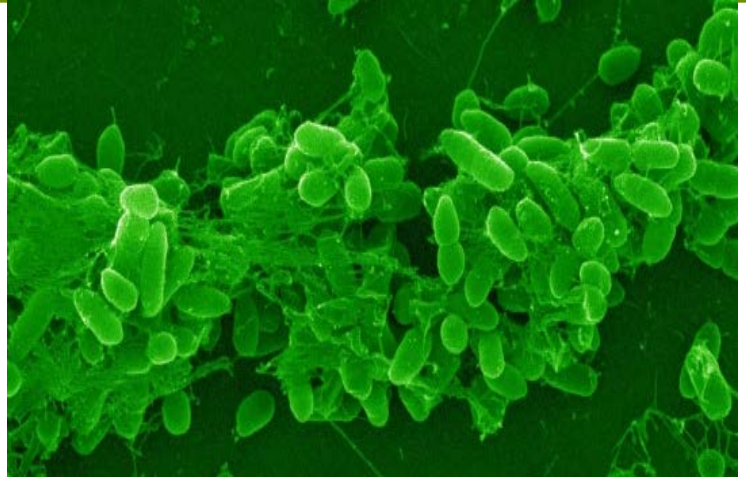
- Brief Introduction to biofilm
- D-amino acid treatment
- Anti-biofilm peptide
- Drugs targeting oscillation

What is biofilm?



- Microorganisms stick on a surface with proteins and polysaccarides
- Antibiotics resistance: 10~1000 times
- Matured biofilm: release planktonic bacteria

Chopra L, et al. (2015) Scientific Reports 5:13412.



D-amino acid treatment

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Clin Orthop Relat Res (2015) 473:3951–3961
DOI 10.1007/s11999-015-4465-9

BASIC RESEARCH

D-amino Acid Inhibits Biofilm but n in an Ovine Model

Andrew J. Harmata PhD, Yun Ma PhD, Carlos J. Sanch
Katarzyna J. Zienkiewicz MS, Florent Elefteriou PhD,

Contents lists available at ScienceDirect

Microbial Pathogenesis

journal homepage: www.elsevier.com/locate/micpath

The effects of D-Tyrosine combined with amikacin on the biofilms of *Pseudomonas aeruginosa*

Pengfei She [1], Lihua Chen [1], Hongbo Liu, Yaru Zou, Zhen Luo, Asmaa Koronfel, Yong Wu*

DOI 10.1000/jmm.0.075796 ... 013, Hunan, PR China

Journal of Medical Microbiology (2014), 63, 1369–1376

D-Amino acids i *Staphylococcus* infections

World J Microbiol Biotechnol (2012) 28:3067–3074
DOI 10.1007/s11274-012-1116-0

ORIGINAL PAPER

A synergistic D-tyrosine and tetrakis hydroxymethyl phosphonium sulfate biocide combination for the mitigation of an SRB biofilm

Biomaterials 34 (2013) 7533–754

Contents lists available at SciVerse

Biomaterials

journal homepage: www.elsevier.com

JOURNAL OF BACTERIOLOGY, Oct. 2011, p. 5616–5622 Vol. 193, No. 20
0021-9193/11/$12.00 doi:10.1128/JB.05534-11
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Inhibitory Effects of D-Amino Acids on *Staphylococcus aureus* Biofilm Development[▽]†

Allon I. Hochbaum,[1,2]§ Ilana Kolodkin-Gal,[3]§ Lucy Foulston,[3] Roberto Kolter,[4] Joanna Aizenberg,[1,2] and Richard Losick[3]*

Cell. Mol. Life Sci. (2011) 68:817–831
DOI 10.1007/s00018-010-0571-8

REVIEW

Emerging knowledge of regu in bacteria

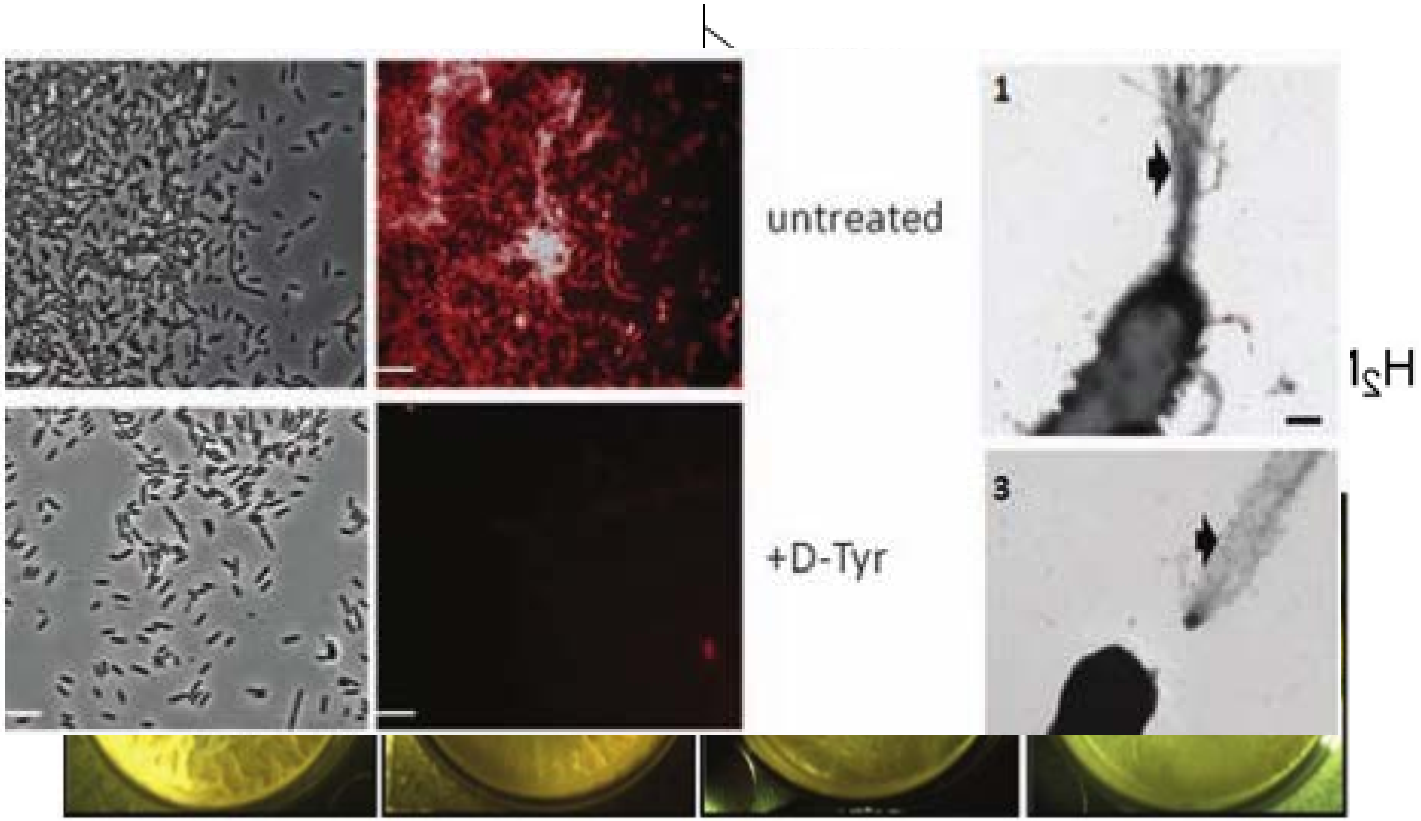
Felipe Cava · Hubert Lam · Miguel A. de Pe
Matthew K. Waldor

Published in final edited form as:
Science. 2010 April 30; 328(5978): 627–629. doi:10.1126/science.1188628.

D-Amino Acids Trigger Biofilm Disassembly

Illana Kolodkin-Gal[1], Diego Romero[2], Shugeng Cao[3], Jon Clardy[3], Roberto Kolter[2], and Richard Losick[1,*]

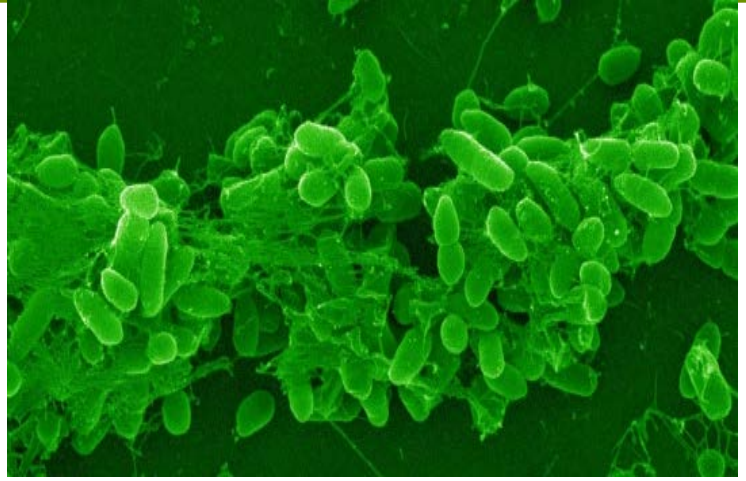
Introduction of D-Amino Acid



Ilana KG, et al. (2010) Science 328(5978).

Effects of D-Amino Acid

- D-tyrosine is most effective on both preventing biofilm formation and disrupting existing biofilm by incorporation into the cell wall
- It also inhibits biofilm formation of *Staphylococcus aureus, Escherichia coli* and *Pseudomonas aeruginosa* biofilm



Anti-biofilm peptide

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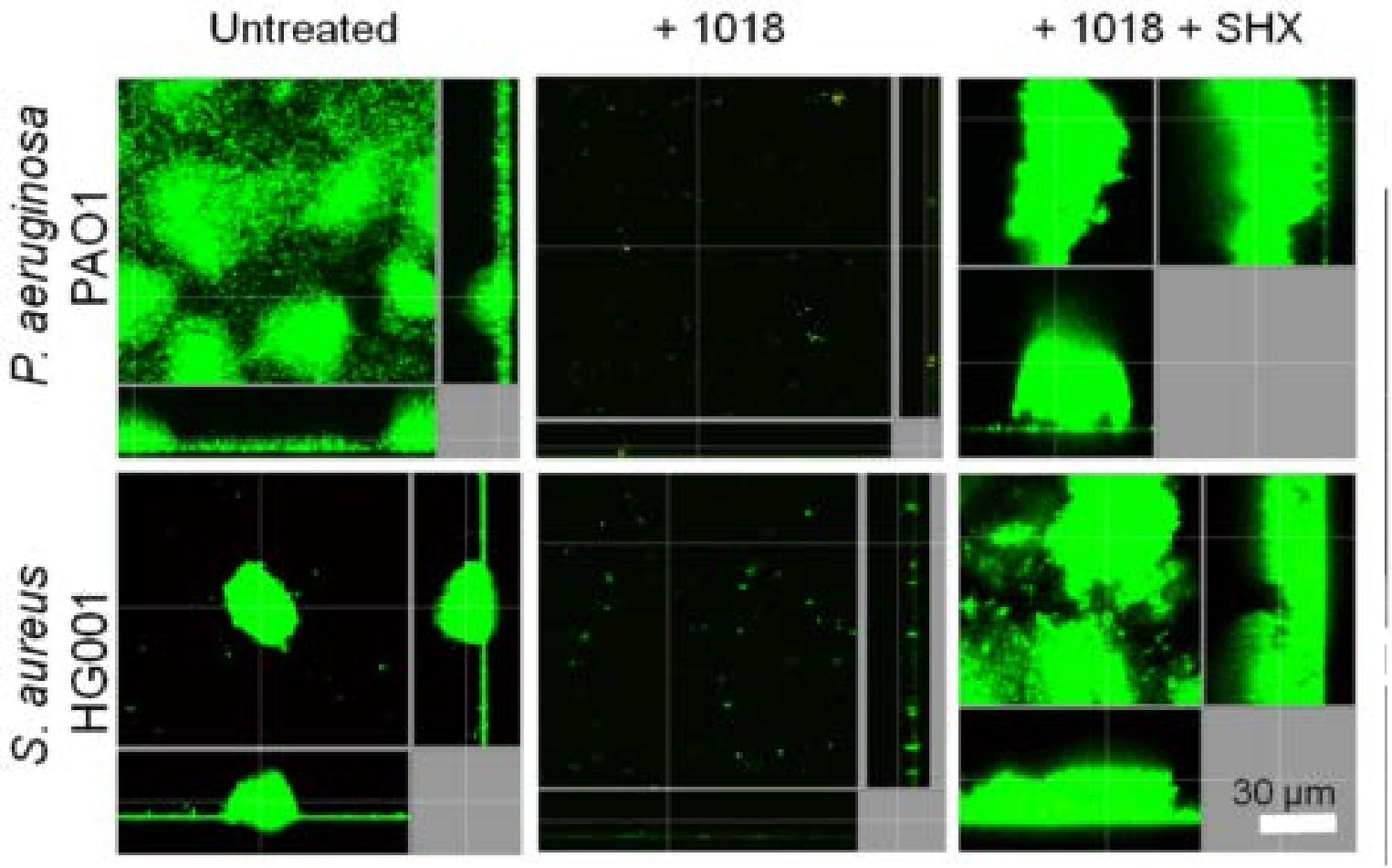
Target of Anti-biofilm Peptide

- Peptide: immunomodulatory peptide IDR (innate defense regulator): 1018 (VRLIVAVRIWRR-NH_2)
- Target: guanosine 5'-di(tri)phosphate 3'-diphosphate [(p)ppGpp] (signal activating stringent response as second messenger)
- Principle: inhibition of synthesis of (p)ppGpp and stress response through enzymes RelA and SpoT

de la Fuente-Núñez C, et al. (2015) PLoS One 10(7).

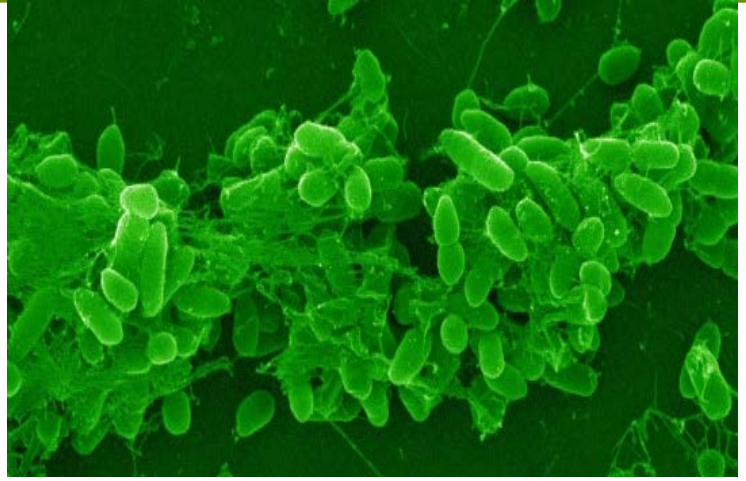
Affectivity of Anti-biofilm Peptide



de la Fuente-Núñez C, et al. (2014) PLoS Pathogens 10(5).

Effects of Anti-biofilm Peptide

- Inhibit growth of biofilm
- Eradicate existing biofilm
- Increase affectivity of disinfectants (e.g. chlorhexidine)



Oscillation: Introduction and Inspiration

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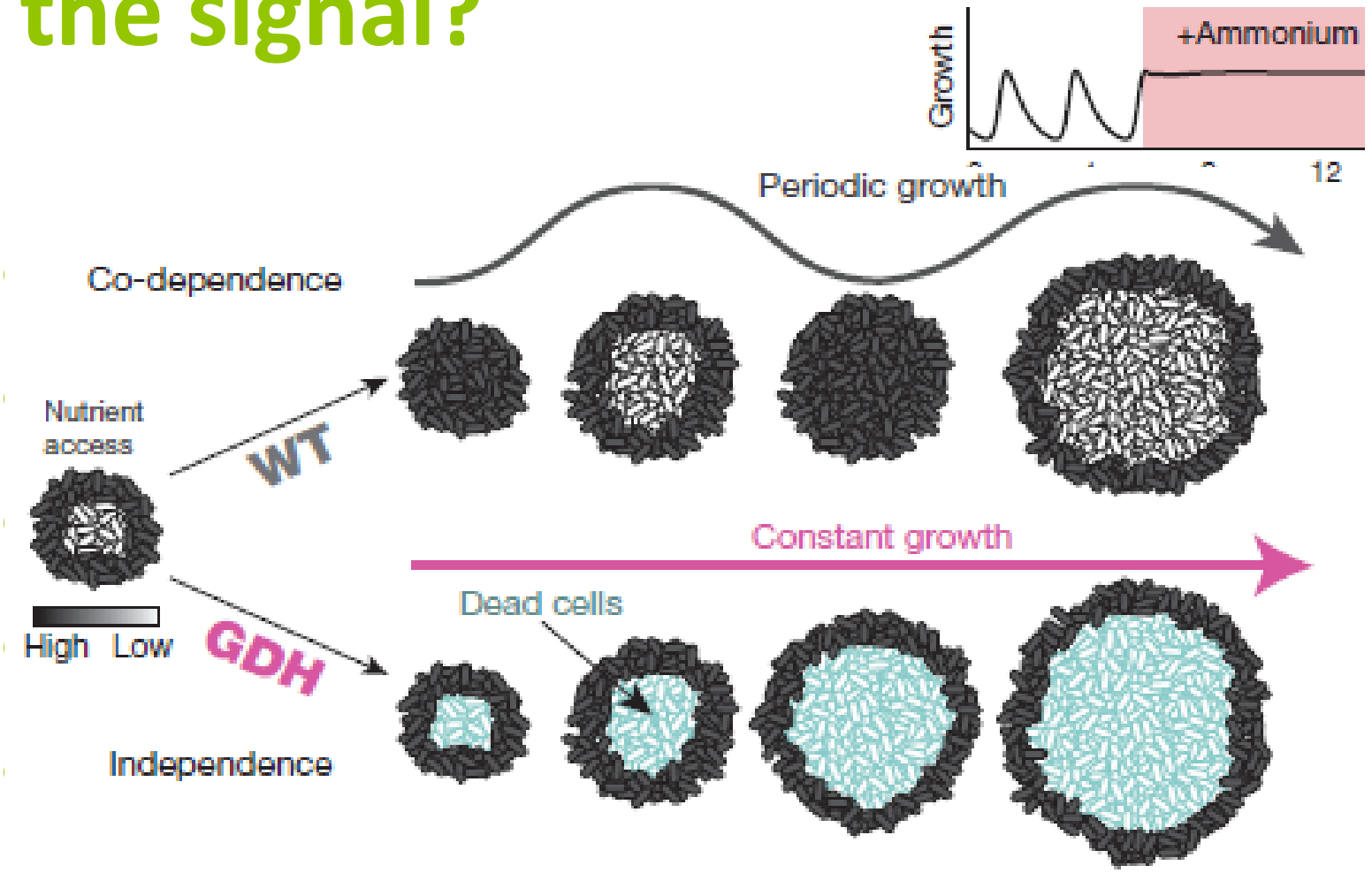
Introduction of Oscillation

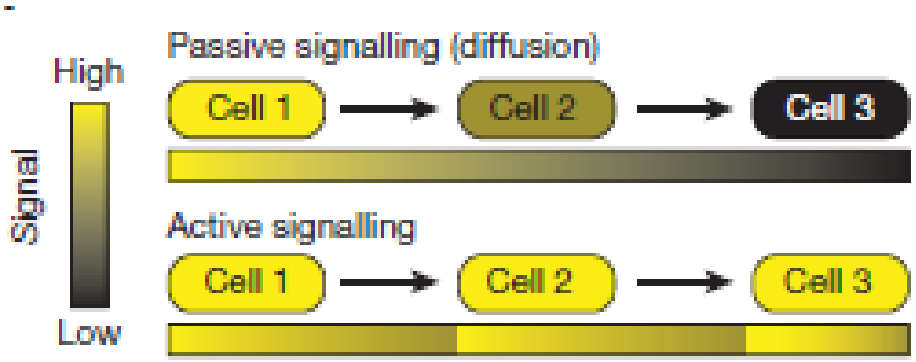
- Biofilm growth has oscillations (pauses growth periodically)
- Biofilm periphery grow → absorb nutrient → biofilm interior starve → (how?) biofilm periphery pause growth → nutrient access biofilm interior → (how?) biofilm periphery grow →→ (oscillation repeats)
- Hypothesis: nutrient (e.g. glutamate) triggers metabolic feedback/ion channel communication
- Note: glutamate –GDH→ ammonium + glutamine

Hypothesis 1: Ammonium, the signal?



Süel GM, et al. (2015) Nature 523(7562).

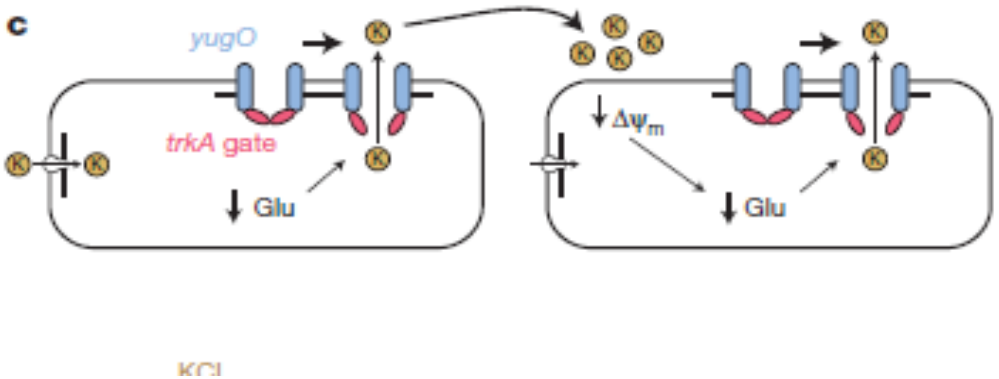
Hypothesis 2: Ion channel, the signal?

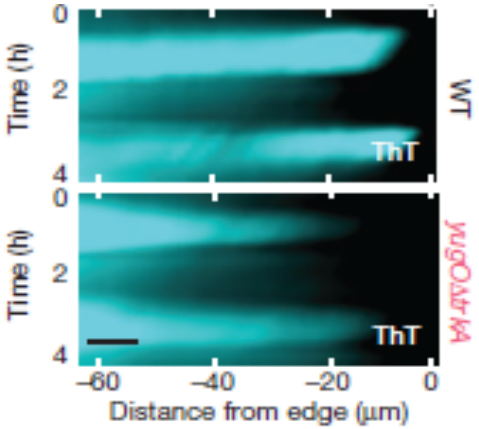


Süel GM, et al. (2015) Nature 527(7576).

Hypothesis 2: Ion channel, the signal?

- Result 4: existence of channel (yugO) and its gate domain (trkA) [gate opens when glutamate limits, leads to potassium efflux]
- Result 5: removal of trkA domain leads to membrane potential constancy loss





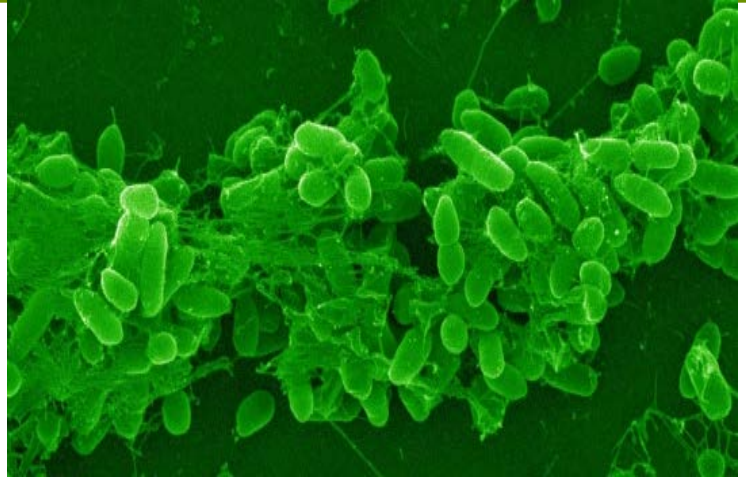
Süel GM, et al. (2015) Nature 527(7576).

Discussion of Oscillation

- Biocides that lead to death might lead to growth; signals that lead to growth might lead to death
- Oscillations of biofilm growth showed that inhibiting growth of colony periphery might lead to growth of the biofilm interior, vice versa
- To eliminate biofilm growth, metabolic products (e.g. ammonium) could be utilized at the same time with disinfectants (e.g. H_2O_2)
- Drugs targeting potassium channel could be utilized by interfering oscillation and metabolic coordination
- Not only structural similarities between bacterial and human potassium ion channels, but also their possible functional similarities with respect to electrical communication should be noticed

Conclusion

- New strategies have been updated for biofilm growth inhibition and disruption
- New methods could be developed according to these strategies



Thank you!

Q&A Session

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Target of Anti-biofilm Peptide

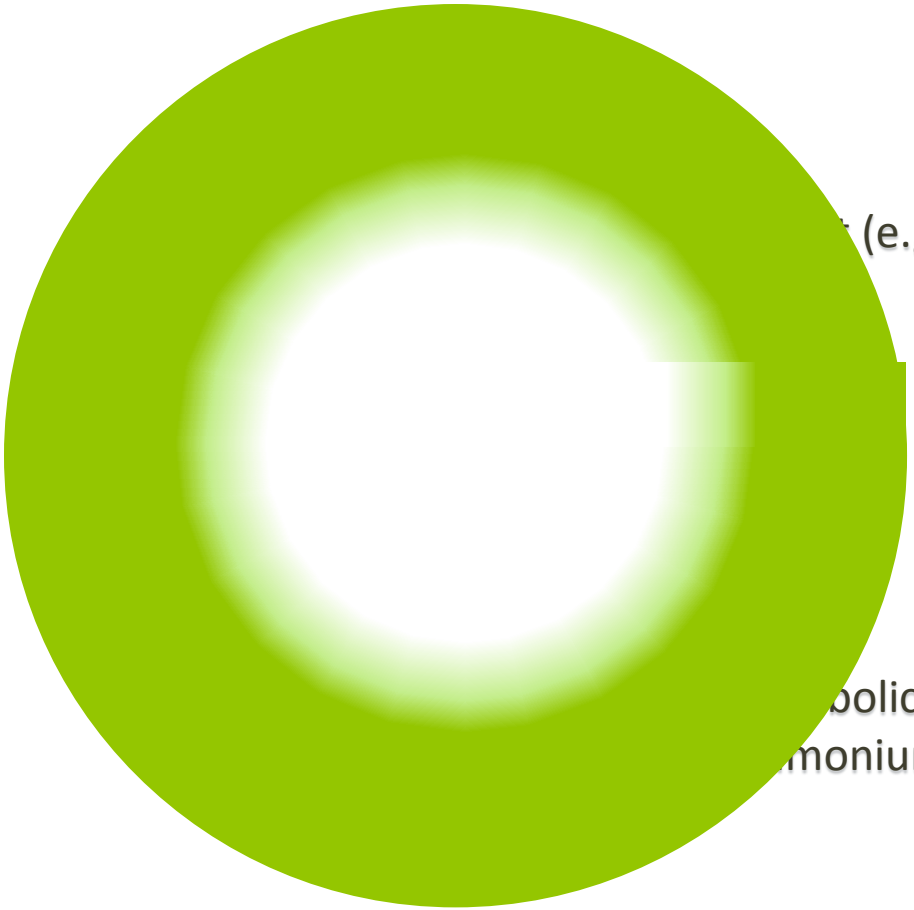
Name	Target	Reference
Cationic antimicrobial peptides	lipopolysaccharides and lipoteichoic acids	Han HM, et al. (2015) Amino Acids
Cinnamic acid derivative ultrashort tetra-peptide	-	Laverty G, et al. (2015) J Pept Sci. 21(10):770-8
Bacteriocins	Membrane permeability	Chopra L, et al. (2015) Sci Rep. 5:13412.
14-Helical β-peptides	-	Raman N, et al. (2015) Pharmaceuticals 8(3)
Coryxin (Asn-Arg-Asn-Gln-Pro-Asn-Ser)	-	Dalili D, et al. (2015) Colloids Surf B Biointerfaces 135
Peptide 1018	(p)ppGpp	de la Fuente-Núñez C, et al. (2015) PLoS One 10(7)
Esculentin-1a(1-21)NH2	Bacterial lipopolysaccharide (LPS)	Di Grazia A, et al. (2015) Amino Acid. 47(12):2505-19

Conclusion

Treatment	Advantage	Disadvantage
D-Amino Acid	Easy to produce, effective	Resistance (e.g. yqrM6)
Anti-biofilm Peptide (Peptide 1018)	Could inhibit growth of biofilm, decrease resistance of disinfectant	Resistance (e.g. overexpression of RelA/SpoT)
Metabolic product (e.g. ammonium)	Easy to produce, decrease resistance of disinfectants	Should be utilized together with disinfectant
Drugs targeting ion channels	Low resistance	Might need further study

Introduction of Oscillation

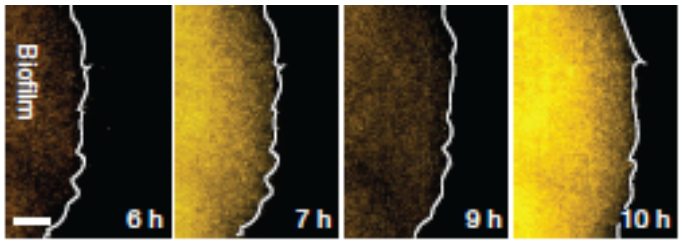
1.5-3 hours

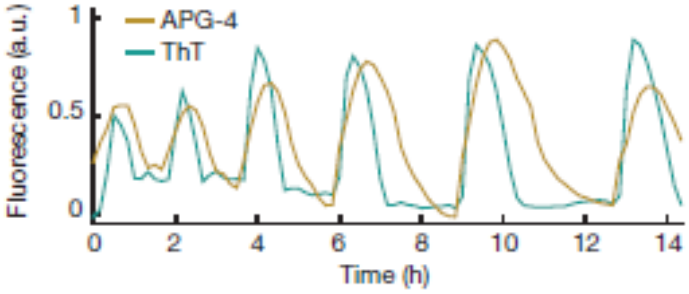


(e.g. glutamate)

bolic products (e.g.
monium)

Introduction of Oscillation





1.5-3 Hours (Oscillation of Biofilm Growth)

Radius (from interior to periphery)