

抗菌薬耐性微生物に対する耐性を持つ共生細菌の同定

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略歴：Eric G. Pamer 医師は、メモリアル・スローン・ケタリングがんセンター (MSKCC) において、Head of the Division of Subspecialty Medicine、Enid A. Haupt Chair in Clinical Investigation、および Director of the Lucille Castori Center for Microbes, Inflammation & Cancer の要職を務めている。博士はケース・ウェスタン・リザーブ大学医学部より MD の学位を授与され、カリフォルニア大学サンディエゴ校 (UCSD) メディカルセンターにおいて内科医学および感染症学の臨床実習を修了した。UCSD (Charles E. Davis 博士に師事)、スクリプス研究所 (Maggie So 博士に師事)、ワシントン大学 (Michael Bevan 博士に師事) にてポストドクとして勤めた後、イェール大学に籍を移した。その後、2000年に自身の研究室を MSKCC に移し、そこで Chief of the Infectious Diseases Service の要職を 15年間に渡って務めた後に現職に至る。

要約：抗生物質耐性菌を含む病原細菌によって引き起こされる感染は、一般的にそれらが粘膜表面、特に腸上皮へ定着するところから始まる。バンコマイシン耐性 *Enterococcus faecium*、*Klebsiella pneumoniae* および *Clostridium difficile* は、抗生物質に対して高い耐性を有するが、腸内細菌叢はこれらが引き起こす感染に対する抵抗性を付与する。種々の抗生物質により処置したネズミおよびヒトの腸内細菌叢のメタゲノムシーケンス解析により、これらの一般的な院内感染原因菌に対する抵抗性獲得に関与する腸内細菌が同定され始めている。抗生物質治療後に、多様性に富む腸内細菌叢を移植する方法は、抗生物質耐性菌による感染症およびその患者間伝播を低減し得る手段として非常に有望である。

参考文献

- 1) Abt MC, Buffie CG, Susac B, Becattini S, Carter RA, Leiner I, Keith JW, Artis D, Osborne LC, Pamer EG. TLR-7 activation enhances IL-22-mediated colonization resistance against vancomycin-resistant enterococcus. *Science Translational Medicine*. 2016 ; 8 (327) : 327ra25.
- 2) Xiong H, Keith JW, Samilo DW, Carter RA, Leiner IM, Pamer EG. Innate Lymphocyte/Ly6C (hi) Monocyte Crosstalk Promotes *Klebsiella pneumoniae* Clearance. *Cell*. 2016 ; 165 (3) : 679-89.
- 3) Caballero S, Kim S, Carter RA, Leiner IM, Sušac B, Miller L, Kim GJ, Ling L, Pamer EG. Cooperating Commensals Restore Colonization Resistance to

- Vancomycin-Resistant *Enterococcus faecium*. *Cell Host Microbe*. 2017 ; 21 (5) : 592-602.
- 4) Becattini S, Littmann ER, Carter RA, Kim SG, Morjaria SM, Ling L, Gyaltsen Y, Fontana E, Taur Y, Leiner IM, Pamer EG. Commensal microbes provide first line defense against *Listeria monocytogenes* infection. *Journal of Experimental Medicine*. 2017 ; 214 (7) : 1973-1989.
 - 5) Lewis BB, Carter RA, Ling L, Leiner I, Taur Y, Kamboj M, Dubberke ER, Xavier J, Pamer EG. Pathogenicity Locus, Core Genome, and Accessory Gene Contributions to *Clostridium difficile* Virulence. *MBio*. 2017 ; 8 (4) . pii : e00885-17.
 - 6) Haak BW, Littmann ER, Chaubard JL, Pickard AJ, Fontana E, Adhi F, Gyaltsen Y, Ling L, Morjaria SM, Peled JU, van den Brink MR, Geyer AI, Cross JR, Pamer EG, Taur Y. Impact of gut colonization with butyrate producing microbiota on respiratory viral infection following allo-HCT. *Blood*. 2018 ; Apr 19. pii : blood-2018-01-828996.
 - 7) Taur Y, Coyte K, Schluter J, Gjonbalaj M, Littmann E, Ling L, Miller L, Gyaltsen Y, Fontana E, Morjaria S, Gyurkocza B, Perales MA, Castro-Malaspina H, Tamari R, Ponce D, Koehne G, Barker J, Jakubowski A, Papadopoulos E, Dahi P, Sauter C, Shaffer B, Young J, Peled J, Meagher R, Jenq R, van den Brink M, Giralt S, Pamer E, Xavier J. Microbiota-Remediation After Antibiotic-Induced Loss of Commensal Bacteria. *Science Translational Medicine*. In Press

Identifying commensal bacteria that provide resistance against antibiotic-resistant pathogens

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Abstract : Identifying commensal bacteria that provide resistance against antibiotic-resistant pathogens.

Infections caused by antibiotic-resistant bacteria generally begin with colonization of mucosal surfaces, in particular the intestinal epithelium. The intestinal microbiota provides resistance to infection with highly antibiotic-resistant bacteria, including Vancomycin Resistant *Enterococcus faecium*, *Klebsiella pneumoniae* and *Clostridium difficile*. Metagenomic sequencing of the murine and human microbiota following treatment with different antibiotics is beginning to identify bacterial taxa that are associated with resistance to these common, hospital-acquired pathogens. Reintroduction of a diverse intestinal microbiota following antibiotic treatment provides an important potential avenue to reduce antibiotic-resistant infections and their transmission from patient-to-patient.

References

- 1) Abt MC, Buffie CG, Susac B, Becattini S, Carter RA, Leiner I, Keith JW, Artis D, Osborne LC, Pamer EG. TLR-7 activation enhances IL-22-mediated colonization resistance against vancomycin-resistant enterococcus. *Science Translational Medicine*. 2016 ; 8 (327) : 327ra25.
- 2) Xiong H, Keith JW, Samilo DW, Carter RA, Leiner IM, Pamer EG. Innate Lymphocyte/Ly6C (hi) Monocyte Crosstalk Promotes *Klebsiella*

- pneumoniae Clearance. *Cell*. 2016 ; 165 (3) : 679-89.
- 3) Caballero S, Kim S, Carter RA, Leiner IM, Sušac B, Miller L, Kim GJ, Ling L, Pamer EG. Cooperating Commensals Restore Colonization Resistance to Vancomycin-Resistant *Enterococcus faecium*. *Cell Host Microbe*. 2017 ; 21 (5) : 592-602.
 - 4) Becattini S, Littmann ER, Carter RA, Kim SG, Morjaria SM, Ling L, Gyaltsen Y, Fontana E, Taur Y, Leiner IM, Pamer EG. Commensal microbes provide first line defense against *Listeria monocytogenes* infection. *Journal of Experimental Medicine*. 2017 ; 214 (7) : 1973-1989.
 - 5) Lewis BB, Carter RA, Ling L, Leiner I, Taur Y, Kamboj M, Dubberke ER, Xavier J, Pamer EG. Pathogenicity Locus, Core Genome, and Accessory Gene Contributions to *Clostridium difficile* Virulence. *MBio*. 2017 ; 8 (4) . pii : e00885-17.
 - 6) Haak BW, Littmann ER, Chaubard JL, Pickard AJ, Fontana E, Adhi F, Gyaltsen Y, Ling L, Morjaria SM, Peled JU, van den Brink MR, Geyer AI, Cross JR, Pamer EG, Taur Y. Impact of gut colonization with butyrate producing microbiota on respiratory viral infection following allo-HCT. *Blood*. 2018 ; Apr 19. pii : blood-2018-01-828996.
 - 7) Taur Y, Coyte K, Schluter J, Gjonbalaj M, Littmann E, Ling L, Miller L, Gyaltsen Y, Fontana E, Morjaria S, Gyurkocza B, Perales MA, Castro-Malaspina H, Tamari R, Ponce D, Koehne G, Barker J, Jakubowski A, Papadopoulos E, Dahi P, Sauter C, Shaffer B, Young J, Peled J, Meagher R, Jenq R, van den Brink M, Giralt S, Pamer E, Xavier J. Microbiota-Remediation After Antibiotic-Induced Loss of Commensal Bacteria. *Science Translational Medicine*. In Press