

Commensals of two kinds: Promoter or Eliminator of *Vibrio cholerae* infection



Speaker: Sang Sun Yoon, Dept of Microbiology and Immunology, Yonsei University College of Medicine, Seoul, Korea
Date: 11th February 2020
Time: 11 AM
Venue: Seminar Room 1

About the talk:

Indigenous microbes inside the host intestine maintain a complex self-regulating community. The mechanisms by which gut microbes interact with intestinal pathogens remain largely unknown. The team identified a commensal *Escherichia coli* strain whose expansion predisposes mice to infection by *Vibrio cholerae*, a human pathogen. They refer to this strain as 'atypical' *E. coli* (*atEc*) because of its inability to ferment lactose. The *atEc* strain is extremely resistant to reactive oxygen species (ROS) and proliferates extensively during antibiotic treatments. Intestinal ROS levels are decreased in *atEc*-transplanted mice, favoring proliferation of ROS-sensitive *V. cholerae*. An *atEc* mutant defective in ROS degradation fails to facilitate *V. cholerae* infection when pre-transplanted. A species of genus *Bacteroides*, otherwise a dominant gut microbe, was completely eliminated upon treatment with clindamycin (CL), an antibiotic that specifically kills anaerobes. CL-treated and therefore *Bacteroides*-depleted mice developed cholera-like symptoms when infected with *V. cholerae*. Furthermore, cultivated *Bacteroides* cells killed *V. cholerae* *in vitro*, demonstrating antagonistic relationship between the *Bacteroides* sp. and *V. cholerae*. Together, their results suggest that enteric infection is an event that occurs depending on the composition of intestinal microbiota and the *Bacteroides* sp. has potential to be developed as an anticholera intervention.

CURRICULUM VITAE

Name: Sang Sun Yoon

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Education and Training:

Feb. 1998, B.S	Chemistry and Chemical Engineering	Hanyang University Seoul, Korea
Aug. 2000, M.S	Biochemical Engineering	KAIST Taejun, Korea
Dec. 2004, Ph.D.	Microbial Pathogenesis	University of Cincinnati, College of Medicine Cincinnati, OH. USA
Aug. 2007, PostDoc	Microbial Pathogenesis	Harvard Medical School, Boston, MA. USA

Professional Career:

Sep. 2007 – Feb. 2009

Assistant Professor
Department of Microbiology and Immunology
University of Otago
Dunedin, New Zealand

Mar. 2009 – present

Assistant, Associate and Full (Tenured) Professor
Department of Microbiology and Immunology
Yonsei University College of Medicine
Seoul, Korea

Research Experiences:

Sep.1998 - Aug. 2000.

Department of Chemical Engineering, KAIST

M.S. (Advisor: **Dr. Sang Yup Lee**)

Thesis Title: Proteome Analysis of Recombinant *Escherichia coli* Engineered to Produce Polyhydroxyalkanoates.

Sep. 2000 - Dec. 2004.

Department of Molecular Genetics, Biochemistry and Microbiology

University of Cincinnati College of Medicine

Ph.D. (Advisor: **Dr. Daniel J. Hassett**)

Thesis Title: Mechanistic Dissection of Anaerobic Metabolism of *Pseudomonas aeruginosa*: Implications for the Treatment of Cystic Fibrosis Airway Disease.

Dec. 2004 - Aug. 2007.

Department of Microbiology and Molecular Genetics, Harvard Medical School

Postdoctoral Fellow (Advisor: **Dr. John J. Mekalanos**)

Project Title:

1. Molecular Basis of *Vibrio cholerae* Population Switchover from Classical to El Tor Biotype.
2. Innate Immune Response against Sheathed *Vibrio cholerae* Flagellum.
3. ImmunoProteomics: Identification of Novel Immunostimulatory Bacterial Proteins by **Expressed Protein Screen for Immune Activators (EPSIA)** Technology.

Academic activity:

Associate editor, The Journal of Microbiology, 2011-2014

Review editor, Frontiers in Cellular and Infection Microbiology, 2011-present

Served as an “*ad hoc*” reviewer in Journals including

Infection and Immunity, Applied and Environmental Microbiology, Journal of Bacteriology
Antimicrobial Agents and Chemotherapy, FEMS Microbiology Letters, Microbes and Infection
PLoS Pathogens, mSystems, Scientific Reports, Genome Biology, Nature Communications

Honors and Awards:

- 1994-1998. Hanyang University, Excellence Scholarship (**Full-Tuition Waiver**)
- 1998. B.S. with **summa cum laude**, Hanyang University
- Nov. 2003. **Best Poster Award**, Graduate Student Research Forum (Poster Presentation)
University of Cincinnati College of Medicine
- June 2004. **Distinguished Dissertation Fellowship Award for Life Sciences**, University of Cincinnati
- July 2004. **Graduate Student Scientific Award**, University of Cincinnati, College of Medicine
- Dec. 2006. **Best Paper Award**, US-Japan Joint conference on Cholera and Other Bacterial Enteric Infections.
- Oct. 2011. **“New Scientist Award” (KRIBB-sponsored)**, The Microbiological Society of Korea
- June 2014. **Donghwa Holdings Research Award**, Yonsei University College of Medicine
- Dec. 2016. **Top 5 Research of the Year in Biomedical Sciences**, BRIC
- Mar. 2017. **Best Lecturer Award in 2017**, Yonsei University College of Medicine
- Jan. 2018. **Red Ribbon Lecture**, Korean Society for Molecular and Cellular Biology

Research interests

- Bacterial Pathogenesis
- Host-Microbe Interaction
- Commensal Microbes-Pathogen Interaction
- Microbiome
- Microbial Genomics

Publications (as of Jan. 2020)

60. A. Jo, J. Won, C. H. Chil, J. Y. Choi, K.M. Lee, **S.S. Yoon***, H.J. Kim*, Nasal commensal *Staphylococcus epidermidis*-driven Serpine1 induction in nasal epithelium prevents influenza virus invasion of upper airway, submitted
59. D. Lee, E.J. Kim, Y. Baek, J. Lee, Y. Yoon, G.B. Nair, **S.S. Yoon***, D.W. Kim* Alterations in glucose metabolism in *Vibrio cholerae* serogroup O1 El Tor biotype strains, **Sci. Rep.** 2020 10(1):1-10.
58. K.B. Min and **S.S. Yoon*** Pleiotropic functions of *Pseudomonas aeruginosa* DksA1 revealed by transcriptome analysis, **J. Biol. Chem.**, revision submitted
57. J.S. You, J.H. Yong, G.H. Kim, K.T. Nam, J.H. Ryu, M.Y. Yoon* and **S.S. Yoon***, Commensal-derived Metabolites Govern *Vibrio cholerae* Pathogenesis in Host Intestine, **Microbiome**, 2019, 7(1):132
56. Jeon YJ, Jo A, Won J, Lee KM, **Yoon SS**, Choi JY, Kim HJ. Interleukin-17C protects nasal epithelium from *Pseudomonas aeruginosa* infection. **Am J Respir Cell Mol Biol.** 2019 Jul 18.
55. H.J. Kim, A. Jo, Y.J. Jeon, S. An, K.M. Lee, **S.S. Yoon*** and J.Y. Choi*, Nasal commensal *Staphylococcus epidermidis* enhances IFN- λ -dependent immunity against influenza virus, **Microbiome**, 2019, 7(1):80
54. Hwang W. and **Yoon S.S.***, Virulence Characteristics and a Mode of Antibiotic Resistance of Multidrug-Resistant *Pseudomonas aeruginosa*, **Sci. Rep.** 2019 Jan 24;9(1):487.
53. Kim CY, Lee M, Lee K, **Yoon SS**, Lee I. Network-based genetic investigation of virulence-associated phenotypes in methicillin-resistant *Staphylococcus aureus*. **Sci. Rep.** 2018 Jul 17;8(1):10796.
52. Jung IY, Jeong SJ, Lee KM, Ahn JY, Ku NS, Han SH, Choi JY, Yong D, **Yoon SS**, Song YG, Jeong SH, Kim JM, Lee K., Risk factors for mortality in patients with *Pseudomonas aeruginosa* pneumonia: Clinical impact of mucA gene mutation. **Respir. Med.** 2018 Jul; 140: 27-31.
51. Kim B, Park JS, Choi HY, **Yoon SS**, Kim WG., Terrein is an inhibitor of quorum sensing and c-di-GMP in *Pseudomonas aeruginosa*: a connection between quorum sensing and c-di-GMP. **Sci Rep.** 2018 Jun 5; 8(1): 8617.
50. Kim HY, Yu SM, Jeong SC, **Yoon SS**, Oh YT*, Effects of *flaC* mutation on stringent response-mediated bacterial growth, toxin production, and motility in *Vibrio cholerae*. **J Microbiol Biotechnol.** 2018 Mar 15. doi: 10.4014/jmb.1712.12040.
49. H.Y. Kim, J. Go, K.M. Lee, Y.T. Oh*, and **S.S. Yoon***, Guanosine tetra- and pentaphosphate increase antibiotic tolerance by reducing reactive oxygen species production in *Vibrio cholerae*. **J. Biol. Chem.**, 2018 Apr 13;293(15):5679-5694.
48. M.Y. Yoon and **S.S. Yoon***, Disruption of the gut ecosystem by antibiotics (invited review). **Yonsei Medical Journal**, 2018, 59: 4-12.
47. M. Toyofuku and **S.S. Yoon***, Nitric oxide, an old molecule with noble functions in *Pseudomonas*

aeruginosa biology (Invited review). **Advances in Microbial Physiology**, 2018, 72: 117-145.

46. Lee K, Lee KM, Kim D, **S.S. Yoon***, Molecular determinants of the matrix thickening of a dual-species *Pseudomonas aeruginosa* and *Enterococcus faecalis* biofilm. **Appl Environ Microbiol.** 2017 Aug 25. pii: AEM.01182-17. doi: 10.1128/AEM.01182-17.

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44. Lee K and **S.S. Yoon***, *Pseudomonas aeruginosa* Biofilm, a Programmed Bacterial Life for Fitness. **J. Microbiol. Biotechnol.**, 2017 Jun 28;27(6):1053-1064.

43. Lee KM, Lee K, Go J, Park IH, Shin JS, Choi JY, Kim HJ, **S.S. Yoon***, A Genetic Screen Reveals Novel Targets to Render *Pseudomonas aeruginosa* Sensitive to Lysozyme and Cell Wall-Targeting Antibiotics. **Front. Cell Infect. Microbiol.** 2017 Mar 1; 7:59.

42. Alrahman MA and **S.S. Yoon***, Identification of essential genes of *Pseudomonas aeruginosa* for its growth in airway mucus. **J. Microbiol.**, 2017 Jan; 55(1):68-74.

41. Y.T. Oh, H.Y. Kim, E.J. Kim, J. Go, W. Hwang, H.R. Kim, D.W. Kim*, and **S.S. Yoon***, Selective and Efficient Elimination of *Vibrio cholerae* with a Chemical Modulator that Targets Glucose Metabolism, **Front. Cell Infect. Microbiol.** 2016 Nov 16; 6:156.

40. S. Hwang, C.Y. Kim, S.G. Ji, J. Go, H. Kim, S. Yang, H.J. Kim, A. Cho, **S.S. Yoon***, and I. Lee*, Network-assisted investigation of virulence and antibiotic-resistance systems in *Pseudomonas aeruginosa*. **Scientific Reports**, 2016, 6:26223

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*** Selected as a 2016 Top 5 paper in Biomedicine by BRIC**

38. K. Lee, K.-M. Lee, J. Go, J. C. Ryu, J.-H. Ryu, and **S.S. Yoon***, The Ferrichrome Receptor A as a New Target for *Pseudomonas aeruginosa* Virulence Management, **FEMS Microbiology Letters**, 2016, 363 (11)

37. Y.T. Oh, K.-M. Lee, W. Bari, H.Y. Kim, and **S.S. Yoon***, Cholera toxin production induced upon anaerobic respiration is suppressed by glucose fermentation in *Vibrio cholerae*. **J. Microbiol. Biotechnol.** 2016, 26(3):627-36

36. H.J. Kim, H. S. Kim, J. M. Lee, **S.S. Yoon*** and D. Yong*, Rapid Detection of Carbapenemase-producing *Pseudomonas aeruginosa* and *Acinetobacter baumannii* from Clinical Isolates by Loop-mediated Isothermal Amplification, **Annals of Laboratory Medicine**, 2016, 36(1):15-22

35. M. Gi, K.M. Lee, S. C. Kim, J. H. Yoon, **S.S. Yoon***, and J. Y. Choi* A novel siderophore system is essential for the growth of *Pseudomonas aeruginosa* in airway mucus, **Scientific Reports**, 2015,

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34. Y.T. Oh, K.M. Lee, W. Bari, D.M. Raskin, and **S.S. Yoon***. (p)ppGpp, a small nucleotide regulator, directs the metabolic fate of glucose in *Vibrio cholerae*, *J. Biol. Chem.*, 2015, 290:13178-13190
33. **S.S. Yoon**, E. Kim, W-J. Lee*. Functional metagenomics for understanding gut microbiota-animal mutualism (Review article), *Current Opinion in Microbiology*, 2015, 24:38-46
32. M.Y. Yoon, K. Lee and **S.S. Yoon***. Protective role of gut commensal microbes against intestinal infections (Review article), *J. Microbiol.*, 2014, 52(12): 983-989
31. K.B. Min, K-M. Lee, Y. T. Oh and **S.S. Yoon***. Nonmucoïd Conversion of Mucoïd *Pseudomonas aeruginosa* Induced by Sulfate-stimulated Growth. *FEMS Microbiology Letters*, 2014, 360(2):157-166
30. M. Gi, J. Jeong, K. Lee, Y. Park, M. Toyofuku, **S.S. Yoon***, J. Y. Choi*. A Drug Repositioning Screen Identified Pentetic Acid as a Potential Therapeutic Agent to Suppress Elastase-mediated Virulence of *Pseudomonas aeruginosa*. *Antimicrob. Agents and Chemother.*, 2014, 58(12):7205-14

***Highlighted in MDLinx**

(http://www.mdlinx.com/infectious-disease/news-article_rdn.cfm/5725281/pseudomonas-aeruginosa)

29. Jeong S. J., **Yoon S.S.**, Bae I. K., Jeong S. H., Kim J. M., Lee K. Risk factors for mortality in patients with bloodstream infections caused by carbapenem-resistant *Pseudomonas aeruginosa*: clinical impact of bacterial virulence and strains on outcome. *Diagn Microbiol Infect Dis.* 2014 Jul 17. [Epub ahead of print]
28. H. J. Kim, Y. J. Kim, D. E. Yong, K. Lee, J. H. Park, J. M. Lee* and **S.S. Yoon***. Loop-mediated Isothermal Amplification of *vanA* Gene Enables Rapid and Naked-eye Detection of Vancomycin-Resistant Enterococci Infection. *J. of Microbiol. Methods*, 2014, 104:61-6
27. J. Go, K-M. Lee, Y. Park, **S.S. Yoon***. Extended Longevity and Robust Early-stage Development of *Caenorhabditis elegans* by a Soil Microbe, *Lysinibacillus sphaericus*, *Environmental Microbiology Reports*, 2014, 6(6):730-737

***Selected as a "Must-read" paper by Faculty of 1,000 (<http://f1000.com/prime/725394030>)**

26. Y. T. Oh, Y. Park, M. Y. Yoon, W. Bari, J. Go, K-M. Lee, and **S.S. Yoon***. Cholera toxin production during anaerobic TMAO respiration is mediated by stringent response in *Vibrio cholerae*, *J. Biol. Chem.* 2014, 289(19): 13232-42

25. M. Y. Yoon, K-M. Lee, J. Go, Y. Y. Yoon, Park, S. C. Kim, and G. W. Tannock, **S.S. Yoon***. Functional Screen of a Metagenomic Library Reveals Operons Responsible for Enhanced Intestinal Colonization by Gut Commensals. *Appl. Environ. Microbiol.*, 2013, 79(12): 3829-38

***Selected as a "Spotlight" of the issue**

***Selected as a "Must-read" paper by Faculty of 1,000 (<http://f1000.com/prime/718028126>)**

24. Kim M.J., Bae I. K., Jeong S. H., Kim S. H., Song J. H., Choi J. Y., **Yoon S.S.**, Thamlikitkul V., Hsueh P. R., Yasin R. M., Lalitha M. K., Lee K. Dissemination of metallo- β -lactamase-producing *Pseudomonas aeruginosa* of sequence type 235 in Asian countries. *J. Antimicrob. Chemother.* 2013 Jul 9. [Epub ahead of print]

23. S. J. Jeong, **S.S. Yoon**, S. H. Han, D. E. Yong, C. O. Kim, J. M. Kim. Evaluation of humoral immune response to nosocomial pathogens and functional status in elderly patients with sepsis. **Arch. Gerontol. Geriatr.**, 2013 Aug. 30. [Epub ahead of print]

22. J. M. Park, K-B Kim, J-E Lee, Y. Park, **S.S. Yoon**, H. M. Jeong, H-I. Lee, Thermoresponsive Fluorinated Polyacrylamides with Low Cytotoxicity, **Polymer Chemistry**, 2013, (4):2219-2223

21. K-M. Lee, Y. Park, Wasimul B., M. Y. Yoon, J. Go, S. C. Kim, **S.S. Yoon***. Activation of Cholera Toxin Production by Anaerobic Respiration of Trimethylamine N-oxide in *Vibrio cholerae*, **J. Biol. Chem.**, 2012, 287(47): 39742-39752

20. Wasimul B., K-M. Lee, **S.S. Yoon***. Structural and Functional Importance of Outer Membrane Proteins in *Vibrio cholerae* flagellum. **J. of Microbiol.**, 2012, 50(4): 631-637

19. S. Kim, M. Rahman, S. Y. Seol, **S.S. Yoon***, J. Kim*. *Pseudomonas aeruginosa* Bacteriophage PA10 Requires Type IV Pili for Infection and Shows Broad Bactericidal and Biofilm Removal Activities. **Appl. Environ. Microbiol.** 2012, 78(17):6380-6385 (*co-corresponding authors)

18. K-M. Lee, J. Go, M. Y. Yoon, Y. Park, S. C. Kim, D. E. Yong, and **S.S. Yoon***. Vitamin B12-mediated Restoration of Defective Anaerobic Growth Leads to Reduced Biofilm Formation in *Pseudomonas aeruginosa*. **Infection and Immunity**, 2012, 80(5):1639-1649

***Highlighted in Global Medical Discovery**

17. K-M. Lee, J. Lim, S. Nam, M. Y. Yoon, Y-K. Kwon, B.Y. Jung, S. Park, **S.S. Yoon***. Inhibitory Effects of Broccoli Extract on *Escherichia coli* O157:H7 Quorum Sensing and *in vivo* Virulence. **FEMS Microbiology Letters**, 2011, 321(1):67-74

16. Wasimul B., Y.-J. Song and **S.S. Yoon***. Suppressed Induction of Proinflammatory Cytokines by a Unique Metabolite Produced by *Vibrio cholerae* O1 El Tor Biotype in Cultured Host Cells. **Infection and Immunity**, 2011, 79(8):3149-3158

15. K-M. Lee, M. Y. Yoon, Y. J. Park and **S.S. Yoon***. Anaerobiosis-induced Loss of Cytotoxicity is Due to Inactivated Quorum Sensing in *Pseudomonas aeruginosa*. **Infection and Immunity**, 2011, 79(7):2792-2800

14. M.Y. Yoon, K-M. Lee, Y.J. Park and **S.S. Yoon***. Contribution of Cell Elongation to the Biofilm Formation of *Pseudomonas aeruginosa* during Anaerobic Respiration. **PLoS One**, 2011, 6:e16105.

***Selected as a "Must-read" paper by Faculty of 1,000 (<http://f1000.com/9026960>)**

13. **S.S. Yoon***, Anaerobiosis of *Pseudomonas aeruginosa*: Implications for Treatment of Airway Infection. **Journal of Bacteriology and Virology**, 2010, 40:59-66

12. M.Y. Yoon, K-M. Lee, S.H. Jeong, J. Kim and **S.S. Yoon***. Heterogeneous virulence potentials and high antibiotics resistance of *Pseudomonas aeruginosa* strains isolated from Korean pneumonia patients. **The Journal of Microbiology**, 2010, 48:518-25

11. Ann Thanawastein, Wagner R. Montor, Joshua LaBaer, John J. Mekalanos, and **S.S. Yoon***. *Vibrio cholerae* proteome-wide screen for immunostimulatory proteins identifies phosphatidylserine

decarboxylase as a novel toll-like receptor 4 agonist. *PLoS Pathogens*, 2009, 5(8): e1000556

10. A. Rolfs, W. Montor, **S.S. Yoon**, Hu, Yanhui, Bhullar, Bhupinder, Kelley, Fontina, McCarron, Seamus, Jepson, Daniel A., Shen, Binghua, Taycher, Elena, Mohr, Stephanie E., Zuo, Dongmei, Williamson, Janice, Mekalanos, John, LaBaer, Joshua, Production and sequence validation of a complete full length ORF collection for the pathogenic bacterium *Vibrio cholerae*. *PNAS*, 2008, 105:4364-9.

9. **S.S. Yoon** and John J. Mekalanos. Decreased Potency of *Vibrio cholerae* Sheathed Flagellum to Trigger Host Innate Immunity. *Infection and Immunity*, 2008, 76:1282-8.

8. **S.S. Yoon**, A.C. Karabulut, J.D. Lipscomb, R.F. Hennigan, S.V. Lymar, S.L. Groce, A.B. Herr, M.L. Howell, P.J. Kiley, M.J. Schurr, B.Gaston, K.Choi, H.P. Schweizer and D.J Hassett. Two-Pronged Survival Strategy for *Pseudomonas aeruginosa*, Lacking the Capacity to Degrade Nitric Oxide During Anaerobic Respiration. *The EMBO Journal*. 2007. 26:3662-72.

7. **S.S. Yoon** and John J. Mekalanos. 2,3-Butanediol synthesis and the emergence of the *Vibrio cholerae* El Tor biotype. *Infection and Immunity*. 2006. 74:6547-6556

***Selected as a "Spotlight" of the issue**

6. **S.S. Yoon**, Coakley R, Lau GW, Lymar SV, Gaston B, Karabulut AC, Hennigan RF, Hwang S, Buettner G, Schurr MJ, Mortensen JE, Burns JL, Speert D, Boucher RC and D.J. Hassett. Anaerobic Killing of Mucoid *Pseudomonas aeruginosa* by Acidified Nitrite Derivatives under Cystic Fibrosis Airway Conditions. *Journal of Clinical Investigation*. 2006. 116:436-446.

5. **S.S. Yoon** and D.J. Hassett. Chronic *Pseudomonas aeruginosa* Infection In Cystic Fibrosis Airway Disease: Understanding Metabolic Changes That Unravel Novel Drug Targets. *Expert Reviews of Anti-Infective Therapy* 2004. 2:611-623

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3. D.J. Hassett, J. Cuppoletti, B. Trapnell, J.J. Rowe, **S.S. Yoon**, G.M. Hilliard, K. Parvatiyar, M.C. Kamani, D.J. Wozniak, and S.-H. Huang. Anaerobic metabolism and quorum sensing By *Pseudomonas aeruginosa* in Biofilms in Chronically Infected Cystic Fibrosis Airways: Rethinking Antibiotic Treatment Strategies and Drug Targets. *Adv. Drug Delivery Rev.* 2002. 54: 1425-1443.

2. **S.S. Yoon**, R.F. Hennigan, G.M. Hilliard, U.A. Ochsner, K. Parvatiyar, M.C. Kamani, H.L. Allen, T.R. DeKievit, P.R. Gardner, U. Schwab, J.J. Rowe, B.H. Iglewski, T.R. McDermott, R.P. Mason, D.J. Wozniak, R.E.W. Hancock, M.R. Parsek, T.L. Noah, R.C. Boucher and D.J. Hassett. *Pseudomonas aeruginosa* Anaerobic Respiration in Biofilms: Relationships to Cystic Fibrosis Pathogenesis. *Developmental Cell* 2002. 3: 631-642.

***Editorial comments on this paper**

- Costerton JW. Anaerobic biofilm infections in cystic fibrosis. *Molecular Cell*. 2002. 10:699
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1. Han MJ, **S.S. Yoon** and Lee SY. Proteome analysis of metabolically engineered *Escherichia coli* producing Poly (3-hydroxybutyrate). *J. Bac.* 2001. 183:301-8.