In vitro EXOPROTEOME PROFILE OF *Stenotrophomonas maltophilia* IN IRON DEPLETED CONDITION

By

ADLEEN BINTI AZMAN

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Master of Science

December 2015

FPSK (m) 2015 84

This thesis is dedicated to my beloved family for the support and encouragement throughout my Master's Degree

Abstract of the thesis presented to the Senate of Universiti Putra Malaysia in fulfillment of the requirements for the degree of Master of Science

In vitro EXOPROTEOME PROFILE OF _Stenotrophomonas Maltophilia_ IN IRON DEPLETED CONDITION

By

ADLEEN BINTI AZMAN

December 2015

Chairman : Associate Professor Vasantha Kumari Neela, PhD
Faculty : Medicine and Health Sciences

Stenotrophomonas maltophilia has been recently identified as the third most common nosocomial infection in the hospital especially among immunocompromised patients. Management of *S. maltophilia* infection is an inordinate challenge in the hospital due to its intrinsic and acquired resistance to most of the antibiotics. Although *S. maltophilia* is frequently associated with increased morbidities and mortalities, the pathogenesis mechanisms of *S. maltophilia* are still not very clear. This is due to *S. maltophilia* which entered hospital setting from environmental sources heavily colonizes the respiratory tract and other anatomical sites, without showing a clear cut infection in human. Hence, the debate about whether *S. maltophilia* is a true pathogen or a colonizer is still an ongoing investigation.

Iron is an essential factor for their survival. In the host environment, the level of iron is ~10^{11} times below than the level required for microorganism and is mostly unavailable as it is bound together with host protein. Microbes develop multiple mechanisms such as siderophores secretion to forage for free iron in an iron limited environment. Under iron starvation, microbes also secrete other virulence potential exoproteins. The present study was aimed at investigating the effect of iron depletion in secretion of proteomes in *S. maltophilia*.

Briefly, four strains of the *S. maltophilia* LMG959 (environment), ATCC 13637, CS17 and CS24 (clinical) were grown in normal and iron depleted medium. The siderophores production was screened qualitatively and quantitatively using CAS plate and liquid assay. Followed by, nematocidal assay was performed to test the ability of *S. maltophilia* supernatant grown in iron depleted medium to kill the nematode *Caenorhabditis elegans*. Lastly, the putative proteins expressed

during the stressed condition were identified by Isobariq Tags for Relative and Absolute Quantification (ITRAQ) mass spectrometry.

Initial screening of siderophores production exhibited largest yellow zone for CS17 and CS24 (10 mm) followed by ATCC13637 (8 mm), LMG959 (6 mm). The siderophores production was further confirmed quantitatively and the highest was detected in both clinical isolates (30.8% [$p<0.05$] and 29.4%) at 72 h followed by ATCC 13637 (8%) and LMG959 (4%) in iron depleted medium ($p>0.05$). Isolates grown under iron-depleted condition (ATCC 13637: 63%; CS17: 96%; CS24: 97%) showed more nematocidal activity than in normal condition (ATCC 13637: 43%; CS17: 76%; CS24: 79%) ($p>0.05$). None of the worms were killed when infected with LMG959. Based on the above result, only CS17 and LMG959 are subjected to ITRAQ analysis. ITRAQ analysis revealed a total of 122 proteins showed altered expression in response to iron starvation with 96 being up-regulated and 26 were down-regulated for both isolates. ITRAQ analysis identified higher expression of several iron acquisition and pathogenic potential proteins in both isolates grown in iron depleted condition. In another study, clinical and environment isolates grown under normal condition were compared to identify the proteomic profiles. ITRAQ analysis discovered 81 proteins that exhibited differently expressed with 40 proteins up-regulated and 41 proteins down-regulated. In normal condition, several proteins such as Elongation factor G, Endoribonuclease and Fimbrial protein expressed in higher fold in clinical isolate compared to environmental isolate.

In conclusion, *S. maltophilia* produced siderophores under iron depleted condition. Based on nematocidal assay, eventhough there is no significant difference in killing rates between iron depleted and normal condition but *S. maltophilia* did show an increased of ~20% of its killing rates in iron depleted medium except for LMG959. ITRAQ analysis revealed *S. maltophilia* altered the expression of metabolic, iron acquisition and pathogenic potential proteins under iron starvation. A comparison of clinical and environmental isolates grown in normal medium revealed that clinical isolates expresses more pathogenic potential proteins compared to environmental isolate. The data obtained in the present study, clearly indicates that under iron depleted condition, *S. maltophilia* are capable of altering the expression of its proteomes to ensure their survival in the host.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

In vitro EXOPROTEOME PROFIL PADA _Stenotrophomonas Maltophilia_ DALAM KEADAAN KEKURANGAN ZAT BESI

Oleh

ADLEEN BINTI AZMAN

Disember 2015

Pengerusi : Professor Madya Vasantha Kumari Neela, PhD
Fakulti : Perubatan dan Sains Kesihatan

Stenotrophomonas maltophilia telah dikenal pasti sebagai jangkitan nosokomial ketiga paling kerap ditemui di hospital terutamanya di kalangan pesakit yang mempunyai sistem imun yang rendah. Pengurusan terhadap jangkitan *S. maltophilia* merupakan satu cabaran besar di hospital kerana sifat mikrob yang mempunyai daya tahan intrinsik dan daya tahan dapatan terhadap antibiotik. Walaupun *S. maltophilia* sering dikaitkan dengan kadar morbiditi dan mortaliti, mekanisma patogenesisnya masih belum diketahui dengan jelas. Hal ini disebabkan oleh *S. maltophilia* yang berada di persekitaran kebiasaannya mendominasi saluran pernafasan dan bahagian-bahagian anatomi lain tanpa menunjukkan tanda-tanda jangkitan yang jelas pada manusia. Oleh itu, persoalan samada *S. maltophilia* merupakan patogen atau tidak masih menjadi tanda tanya dikalangan penyelidik.

Zat besi merupakan salah satu faktor penting untuk kelangsungan hidup mikroorganisma. Dalam persekitaran perumah, tahap zat besi adalah ~ 10^{11} kali lebih rendah dari tahap minimum yang diperlukan mikroorganisma untuk hidup dan kebanyakan zat besi terikat dengan protin perumah. Mikrooganisma mempunyai pelbagai mekanisma bagi mendapatkan zat besi dari persekitaran. Antaranya adalah secara perembesan siderophores yang bertujuan untuk mendapatkan zat besi yang tidak terikat dengan protin perumah dan kemampuan membebaskan eksoprotin yang mengandungi faktor virulen.

Kajian ini bertujuan untuk mengenalpasti kesan kekurangan zat besi kepada rembesan protin pada *S. maltophilia*. Secara ringkasnya, empat pencilan *S. maltophilia* LMG 959 (pencilan alam sekitar), SM13637 (ATCC), CS17 dan CS24 (pencilan klinikal) telah dibiakkan dalam medium biasa dan medium rendah zat besi. Penghasilan Siderophores telah disaring secara kualitatif dan kuantitatif

menggunakan piring CAS dan cecair CAS asai, diikuti dengan ujian nematocidal asai yang dilakukan untuk menguji keupayaan supernatan *S. maltophilia* yang dibiakkan dalam medium rendah zat besi untuk membunuh nematod, *Caenorhabditis elegans*. Akhir sekali, protin yang dirembeskan oleh mikrob yang berada dalam keadaan tertekan telah dikenalpasti menggunakan spektrometri massa ITRAQ.

Penyaringan awal pengeluaran siderophores menunjukkan bahawa zon kuning terbesar telah dihasilkan oleh CS17 dan CS24 dengan 10 mm diameter manakala ATCC13637 dan LMG959 menghasilkan 8 mm , 6 mm zon kuning. Penghasilan siderophores disah kan secara quantitatif dan didapati penghasilan siderophores yang tinggi telah dikesan pada pencilan klinikal CS17 dan CS24 (30.8% dan 29.4%) pada jam ke-72 diikuti oleh ATCC13637 (8%) dan LMG959 (4%). Pencilan yang berada dalam persekitaran rendah zat besi (ATCC 13637 : 63%; CS17: 96%; CS24: 97%) menunjukkan tahap aktiviti nematocidal yang lebih tinggi daripada keadaan normal (ATCC 13637 : 43%; CS17: 76%; CS24: 79%). Tiada nematoda pun yang terbunuh pada pencilan LMG959. Berdasarkan analisa spektrometri massa ITRAQ, sebanyak 122 jenis protin dikenalpasti menunjukkan perubahan terhadap persekitaran rendah kekurangan zat besi dimana 96 protin mengalami peningkatan menaik dan 26 protin mengalami penurunan. Perbandingan antara pencilan klinikal dengan pencilan persekitaran yang dibiakkan dalam keadaan normal menunjukkan bahawa 81 jenis protin mengalami perubahan dengan 40 jenis protin meningkat dan 41 jenis protin menurun. Analisa ini juga mengenal pasti kadar rembesan beberapa protin yang mempunyai sifat pengambilalihan zat besi dan keupayaan virulen yang lebih tinggi dalam pencilan-pencilan yang dibiakkan dalam medium rendah zat besi.

Di perbandingan yang lain, pencilan persekitaran dan klinikal dalam keadaan normal dibandingkan dengan mengenal pasti proteomes profil pencilan. Analisis ITRAQ menemui 81 protein menunjukkan perubahan dengan 40 protein mengalami peningkatan menaik dan 41 protein mengalami penurunan. Dalam keadaan normal, beberapa protein seperti faktor Pemanjangan G, Endoribonuclease dan protein Fimbrial dinyatakan dalam kali ganda lebih tinggi dalam pencilan klinikal berbanding pencilan persekitaran.

Kesimpulannya, *S. maltophilia* menghasilkan siderophores dalam keadaan kekurangan zat besi. Berdasarkan aktiviti nematocidal, dalam keadaan kurang zat besi, *S. maltophilia* pencilan klinikal mampu membunuh lebih banyak nematode, C. elegans berbanding pencilan persekitaran. Analisis ITRAQ menunjukkan *S. maltophilia* menghasilkan metabolik protin, pengambilan zat besi dan protein yang berpotensi patogenik dalam keadaan kekurangan zat besi. Perbandingan pencilan klinikal dan persekitaran dibiakkan dalam medium biasa menunjukkan bahawa pencilan klinikal menghasilkan lebih banyak protein yang bersifat patogenik berbanding pencilan persekitaran. Berdasarkan data yang diperolehi dalam kajian ini, dalam keadaan kekurangan zat besi, *S. maltophilia* mampu mengubah proteomes untuk memastikan kelangsungan hidup mereka dalam perumah.

ACKNOWLEDGEMENTS

I would like to express my gratitude to all those who have made this project a success in one way or another. First of all, special thanks to my supervisor Associate professor Dr Vasantha Kumari Neela who gave me full support and guiding me throughout the entire project. I was very grateful on Dr Neela's willingness to spend her valuable time meeting me throughout my master's programme, giving me constructing advice as well as providing me the ideas to complete this thesis. I greatly appreciate her effort in guiding me especially in reading and checking my early draft and suggested some improvement to make a better thesis. I was able to obtain a great feedback from her in the process of doing the analysis.

The gratitute is also addressed to my co-supervisors, Associate professor Dr Rukman Awang Hamat, Dr Suresh Kumar and Associate professor Dr Syafinaz Amin Nordin for their contribution in giving suggestions and advices throughout completing this project. Also my sincere gratitute goes to Associate Professor Dr Malina Osman for her expert, sincere and valuable guidance and encouragement extended to me.

Next, I would like to express my appreciation and thankfulness to all members in medical microbiology and parasitology laboratory. They gave me the best help that they could possibly offer. Their kindness is well appreciated and makes life easier. Not forgotten, special acknowledge to my family members who always stand behind me and give me loads of advices and encouragements throughout the process of finishing this project. Last but not least, thanks to everyone who have contributed directly or indirectly in completing this project and thesis.

This thesis was submitted to the senate of Universiti Putra Malaysia and has been accepted as fulfillment of requirement for degree of Master of Science. The members of the Supervisory Committee were as follows:

Vasantha Kumari Neela, PhD
Associate Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Chairman)

Rukman bin Awang Hamat, MBBS, MPath
Professor (Medical)
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

Suresh Kumar, PhD
Associate Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

Syafinaz Amin Nordin, MBChB, MPath,MHEd
Professor (Medical)
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

BUJANG BIN KIM HUAT, PhD
Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

Date: 10th March 2016

Declaration by graduate student

I hereby confirm that:

- this thesis is my original work;
- quotations, illustrations and citations have been duly referenced;
- this thesis has not been submitted previously or concurrently for any other degree at any other institutions;
- intellectual property from the thesis and copyright of thesis are fully-owned by Universiti Putra Malaysia, as according to the Universiti Putra Malaysia (Research) Rules 2012;
- written permission must be obtained from supervisor and the office of Deputy Vice-Chancellor (Research and Innovation) before thesis is published (in the form of written, printed or in electronic form) including books, journals, modules, proceedings, popular writings, seminar papers, manuscripts, posters, reports, lecture notes, learning modules or any other materials as stated in the Universiti Putra Malaysia (Research) Rules 2012;
- there is no plagiarism or data falsification/fabrication in the thesis, and scholarly integrity is upheld as according to the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) and the Universiti Putra Malaysia (Research) Rules 2012. The thesis has undergone plagiarism detection software.

Signature: _____ Date: _____

Name and Matric No.: Adleen Bt Azman _____

Declaration by members of Supervisory Committee

This is to confirm that:

- the research conducted and the writing of this thesis was under our supervision;
- supervision responsibilities as stated in the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) are adhered to.

Signature: _____
Name of Chairman of Supervisory Committee: Vasantha Kumari Neela

Signature: _____
Name of Member of Supervisory Committee: Rukman Awang Hamat

Signature: _____
Name of Member of Supervisory Committee: Suresh Kumar

Signature: _____
Name of Member of Supervisory Committee: Syafinaz Amin Nordin

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVATIONS

%	Percentage
oC	Degree celcius
≤	Less than
≥	More than
µl	microliter
µm	Micrometer
2DGE	Two dimensional Gel Electrophoresis
ATCC	American Type Culture Collection
BCCM	Belgium coordinate Collection Microbiology
BHI	Brain Heart Infusion
BSA	Bovine Serum Albumin
CAS	Chrome Azurol S
CF	Cystic Fibrosis
CS17	Clinical isolate
DC	Detergent compatible
ddH2O	distilled water
DIP	2,2 dipyridyl
DNA	Deoxyribonucleic acid
Fe(II)/Fe2+	Ferrous iron
Fe(III)/Fe3+	Ferric iron
FUDR	Fluorodeoxyuridine
Fur	Ferric uptake regulation protein
g	gram

h	Hours
HCL	Hydrochloric acid
HPLC	High-performance liquid chromatography
HSCT	Hematopoietic stem cell transplantation
ICU	Intensive Care Unit
ITRAQ	Isobariq Tagging for Relative and Absolute quantification
LMG959	Environmental isolate
M	Molar
min	minutes
ml	mililiter
mm	milimeter
MS	Mass spectometry
NaOH	Sodium Hydroxide
NGM	Nematode Growth Media
nm	nanometer
OD	Optical Density
PAH	Pulmonary alveolar hemorrhage
PBS	Phosphate Buffered Saline
pH	Puissanse hydrogen (Hydrogen ion concentration)
RAST	Rapid Annotation Subsystem Technology
RC	Reducing agent compatible
RC-DC	Reducing agent and detergent compatible
rpm	Revolutions per minute
s	seconds
SCX	Strong cation exchange liquid chromatography

T	Time
TCA	trichloroacetic acid
TOF	Time-of-flight
UPM	Universiti Putra Malaysia
w/v	weight per volume

CHAPTER 1

INTRODUCTION

Historically, *Stenotrophomonas maltophilia* is an environmental microbe that is commonly isolated from soil, plant roots, tap water and environment. During recent years, *S. maltophilia* has entered hospital setting and became a successful nosocomial pathogen. Properties which made *S. maltophilia* a successful nosocomial pathogen includes its natural resistance to multiple drugs, harboring antibiotic resistance genes, multidrug resistance pumps and various gene transfer mechanisms involved in the acquisition of antimicrobial resistance (Brooke, 2012). Although *S. maltophilia* is not a truly pathogen, but mortality rates associated with this microbe range from 20-70% especially among immune-compromised patients (Jang *et al*., 1992; Victor *et al*., 1994; Brooke, 2012). Infections that are associated with *S. maltophilia* include respiratory tract infections, biliary sepsis, endocarditis, urinary tract infection and meningitis.

Despite the clinical importance, information on *S. maltophilia* virulence is limited. Study reported by Figuerdo *et al* (2006) indicated that *S. maltophilia* could behave as a pathogen as its supernatant exerted cytotoxic effects on Vero, HeLa and HEp-2 cells. It caused rounding, loss of intercellular junction and membrane alteration followed by cell death. Nematocidal assay performed by Thomas *et al* (2013) illustrated that *S. maltophilia* are capable of killing *Caenorhabditis elegans* even without direct bacterial contact. Based on the previous findings *S. maltophilia* has few pathogenic properties such as elastase, proteinase, dnase, heparinase, lecithinase, lipase and hyaluronidase (Thomas *et al*., 2014).

It is well known that iron plays an important role in the pathogenesis of microbial infection. Iron is an essential factor for the growth of microorganism which is required for every metabolic process. In human under oxygen rich environment, the soluble iron ferrous is oxidized to insoluble ferric which is not accessible to bacteria while in human blood, the amount of iron is ~10^{11} times lower than the level required for microbes. Iron that is available in human blood is mostly bound together with protein called transferrin and lactoferrin making it inaccessible to microbes thus preventing microbial growth (Garcia *et al*., 2012). To overcome this condition, microbes have developed multiple mechanisms to scavenge the iron from the environment and also to avoid killing by the innate immune system. One of the common mechanisms is the secretion of iron scavenging compounds called siderophores.

Siderophores are low molecular weight compounds which have high affinity to ferric. Siderophores are only produced when the iron is limited in the environment. The production of siderophores indicates that microorganism is under stress (Schwyn and Neilands, 1987; Garcia *et al*., 2012). These siderophores plays an important role in pathogenicity for most microorganisms

as it induces the secretion of other proteins which exhibits detrimental effect on host cells leading to life threatening infection (Hotta *et al*., 2010).

The present study hypothesized that growing *S. maltophilia* in iron depleted condition will induce the production of siderophores and altered the S. maltophilia proteomes protein including pathogenic potential proteins. Therefore, to test the hypothesis, *S. maltophilia* is grown in an iron depleted medium, the stress for iron scavenging is measured through siderophores production. Followed by, nematocidal assay was performed to test the ability of *S. maltophilia* supernatant grown in an iron depleted medium to kill *C. elegans*. Lastly, the proteomes profiling expressed during the iron starvation was identified by mass spectrometry.

1.1 Problem statements

1. There is no conclusive data on *S. maltophilia* proteomes profilling.
2. *S. maltophilia* has received little attention regardless of their alarming presence in the hospital setting.
3. The uncertainty of whether *S. maltophilia* is a true pathogen remained unclear.

1.2 Objectives of the study

General objective

To investigate the effect of iron depletion in secretion of proteomes profilling in *S. maltophilia*

Specific objectives

1. To measure the production of siderophores in normal and iron depleted medium in *S. maltophilia.*
2. To determine the *in vivo* nematocidal activity of *S. maltophilia* grown in normal and iron depleted medium.
3. To identify the proteomes profile of *S. maltophilia* grown in normal and iron depleted condition.
4. To compare the proteomes profile of clinical and environmental *S. maltophilia* grown in normal medium.

REFERENCES

Abbassi, M. S., Touati, A., Achour, W., Cherif, A., Jabnoun, S., Khrouf, N., & Ben Hassen, A. (2009). *Stenotrophomonas maltophilia* responsible for respiratory infections in neonatal intensive care unit: antibiotic susceptibility and molecular typing. *Pathologie Biologie (Paris),* 57(5), 363-367.

Abby, S., Jeffrey, D., Michael, W., Theresa, R., Rachida, B. (2014). Proteomic analysis of keratitis-associated *Pseudomonas aeruginosa*. *Molecular Vision*, 20, 1182-1191.

Abdallah, C., Dumas-Gaudot, E., Renaut, J., & Sergeant, K. (2012). Gel-Based and Gel-Free Quantitative Proteomics Approaches at a Glance. *International Journal of Plant Genomics,* 2012, 17.

Alberts, B., Johnson, A., Lewis, J., Raff, M., Roberts, K., and Walter, P. (2002). Molecular Biology of the Cell, 4th edition New York: Garland Science.

Alexander, M. (1999). Biodegradation and bioremediation. *Academic Press*, p-453.

Aneja, P., & Charles, T. C. (1999). Poly-3-Hydroxybutyrate degradation in *Rhizobium (Sinorhizobium) meliloti*: Isolation and characterization of a gene encoding 3-Hydroxybutyrate dehydrogenase. *Journal of bacteriology*. 181(3), 849–857.

Ann, J. M. M., & Barclay, R. (2010). Bacteria, Iron and Pathogenicity. *Biochemical Education*, 11(2), 54–63.

Apisarnthanarak, A. (2003). Risk factors for *Stenotrophomonas maltophilia* bacteremia in oncology patients: a case-control study. *Infection Control and Hospital Epidemiology* 24(4), 269 –274.

Araoka, H., Baba, M., Yoneyama, A. (2010). Risk factors for mortality among patients with *Stenotrophomonas maltophilia* bacteremia in Tokyo, Japan, 1996–2009. *European Journal of Clinical Microbiology and Infectious Diseases*, 29, 605–608.

Arvanitidou, M., Vayona, A., Spanakis, N., & Tsakris, A. (2003). Occurrence and antimicrobial resistance of Gram-negative bacteria isolated in haemodialysis water and dialysate of renal units: results of a Greek multicentre study. *Journal of Applied Microbiology*, 95(1), 180-185.

Berg, G., Eberl, L., & Hartmann, A. (2005). The rhizosphere as a reservoir for opportunistic human pathogenic bacteria. *Environmental Microbiology*, 7(11), 1673–1685.

Betty Zou, S., Hervé, R., Michael, I., & William, W. N. (2011). Elongation factor P mediates a novel post-transcriptional regulatory pathway critical for bacterial virulence. *Virulence*, 2(2), 147-151.

Braun, V., Hantke, K., & Koster, W. (1998). Bacterial iron transport: mechanisms, genetics and regulation. In: Metal Ions in Biological systems. Sigel, A., Sigel, H., editors. Iron transport and storage in Microorganisms, Plants and Animals. *New York: Marcel Dekker*; p. 67-145.

Britigan, B. E., Hayek, M. B., Doebbeling, B. N., & Fick, R. B. (1993). Transferrin and lactoferrin undergo proteolytic cleavage in the *P.aeruginosa* infected lungs of patient with CF*. Infection and Immunity*, 61(12), 5049-5055.

Brooke, J. S., Vo, A., Watts, P., & Davis, N. A. (2008). Mutation of a lipopolysaccharide synthesis gene results in increased biofilm of *Stenotrophomonas maltophilia* on plastic and glass surfaces. *Annals of Microbiology,* 58(1), 35–40.

Brooke, J.S. (2012). *Stenotrophomonas maltophilia*: an Emerging Global Opportunistic Pathogen. *Clinical Microbiology Reviews*, 25(1), 2–41.

Buchanan, S., Smith, B., Venkatramani, L., Xia, D., Esser, L., Palnitkar, M., Chakraborty, R., Van der Helm, D., & Deisenhofer, J. (1999). "Crystal structure of the outer membrane active transporter FepA from *Escherichia coli*". *Nature Structural Biology*, 6(1), 56–63.

Bullen, J. J., Rogers, H. J., Spalding, P. B., & Ward, C. G. (2005). Iron and infection: the heart of the matter. *FEMS Immunology and Medical Microbiology*, 43(3), 325–330.

Cartron, M. L., Maddocks, S., Gillingham, P., Craven, C.J., & Andrews, S. C. (2006). Feo-transport of ferrous iron into bacteria. *Biometals,* 19(2), 143–157.

Caswell-Chen, E. P., Chen, J., Lewis, E. E., Douhan, G. W., Nadler, S. A., & Carey, J. R. (2005). Revising the standard wisdom of C. elegans natural history: Ecology of longevity. *Science of Aging Knowledge Environment*, 2005 (40), 30.

Cervia, J. S. (2010) Point of use water filtration reduces healthcare-associated infections in bone marrow transplant recipients. *Transplant Infectious Disease*, 12(3), 238-241.

Chang ,Y.T., Lin, C.Y., Lu, P.L., Lai, C.C., Chen, T.C., Chen, C.Y., Wu, D.C., Wang, T.P., Lin, C.M., Lin, W.R., and Chen, Y.H. (2014). *Stenotrophomonas maltophilia* bloodstream infection: comparison between community-onset and hospital-acquired infections. *Journal of Microbiology, Immunology and Infection,* 47(1), 28-35.

Chatterjee, S., Sonti, R. V. (2002). rpfF mutants of *Xanthamonas oryzae pv*. *Oryzae* are deficient for virulence and growth under low iron conditions. *Molecular Plant-Microbe Interactions,* 15(5), 463-471.

Cheng-Wen, L., Hsin-Chieh, L., Yi-Wei, H., Tung-Ching, C. & Tsuey-Ching, Y. (2011). Inactivation of mrcA gene derepresses the basal-level expression of L1 and L2 b-lactamases in *Stenotrophomonas maltophilia*. *Journal of Antimicrobial Chemotherapy*, 66(9), 2033 –2037.

Christopher, F. H. (2001). ABC transporters: physiology, structure and mechanism. *Research in Microbiology*, 152 (2001), 205–210.

Christopher, L., Bissoon, S., Singh, S., Szendefy, J., & Szakacs, G. (2005). Bleach-enhancing abilities of *Thermomyces lanuginosus* xylanases produced by solid state fermentation. *Process Biochemistry*, 40(10), 3230–3235.

Ciacci-Woolwine, F., McDermott, P. F., Mizel, S. B. (1999). Induction of cytokine synthesis by flagella from gram-Negative bacteria may be dependent on the activation or differentiation state of human monocytes. *Infection and Immunity,* 67(10), 5176–5185.

Collins, H. L. (2003). The role of iron in infections with intracellular bacteria. *Elsevier Immunology Letter*, 85(2), 193-195.

Crosa, J. H., & Walsh, C. T. (2002). Genetics and assembly line enzymology of siderophore biosynthesis in bacteria. *Microbiology and Molecular Biology Reviews,* 66(2), 223-249.

Denton, M., & Kerr, K. G. (1998). Microbiological and clinical aspects of infection associated with *Stenotrophomonas maltophilia*. *Clinical Microbiology Reviews*, 11(1), 57-80.

Denton, M., Rajgopal, A., Mooney, L., Qureshi, A., Kerr, K. G., Keer, V., Pollard, K., Peckham, D. G., & Conway, S. P. (2003). *Stenotrophomonas maltophilia* contamination of nebulizers used to deliver aerosolized therapy to inpatients with cystic fibrosis. *Journal of Hospital Infection*, 55 (3), 180-183.

Der Vartanian, M. (1988). Differences in excretion and efficiency of the aerobactin and enterochelin siderophores in a bovine pathogenic strain of *Escherichia coli*. *Infection and Immunity*, 56(2),413-418.

DeSouza, L., Diehl, G., Rodrigues, M. J., Guo, J., Romaschin, A. D., Colgan, T. J., Siu. K. W. M. (2005) Search for cancer markers from endometrial tissues using differently labeled tags iTRAQ and iCAT with multidimensional liquid chromatography and tandem mass spectrometry, *Journal of Proteome Research*, 4(2), 377-386.

Downhour, N. P., Petersen, E. A., Krueger, T. S., Tangella, K. V., & Nix, D. E. (2002). Severe cellulitis/myositis caused by *Stenotrophomonas maltophilia*. *Annals of Pharmacotherapy*, 36(1), 63-66.

Dumont, A.L., Karaba, S.M., Cianciotto, N.P. (2015). Type II Secretion-Dependent Degradative and Cytotoxic Activity Mediated by *Stenotrophomonas maltophilia* Serine Proteases StmPr1 and StmPr2. *Infection and immunology*, 83 (10), 3825-3837.

Eaves-Pyles, T.D., Wong, H.R., Odoms, K. and Pyles, R.B. (2001). *Salmonella* flagellin-dependent proinflammatory responses are localized to the conserved amino and carboxyl regions of the protein.*The Journal of Immunology*, 167, 7009–7016.

Evans, F. F., Raftery, M. J., Egan, S., Kjelleberg, S. (2007). Profiling the secretome of the marine bacterium *Pseudoalteromonas tunicata* using amine-specific isobaric tagging (iTRAQ). *Journal of Proteome Research*, 6 (3), 967-975.

Falagas, M. E., Kastoris, A. C., Vouloumanou, E. K., & Dimopoulos, G. (2009). Community-acquired *Stenotrophomonas maltophilia* infections: a systematic review. *European Journal of Clinical Microbiology and Infectious,* 28(7), 719 –730.

Falagas, M.E., Kastoris, A.C., Vouloumanou, E.K., and Dimopoulos, G. (2009) Community-acquired *Stenotrophomonas maltophilia* infections: a systematic review. *European Journal of Clinical Microbiology and Infectious Diseases*, 28(7), 719-730.

Feldman, M., Bryan, R., Rajan, S., Scheffler, L., Brunnert, S., Tang, H., Prince, A. (1998). Role of flagella in pathogenesis of *Pseudomonas aeruginosa* pulmonary infection. *Infection and Immunity*, 66(1), 43–51.

Figueirdo, P. M. S. (2006). Cytotoxic activity of clinical Stenotrophomonas maltophilia. Letters in Applied Microbiology, 43(4), 443-449.

Fihman, V., Le Monnier, A., Corvec, S., Jaureguy, F., Tankovic, J., Jacquier, H., Carbonnelle, E., Bille, E., Illiaquer, M., Cattoir, V., and Zahar, J.R. (2012). *Stenotrophomonas maltophilia*--the most worrisome threat among unusual non-fermentative gram-negative bacilli from hospitalized patients: a prospective multicenter study. *Journal of Infection,* 64(4), 391-398.

Furukawa, K. (2003).'Super bugs' for Bioremediation. *Trends in Biotechnology*, *21*(5), 187-190.

Garcia, C. A., Rossi, B. P. D., Alcaraz, E., Vay, C. & Franco, M. (2012). Siderophores of Stenotrophomonas matophilia detection and determination of their chemical nature. *Revista argentina de microbiología*, 44 (3), 150-154

Garcia, C.A., Alcaraz, E.S., Franco, M.A., Passerini de Rossi B.N. (2015). Iron is a signal for *Stenotrophomonas maltophilia* biofilm formation, oxidative stress response, OMPs expression, and virulence. *Frontiers in Microbiology*, 4(6), 926.

García-León, G., Hernández, A., Hernando Amado, S., Alavi, P., Berg, G., & Martínez,J. L. (2014). A function of the major quinolone resistance determinant of *Stenotrophomonas maltophilia* SmeDEF is the colonization of the roots of the plants. *Applied and Environmental Microbiology*, 80(15), 4559-4565.

Gregory, S. M., & James, W. C. (1998) TonB-dependent iron acquisition: mechanisms of siderophore-mediated active transport. *Molecular Microbiology*, 28(4), 675–681.

Gygi, S. P., Rist, B., Gerber, S. A., Turecek, F., Gelb, M. H., & Aaebersold, R. (1999). Quantitative analysis of complex protein mixtures using isotope-coded affinity tags. *Nature Biotechnology*, 17(10), 994-999.

Hacker, J. (1992). Role of fimbrial adhesins in the pathogenesis of Escherichia coli infections. *Canadian Journal of Microbiology*, 38(7), 720-727.

Hatzimichael, E., & Tuthill, M. (2010). Hematopoietic stem cell transplantation. *Stem Cells Cloning*, 3, 105–117.

Hayashi, F., Smith, K. D., Ozinsky, A., Hawn, T. R., Yi, E. C., Goodlett, D. R., Eng, J. K., Akira, S., Underhill, D. M. and Aderem, A. (2001). The innate immune response to bacterial flagellin is mediated by Toll-like receptor 5. *Nature,* 410, 1099–1103.

Henderson, B., & Andrew, M. (2011). Bacterial Virulence in the Moonlight: Multitasking bacterial moonlighting proteins are virulence determinants in infectious disease. *Infection and immunity*, 79(9) 3476–3491.

Höltje, J. V. (1998). Growth of the stress-bearing and shape-maintaining murein sacculus of *Escherichia coli*. *Microbiology and Molecular Biology,* 62(1), 181–203.

Hotta, K., Chu-Young, K., David, T. F. & Andrew, T. K. (2010). Siderophore-mediated iron acquisition in *Bacillus anthracis* and related strains. *Microbiology*, 156(7), 1918–1925.

Ishimaru, C. A. (1993). Biochemical and genetic analysis of siderophores produced by plant-associated *Pseudomonas* and *Erwinia* species. In: Iron Chelation in Plants and Soil Microorganisms. Barton, L.B. & Hemming, B. C. (Eds.). Academic Press, Inc.

Ivanov, V., Stabnikov, V., Zhuang, W. Q., Tay, J. H., Tay, S. T. L. (2005). Phosphate removal from the returned liquor of municipal wastewater

treatment plant using iron-reducing bacteria. *Journal of Applied Microbiology*, 98(5), 1152–1161.

Jang, T. N., Wang, F. D., Wang, L. S., Liu, C. Y., & Liu, I. M. (1992). Xanthomonas maltophilia bacteremia: an analysis of 32 cases. *Journal of the Formosan Medical Association*, 91(12), 1170-1176.

Jin, F., Ding, Y., Ding, W., Reddy, M. S., Fernando, W. G., & Du, B. (2011). Genetic diversity and phylogeny of antagonistic bacteria against *Phytophthora nicotianae* isolated from tobacco rhizosphere. *International Journal of Molecular Sciences,* 12(5), 3055–3071.

Jingjing, Z., Lei, Z., Jinkui, Q., & Hongjuan, N. (2015). Isobaric tags for relative and absolute quantitation (iTRAQ)-based proteomic analysis of *Cryptococcus humicola* response to aluminum stress. *Journal of Bioscience and Bioengineering,* doi:10.1016/j.jbiosc.2015.02.007.

Kaletta, T., & Hengartner, M. O. (2006). Finding function in novel targets: C-elegans as a model organism. *Nature Reviews Drug Discovery*, 5(5), 387–398.

Katunin, V. I., Savelsbergh, A., Rodnina, M.V., & Wintermeyer, W. (2002). Coupling of GTP hydrolysis by elongation factor G to translocation and factor recycling on the ribosome. *Biochemistry,* 41(42), 12806–12812.

Kim, E. J., Sabra, W., & Zeng, A. P. (2003). Iron deficiency leads to inhibition of oxygen transfer and enhanced formation of virulence factors in cultures of *Pseudomonas aeruginosa* PAO1. *Microbiology*, 149(9), 2627-2634.

Lam, H. M., & Winkler, M. E. (1990). Metabolic relationships between pyridoxine (vitamin B6) and serine biosynthesis in *Escherichia coli* K-12. *Journal of Bacteriology*, 172(11), 6518–6528.

Lam, H., Oh, D. C., Cava, F., Takacs, C. N., Clardy, J., de Pedro, M. A., & Waldor, M.K. (2009). D-amino acids govern stationary phase cell wall remodeling in bacteria. *Science*, 325 (5947), 1552–1555.

Lamont, I. L., Beare, P. A., Ochsner, U., Vasil, A. I., and Vasil, M. L. (2002). Siderophore-mediated signaling regulates virulence factor production in *Pseudomonas aeruginosa*. *Proceedings of the National Academy of Sciences USA*, 99(10), 7072–7077.

Latifi, A., Robert, J., Sylvain, L., Michel, H., & Cheng-Cai, Z. (2005). Iron starvation leads to oxidative stress in *Anabaena sp*. Strain PCC 7120. *Journal of Bacteriology*, 187(18), 6596–6598.

Letoffe, S., Heuck, G., Delepelaire, P., Lange, N., Wandersman, C. (2009). Bacteria capture iron from heme by keeping tetrapyrrol skeleton intact. *Proc Natl Acad Sci U S A,*106, 11719–11724.

Lin, Y.T., Huang, Y.W., Chen, S.J., Chang, C.W., Yang, T.C. (2015). The smeYZ efflux pump of *Stenotrophomonas maltophilia* contributes to drug resistance, virulence-related characteristics, and virulence in mice. *Antimicrobial Agents and Chemotheraphy*, 59 (7), 4067-4073.

Mahajan-miklos, S., Tan, M. W., Rahme, L. G., & Ausubel, F. M. (1999). Molecular mechanism of bacterial virulence elucidated using a Pseudomonas aeruginosa - Caenorhabditis elegans pathogenesis model. *Cell press*, 96(1), 47-56.

Mancini, D. A. P., Mendonça, R. M. Z., Dias, A. L. F., Mendonça, R. Z., & Pinto, J. R. (2005). Co-infection between influenza virus and flagellated bacteria. *Revista do Instituto de Medicina Tropical de São Paulo*, 47(5), 275–280.

Martínez,J. L. (2013). Bacterial pathogens: from natural ecosystems to human hosts. *Environmental Microbiology*, 15(2), 325-333.

Matzanke, B. F., Anemuller, S., Schunemann, V., Trautwein, A. X., & Hantke, K. (2004). FhuF, part of a siderophore-reductase system. *Biochemistry*, 43(5), 1386–1392.

Maxwell, C. K. L., Phillip, L. W., Alexandre, B., Catherine, A., Kirsten, J.H., Michael, A.,& Joel, N. M. (2008). *Caenorhabditis elegans*: An Emerging Model in Biomedical and Environmental Toxicology. *Toxicological sciences*, 106(1), 5–28.

Miller, J. F., Mekalanos, J. J., Falkow, S. (1989). Coordinate regulation and sensory transduction in the control of bacterial virulence. *Science*, 243(4893), 916-922.

Miranda, S. P., Cabirol, N., George-Tellez, R., Zamudio-Rivera, L. S. & Fernandez, F. J. (2007). O-CAS a fast and universal method for siderophore detection. *Journal of Microbiological Methods*, 70(1), 127-131.

Mittal, R., Sharma, S., Chhibber, S., & Harjai, K. (2008). Iron dictates the virulence of *Pseudomonas aeruginosa* in urinary tract infections. *Journal of Biomedical Science,* 15(6), 731-774.

Montanari, L. B., Sartori, F. G., Cardoso, M. J., Varo, S. D., Pires, R. H., Leite, C. Q., Prince, K., & Martins, C. H. (2009). Microbiological contamination of a hemodialysis center water distribution system. *Revista do Instituto de Medicina Tropical de São Paulo,* 51(1), 37-43.

Moors, M. A., Li, L. and Mizel, S. B. (2001). Activation of interleukin-1 receptor associated kinase by Gram-negative flagellin. *Infection and Immunity*, 69, 4424–4429.

Mori, M., Kitagawa, T., Sasaki, Y., Yamamoto, K., Onaka, T., & Yonezawa, A. (2012). Lethal pulmonary hemorrhage caused by *Stenotrophomonas*

maltophilia pneumonia in a patient with acute myeloid leukemia. *Kansenshogaku Zasshi*, *86*(3), 300–305.

Munter, R. G., Yinnon, A. M., Schlesinger, Y., Hershko, C. (1998). Infective endocarditis due to *Stenotrophomonas (Xanthomonas) maltophilia*. *European Journal of Clinical Microbiology and Infectious*, 17(5), 353-356.

Mylonakis, E., Ausubel, F.M., Perfect, J.R., Heitman, J., and Calderwood, S.B. (2002). Killing of *Caenorhabditis elegans* by *Cryptococcus neoformans* as a model of yeast pathogenesis. *Proceedings of the National Academy of Sciences of the United State of America*, 26,99(24),15675-15680.

Nakouti, I., and Hobbs, G. (2014). Incorporation of L-lysine and 2,2'-dipyridyl in the growth media promotes desferrioxamine E production by an actinobacterium. *World Journal of Microbiology and Biotechnology*, 30(1), 331-334.

Ochsner, U. A., Wilderman, P. J., & Vasil, M. L. (2002). GeneChip expression analysis of the iron starvation response in *Pseudomonas aeruginosa*: identification of novel pyoverdine biosynthesis gens. *Molecular Microbiology*, 45(5), 1277-1287.

Pal, R. B., & Gokarn, K. (2010). Siderophores and pathogenecity of microorganisms. *Journal of Bioscience and Technology*, 1(3), 127-134.

Palleroni, N. J, Bradbury, J. F. (1993). *Stenotrophomonas*, a new bacterial genus for *Xanthomonas maltophilia* (Hugh 1980). *International journal of systematic bacteriology*, 43, 606–609.

Patel, H. M., & Walsh, C. T. (2001). *In vitro* reconstitution of the Pseudomonas aeruginosa nonribosomal peptide synthesis of pyochelin: characterization of backbone tailoring thiazoline reductase and N-methyltransferase activities. *Biochemistry,* 40(30), 9023-9031.

Pauline, M., Contreras-Martel, C., Viviana, J., Otto, D., Andréa, D. (2006). Penicillin Binding Proteins: key players in bacterial cell cycle and drug resistance processes. *FEMS microbiology reviews*, 30(5), 673-691.

Payne, R. J., Kerbarh, O., Miguel, R. N., Abell, A. D., & Abell, C. (2005) Inhibition studies on salicylate synthase. *Organic and Biomolecular Chemistry,* 3(10), 1825-1827.

Pompilio, A., Valentina, C., Pamela, C., Mauro, N., Andrea, P., Simone, G., Ersilia, F., Vincenzo, S., Raffaele, P., & Giovanni, Di B. (2010). Adhesion to and biofilm formation on IB3-1 bronchial cells by *Stenotrophomonas maltophilia* isolates from cystic fibrosis patients. *BMC Microbiology*, 10, 102.

Potera, C. (1999). Forging a link between biofilms and disease. *Science*, 283(5409), 1837–1838.

Reniere, M.L., Torres, V.J., Skaar, E.P. (2007) Intracellular metalloporphyrin metabolism in *Staphylococcus aureus*. *Biometals*, 20: 333–345.

Rojas, P., Garcia, E., Calderon, G. M., Ferreira, F., Rossa, M. (2009). Successful treatment of Stenotrophomonas maltophilia meningitis in a preterm baby boy. *Journal of Medical Case Reports*, 3, 7389.

Runyen-Janecky, L. J., Reeves, S. A., Gonzales, E. G., & Payne, S. M. (2003). Contribution of the *Shigella flexneri* Sit, Iuc, and Feo iron acquisition systems to iron acquisition *in vitro* and in cultured cells. *Infection and Immunity*, 71(4), 1919–1928.

Saurin, W., Hofnung, M., & Dassa, E. (1999). Getting in or out: early segregation between importers and exporters in the evolution of ATP binding cassette (ABC) transporters. *Journal of Molecular Evolution*, 48(1), 22-41.

Schulze, W. X., & Usadel, B. (2010). Quantitation in mass spectrometry-based proteomics. *Annual Review of Plant Biology*, 61, 491-516.

Schwyn, B. & Neilands, J. B. (1987). Universal Chemical Assay for the Detection Determination of Siderophores'. Analytical Biochemistry, 160(1), 47–56.

Sierro, F., Dubois, B., Coste, A., Kaiserlian, D., Kraehenbuhl, J. P. and Sirard, J. C. (2001). Flagellin stimulation of intestinal epithelial cells triggers CCL20-mediated migration of dendritic cells. *Proceedings of the National Academy of Sciences of the United State of America*, 98, 13722–13727.

Singh, P. K., Parsek, M. R., Greenberg, E.P., & Welsh, M. J. (2002). A component of innate immunity prevents bacterial biofilm development. *Nature*. , 417(6888),552-555.

Sokol, P. A., & Wood, D. E. (1984). Relationship of iron and extracellular virulence factors to *Pseudomonas aeruginosa* lung infections. *Journal of Medical Microbiology*, 18(1984), 125-133.

Somoskovi, A., Wade, M. M., Sun, Z., & Zhang, Y. (2004). Iron enhances the antituberculous activity of pyrazinamideJournal of Antimicrobial Chemotherapy, 53(2), 192-6.

Srinivasan, M. C., & Rele, M. V. (1999). "Microbial xylanases for paper industry," *Current Science*, *77*(1), 137–142.

Sritharan, M. (2006). Iron and bacterial virulence. *Indian Journal of Medical Microbiology*, *24*(3), 163-4.

Sritharan, M. (2000). Iron as a candidate in virulence and pathogenesis in mycobacteria and other microorganisms. *World Journal of Microbiology and Biotechnology,* 16(8-9), 769-80.

Sritharan, M., Yeruva, V. C., Sundaram Sivagami, C. A., Duggirala, S. (2006). Iron enhances the susceptibility of pathogenic mycobacteria to isoniazid, an anti-tubercular drug. *Journal of Microbiology and Biotechnology,* 24(3), 163-164.

Stehr, M., Smau, L., Singh, M., Seth, O., Macheroux, P., Ghisla, S., and Diekmann, H. (1999). Studies with lysine N6-hydroxylase. Effect of a mutation in the assumed FAD binding site on coenzyme affinities and on lysine hydroxylating activity. *The Journal of Biological Chemistry,* 380(1), 47-54.

Steiner, T. S., Nataro, J. P., Poteet-Smith, C. E., Smith, J. A., & Guerrant, R. L. (2000). Enteroaggregative *Escherichia coli* expresses a novel flagellin that causes IL-8 release from intestinal epithelial cells. *The Journal of Clinical Investigation*, 105(12), 1769–1777.

Stiernagle, T. (2006). Maintenance of *C. elegans*. http://dx.doi.org/10.1895/wormbook.1.101.1.

Storz, G., Vogel, J., & Wassarman, K. (2011) "Regulation by small RNAs in bacteria: expanding frontiers", Molecular Cell, 43(6), 880–891.

Sun, H-Y,. (2010). Infections occurring during extracorporeal membrane oxygenation use in adult patients. *The Journal of Thoracic and Cardiovascular Surgery*, 140(5), 1125–1132.

Sutphin, G. L., & Kaeberlein, M. (2009). Measuring *Caenorhabditis elegans* life span on solid media. *Journal of Visualized Experiments,* 12, 1152.

Szymanska, J. (2007). Bacterial contamination of water in dental unit reservoirs. *Annals of Agricultural and Environmental Medicine,* 14, 137-140.

Tammy, C., Solomon, P. S., Bringans, S., Kar-Chun, T., Oliver, R. P., Lipscombe, R. (2010). Quantitative proteomic analysis of G-protein signaling in Stagonospora nodorum using isobaric tags for relative and absolute quantification. *Proteomics*, 10(1), 38-47.

Teng, S. O., Lee, W. S., Ou, T. Y., Hsieh, Y. C., Lee, W. C., & Lin, Y. C. (2009). Bacterial contamination of patients' medical charts in a surgical ward and the intensive care unit: impact on nosocomial infections. *Journal of Microbiology, Immunology and Infection,* 42(1), 86-91.

Thomas, R., Rukman, A. H., Neela, V. (2013). *Stenotrophomonas maltophilia*: pathogenesis model using *Caenorhabditis elegans*. *Journal of Medical Microbiology*, 62(11), 1777-1779.

Thomas, R., Rukman, A. H., Neela, V. (2014). Extracellular enzyme profiling of *Stenotrophomonas maltophilia* clinical isolates. *Virulence*, 5(2), 326–330.

Tindale, A. E., Mehrotra, M., Ottem, D., Page, W. J. (2000). Dual regulation of catecholate siderophore biosynthesis in *Azotobacter vinelandii* by iron and oxidative stress. *Microbiology*, 146(7), 1617-26.

Tzanetou, K., Triantiphillis, T., & Tsoutsos, D. (2004). *Stenotrophomonas maltophilia* peritonitis in CAPD patients: susceptibility to antibiotics and treatment outcome: a report of five cases. *Peritoneal Dialysis International*, 24(4), 401-404.

Van Zyl, E., & Steyn, P. L. (1992). Reinterpretation of the taxonomic position of *Xanthomonas maltophilia* and taxonomic criteria in this genus. *International journal of systematic bacteriology,* 42(1), 193-198.

Vartivarian, S. E., Papadakis, K. A., Palacios, J. A., Manning, J. T., & Anaissie, E. J. (1994). Mucocutaneous and soft tissue infections caused by *Xanthomoans maltophilia*: a new spectrum. *Annals of Internal Medicine*, 121(12), 969-973.

Victor, M. A., Arpi, M., Bruun, B., Jønsson, V., Hansen, M. M. (1994). *Xanthomonas maltophilia* bacteremia in immunocompromised hematological patients. *Scandinavian Journal of Infectious Diseases*, 26(2), 163–170.

Wilks, A. (2002). Heme oxygenase: evolution, structure, and mechanism. *Antioxid Redox Signal*, 4, 603–614.

Wu, W. W., Wang, G., Baek, S. J., Shen, R. F. (2006). Comparative study of three proteomic quantitative methods, DiGE, cICAT and iTRAQ using 2DGE OR LC-MALDITOF/TOF., *Journal of Proteome Research*, 5(5), 651-658.

Ye N., Liang, S., Xiaohong, Q., & Zhihao, S. (2013). Proteomic analysis of *Pseudomonas putida* reveals an organic solvent tolerance-related gene *mmsB. Plos one,* 8(2), e55858.

Yoon, S.S. and Mekalanos, J.J. (2008). Decreased potency of the *Vibrio cholerae* sheathed flagellum to trigger host innate immunity. *Infection and Immunity*, 76, 1282–1288.

Zgair, A.K and Chhibber, S. (2011). Adhesion of *Stenotrophomonas maltophilia* to mouse tracheal mucus is mediated through flagella. *Journal of Medical Microbiology*, 60, 1032–1037.