

## งานวิจัยเรื่องวัณโรค

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ข้าพเจ้าเรื่องราววัณโรคในประเทศไทยเจ็บหายไบนาน เพิ่งมาจะมีข่าวว่าประเทศไทยถูกองค์การอนามัยโรคจัดเป็นหนึ่งใน ๑๔ ประเทศ ที่มีวัณโรคชุกชุม รัฐบาลไทยจึงเสนอให้นักวัณโรคไทยเน้นการศึกษาวิจัยเพื่อลดการแพร่ระบาด<sup>๑</sup> ผู้เขียนทราบเรื่องทำให้อยากกลับไปศึกษาวิจัยวัณโรคอีก เพราะสมัยก่อนสนใจศึกษาเรื่องวัณโรคมก การศึกษาวิจัยช่วงแรกๆ ในชีวิตแพทย์เป็นเรื่องวัณโรค ทำวิจัยไว้ไม่น้อย (ดูเอกสาร) เขียนตำราวัณโรคภาษาไทย ๒ เล่ม (วัณโรคปอดกับวัณโรคนอกปอด) และทำดัชนีนิพนธ์เรื่องความสัมพันธ์ระหว่างความไวเกินต่อทูเบอร์คูลินกับเซรัมโปรตีนในวัณโรค



รูปที่ ๑ ปกหนังสือวัณโรคปอด วัณโรคนอกปอด และดัชนีนิพนธ์

## บทความวิชาการที่ลงพิมพ์ในวารสารทั้งในประเทศ และต่างประเทศมีเกินร้อย ดังตัวอย่างบทความ เอกสารซึ่งพิมพ์เท่าที่จำได้ต่อไปนี้

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๑๓๒. สมชัย บวรกิตติ. สถานการณ์วัณโรคในประเทศไทย เลวลง มีสาเหตุ? *ธรรมศาสตร์เวชสาร* ๒๕๖๐;๑๗:๖๖๙.

มาถึงวันนี้ ณ จุดนี้ จะไปศึกษาเรื่องวัณโรคอีกก็ คงทำยาก ไม่ใช่เพราะเรื่องอายุที่เป็นตัวเลข แต่เป็นเพราะว่าไม่ได้ทำงานในสถาบันวิชาการ (มหาวิทยาลัย) ที่มีผู้ร่วมงาน และอุปกรณ์วิจัยพร้อม และที่สำคัญมากก็คือระดับการศึกษาไม่ใช่แบบเดิมๆ แล้ว วิทยาการความรู้ก้าวหน้าไปมาก ถ้าจะศึกษาที่ต้องลงไปทางอนุเวชศาสตร์ด้านพันธุศาสตร์ และวิทยาภูมิคุ้มกัน ซึ่งผู้ที่ไม่อยู่ในสถาบันวิชาการระดับมหาวิทยาลัยคงไม่มีโอกาสทำได้ ถึงแม้ว่าอาจยังมีความคิดความอ่าน สามารถสร้างโครงการศึกษาวิจัยที่เกิดประโยชน์ได้ เท่าที่ทราบมีนักเวชพันธุศาสตร์ไทยร่วมมือกับนักวิชาการญี่ปุ่นศึกษาหาข้อมูลด้านหน่วยพันธุกรรม ได้ข้อสรุปว่า HSPEP1-MAFB อาจเป็นหน่วยพันธุกรรมภูมิไวรับวัณโรคในคนอายุน้อย (Mahasirimongkol S, Yanai H, Mushiroda T, Promphittayarat W, Wattanapokayakit S, Phromai J, et al. Genome-wide association studies of tuberculosis in Asians identify distinct at-risk locus for young tuberculosis. *J Hum Genet* 2012;57(6):363-7).

### เอกสารข้างล่างนี้เป็นตัวอย่างการศึกษา ด้านอนุเวชศาสตร์ยุคปัจจุบัน ที่มีผู้ศึกษา อย่างกว้างขวาง มีข้อมูลเป็นประโยชน์ เพื่อการศึกษา และอ้างอิง

๑. **Ogus AC**, Yoldas B, Ozdemir T, Uguz A, Olcen S, Keser I, et al. The Arg753Gln polymorphism of the human Toll-like receptor 2 gene in tuberculosis disease. *European Respir J* 2004;23:219-23.

The Arg 753 Gln polymorphism of the TLR2 gene was studied in 151 TB patients compared to 116 healthy control subjects. Findings were that the risk of developing TB was increased for carriers of the **AA and GA genotypes**, respectively. The arginine to glutamine substitution at residue 753 polymorphism of the Toll-like receptor 2 gene influences the risk of developing tuberculosis.

๒. **Fernando SL**, Britton WJ. Genetic susceptibility to mycobacterial disease in humans. *Immunology and Cell Biology* 2006;84:125-37.

๓. **Thoung NTT**, Dunstan SJ, Chau TTH, Thorsson V, Simmons CP, et al. Identification of Tuberculosis Susceptibility genes with Human Macrophage Gene Expression Profiles. *Plos/pathogens* December 5, 2008

๔. **Lorenzi JCC**, Trombone APF, Rocha CD, Almeida LP, Lousada RL, Malardo T, et al. Intranasal vaccination with messenger RNA as a new approach in gene therapy: Use against tuberculosis. *BMC Biotechnology* 2010;10:77-87.

Intranasal vaccination with naked mRNA of Hsp65 protein from *M. leprae* was able to induce protection against virulent strain of *M. tuberculosis*. This immunization was associated with specific production of IL-10 and TNF-alpha in spleen.

๕. **Rowan K**. Gene Linked to Tuberculosis Susceptibility Identified. *Live Sci* August 10, 2010.

The study was conducted by scanning more than 333,000 genes in more than 11,000 people living in Africa, and turned up one gene that was associated with increased susceptibility to TB. Horstmann quoted that the newly identified gene - called rs4331426 - is associated with only a very small increase in a person's risk of susceptibility to TB. Hakonarson said, he agree with Horstmann's conclusion that the gene uncovered by the study is unlikely to cause susceptibility to TB itself, but is likely to lie in proximity to genes that do.

๖. **Andraos C**, Koorsen G, Knight JC, Bornman L. **Vitamin D receptor gene methylation** is associated with ethnicity, tuberculosis and TaqI polymorphism. *Hum Immunol* 2011;72(3):262-8.

Bisulphite conversion and/or pyrosequencing were used to analyse the methylation status of 17 CpGs of VDR and to genotype 7 SNPs in the 3' CPG island (CGI 1060), including the SNPs *Apal* (rs7975232) and *TaqI* (rs731236) in 32 TB cases and 29 controls. The results showed **methylation differences related to TB status and interaction between the disease-associated SNP *TaqI*, population and TB with respect to VDR methylation.**

๗. **Stein CM.** Genetic Epidemiology of Tuberculosis Susceptibility: Impact of Study Design. PLOS/ pathogen January 20, 2011.

Review upon 94 reports on tuberculosis genetics published from year 1941 (Lurie M. Am Rev Tuberc 44:1125) to 2010 (Velez DR, et al. Hum Genet 127:65-73) gave the impression of barely understanding the genetics of tuberculosis. Future studies were suggested to consider phenotype definition and genetic epidemiological principles to understand LTBI and risk of progression to TB.

๘. **Stein CM.** Tuberculosis. Wiley Online Library August 2012. From: <http://www.els.net/WileyCDA/ElsArticle/refId-a00023886.html> เปิดอ่าน 6/12/2560.

There is evidence showing that tuberculosis susceptibility is partially influenced by human genetic factors. Differences in susceptibility between ethnic groups and segregation analysis were noted.

๙. **Zhang J, Zheng L, Zhu D, An H, Yang Y, Liang Y, et al.** Polymorphism in the **interleukin 18 receptor 1 gene** and Tuberculosis Susceptibility among Chinese. PLOS / one October 31, 2014

Genotyping for single-nucleotide polymorphism (SNPs) using Sequenom's iPLEX assays in 1,032 patients with TB and 1,008 controls of Chinese Han origin showed **decreased mRNA levels of *IL18R1* due to rs3755276** may partially mediate the increased susceptibility to TB.

๑๐. **Chen M, Deng J, Su C, Li J, Wang M, Abuaku BK, et al.** Impact of passive smoking, cooing with solid fuel exposure, and **MBL/MASP-2 gene polymorphism** upon susceptibility to tuberculosis. Internat J Infect Dis 2014;29: 1-6.

205 TB patients and 216 healthy controls were subjected to PCR with sequence-specific primer (PCR-SSP) technology leveraged to genotype rs7096206 of MBL genes and rs2273346 and rs6695096 of MASP-2 genes. Findings: **Polymorphism of MBL (rs7096206) and MASP-2 (rs6695096) genes were found associated with susceptibility to TB in non-smokers and there were gene-environment interaction among them.**

๑๑. **Graustein AD, Horne DJ, Arentz M, Bang ND, Chau TTH, Thwaites GE, et al.** **TLR9 gene region polymorphisms and susceptibility to tuberculosis** in Vietnam. Tuberculosis 2015;95:190-6.

The study (N = 339 TB cases and 376 controls) identifies a SNP (rs352142) within the TLR9 gene region that is associated with susceptibility to tuberculous meningitis and a second SNP (rs352143) that was associated with pulmonary tuberculosis.

๑๒. **Fol M, Druszczynska M, Włodarczyk M, Ograczyk E, Rudnicka W.** Immune response gene polymorphisms in tuberculosis. Acta Biochimica Polonica 2015;62(4):633-40.

Review on recent discoveries in genetic studies and influence on TB susceptibility disclosed that the spectrum of innate and adaptive environmental factors may contribute to the clinical manifestation of TB. And that host genetic factors have a potential to influence the susceptibility to M.tb infection and progression to active TB.

## กิตติกรรมประกาศ

รองศาสตราจารย์ นายแพทย์มานพ พิทักษ์ภากร นักเวชพันธุศาสตร์ คณะแพทยศาสตร์ ศิริราชพยาบาล มหาวิทยาลัยมหิดล ได้กรุณาอ่านต้นฉบับ และให้คำแนะนำ