2025年１月15日発行（隔月15日発行）　　ISSN　0022－9776

Kekkaku 結核

▼ 読みたい項目をクリックしてください

Vol. 100　No. 1　January-February　2025

日本結核・非結核性抗酸菌症学会誌

Memorial Lecture by the Imamura Award Winner

EDUCATION AND ACADEMIC ACTIVITY SUPPORT FOR YOUNG DOCTORS THROUGH THE OITA PREFECTURE TUBERCULOSIS MEDICAL SYSTEM ENHANCEMENT PROJECT

[1,2]Kosaku KOMIYA

Key words: Education, Resident, Research

Memorial Lecture by the Imamura Award Winner

RESEARCH TO ELUCIDATE THE PATHOGENESIS OF PULMONARY NONTUBERCULOUS MYCOBACTERIAL (NTM) DISEASE FROM HOST GENE RESPONSES

Masashi MATSUYAMA

Abstract: Although the incidence of pulmonary nontuberculous mycobacterial (NTM) disease is increasing, the pathophysiology of the disease is not fully understood. In Japan, *Mycobacterium avium-intracellulare* complex (MAC) accounts for 90% of the causative organisms. Nontuberculous mycobacteria are ubiquitous in various environments, but they do not cause disease in all individuals. Therefore, it is thought that the disease is largely affected by host factors. The author has studied the host response to pulmonary NTM disease using comprehensive gene expression analysis by RNA sequencing (RNA-seq) and genetically engineered mice.

When wild-type mice were infected intranasally by *Mycobacterium avium*, a clinical isolate obtained from a patient with pulmonary MAC disease, lymphocyte-based inflammation was observed around peribronchovascular bundles in the lung tissue two months after infection. Comprehensive gene expression analysis by RNA-seq showed that the "Th1 pathway" and the "Macrophage Classical Activation Signaling Pathway" were activated.

Primary human airway epithelial cells from healthy subjects were differentiated into human airway epithelium using the air-liquid interface method and infected with *M. avium* or *M. abscessus*, followed by RNA-seq analysis. In both infections, IL-32 expression was upregulated. In contrast, the expression of genes related to cilia was decreased, indicating that the cilia in the respiratory epithelium were damaged.

The author used genetically engineered mice to determine the roles of T-bet, ROR-γt, PD-1, PD-L1, and Nrf2 in a model of pulmonary MAC infection. T-bet is a transcription factor that regulates Th1 cell differentiation and IFN-γ production. T-bet regulated susceptibility and inflammatory responses to *M. avium*. T-bet–deficient mice displayed diminished Th1 responses and development of Th17 responses. Reduced Th1 responses increased susceptibility to systemic MAC infection, and Th17 development induced excessive neutrophilic pulmonary inflammation. In this respect, a fine balance between Th1 and Th17 responses was essential in defining the outcome of MAC infection.

ROR-γt is a transcription factor that regulates Th17 cell differentiation. Overexpression of ROR-γt resulted in Th17 over response along with Th1 response after *M. avium* infection, inducing excessive lung neutrophilic inflammation. In contrast, overexpression of ROR-γt did not affect Th1 cell differentiation or inhibit bacterial growth.

Nrf2 is a transcription factor that is activated in response to oxidative stress. Nrf2-deficient mice were highly susceptible to *M. avium* bacteria compared with wild-type mice. RNA-seq analysis showed that Nramp1 and HO-1 expressions were greatly decreased in the infected lungs of Nrf2-deficient mice. Furthermore, we showed that Nramp1 and HO-1, which are regulated by Nrf2 within alveolar macrophages, are important in defense against *M. avium* infection by promoting phagolysosome fusion and granuloma formation, respectively.

Blockade of the PD-1/PD-L1 pathway activates tumor immunity. The loss of PD-1 or PD-L1 did not affect mortality or the amount of bacteria in the lungs of *M. avium*-infected mice. Interestingly, gene expression levels associated with Th1 immunity did not differ between genotypes, which may explain why susceptibility to infection did not change.

These studies the author performed have shown that host responses involving a specific gene or gene set are associated with the pathophysiology of pulmonary MAC infection.

胃癌術後化学療法中に画像変化を観察できた高齢者結核性肺炎の1例

[1]重森　度　[1]山口　将史　[1]角田　陽子　[1]松田　正
[1]中西　司　[2]大谷　秀司　[2]中井　美里　[1]中野　恭幸

要旨：〔背景〕結核性肺炎は肺結核症において胸部画像所見で細菌性肺炎や器質化肺炎様のconsolidationやすりガラス影を呈する場合とされるが，近年従来認識されていた臨床像と異なる症例の報告が散見される。〔症例〕70歳男性。胃癌に対する切除術後に化学療法が開始された。約半年後の胸部CTで右肺尖部に結節状の新規病変を認めた。当初は発熱や咳嗽などの呼吸器症状はなく，粒状影や空洞性病変も認めなかったため，転移性肺腫瘍や原発性肺癌が疑われて精査が開始された。その後，喀痰抗酸菌塗抹は陰性ながらも結核菌PCR陽性が判明したため，当科紹介となった。紹介時に胸部CTを再検したところ，細菌性肺炎様の像に変化していた。結核性肺炎の診断で抗結核薬の投与を行ったところ，陰影は改善した。〔結語〕本症例は抗癌剤による免疫能低下を契機に，肺尖部の初感染病巣の結核菌の再活性化が生じて短時間に拡大した結果，結核性肺炎の形態をとったと考えられる。比較的短期間に細菌性肺炎様の形態に変化する様子を確認できた示唆に富む症例と考えられたため，ここに報告する。

キーワーズ：浸潤影，高齢者，胃癌術後，結核性肺炎

縦隔リンパ節病変が食道穿孔をきたした外国人若年性結核の1例

[1,2]上田　航大　[1]金澤　　潤　[1]小澤　　優　[1]野中　　水
[1]荒井　直樹　[1]兵頭健太郎　[1]林原　賢治　[1]大石　修司
[1]石井　幸雄　[1]齋藤　武文

要旨：症例は23歳のベトナム人男性。半年前からの前胸部痛，咳嗽を主訴に受診。胸部CTで右肺上葉の粒状影，縦隔リンパ節の腫大および気管分岐下リンパ節内に食道へ連続する低吸収域を認めた。上部消化管内視鏡では食道穿孔の所見を認め，喀痰抗酸菌塗抹陽性，結核菌核酸増幅法陽性であることから縦隔リンパ節結核による食道穿孔と診断した。抗結核薬投与と絶食補液管理で瘻孔部の閉鎖が得られた。その後，喀痰抗酸菌塗抹，培養の陰性化が得られ，治療開始後4カ月で退院とした。食道穿孔の原因となった縦隔リンパ節病変は初期変化群に引き続いて生じた初感染結核であると考えられた。近年増加傾向の外国生まれ結核においては肺外結核が多いことが報告されている。結核による食道穿孔はまれであるが，若年外国生まれ結核の増加により，本例のように重症な初感染結核の増加が予想される。示唆に富む1例であると考え報告を行う。

キーワーズ：初感染結核，縦隔リンパ節結核，外国生まれ結核，肺外結核，食道穿孔