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When a commensal becomes a pathogen

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Sarcoidosis is a granulomatous disease of unknown etiology, affecting persons worldwide. Because the etiologies remain enigmatic, the ability to identify effective therapeutics remains elusive. Sarcoidosis immunology and pathology suggest that infectious agents may have a role in its pathogenesis. Molecular analysis of pathologic tissues remains a viable mechanism for identifying etiologic agents of microbial origin.

In this issue of Sarcoidosis, Vasculitis and Diffuse Lung Diseases, Ichikawa et al, reports the detection of quantitative differences for the presence of *P. acnes* nucleic acids in sarcoidosis bronchoalveolar lavage (BAL), compared to control BAL. By demonstrating a quantitative distinction among sarcoidosis subjects compared to a control population, they provide further credence in an association of *Propionibacterium* species with sarcoidosis pathogenesis. In addition, they note positive correlations of *P. acnes* DNA with angiotensin converting enzyme (ACE) levels, as well as with the number of macrophages in the sarcoidosis BAL. ACE levels often parallel granuloma burden, thus the quantitative correlation of *P. acnes* with ACE and host macrophage levels suggests the microorganisms are present within the granuloma, and more precisely, within the host macrophage. A distinction for the presence of *P. granulosum* was not noted. A recent report cited the efficacy of minocycline in a patient with muscular sarcoidosis whose biopsy was positive for *P. acnes* proteins. Clinically resolving disease occurred while the patient was taking minocycline; however, the granulomas rapidly recurred after tapering minocycline, suggesting that the immunomodulatory effects rather than the antimicrobial effects were affecting disease resolution (1).

The hypothesis supporting a pathogenic role for *P. acnes* can be further strengthened by ascertaining if the presence of *P. acnes* in the sarcoid granuloma reflects pathogenecity or simply commensals that traffic to established granulomas, analogous to that shown to be the case with some mycobacteria (2). This is determined by concomitant molecular analysis of granulomatous controls of known etiology such as histoplasmosis, blastomycosis, and cryptococcus for *P. acnes* DNA. At least 22 of the 30 control subjects in this report may not have had granulomatous inflammation. Also, molecular analysis for housekeeping genes such as 16S rRNA may or may not reflect active infection. A positive analysis demonstrating active expression of microbial virulence factors would support pathogenesis and explain why *P. acnes* is a pathogen in one host and a commensal in another. Simultaneous detection of microbial nucleic acids and immune responses against microbial virulence proteins would certainly indicate pathogenesis, and antibiotics as therapeutics.

Finally, a laudable goal would involve connecting the proverbial dots of pathogenic mycobacteria

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and *Propionibacterium acnes* (formerly *Corynebacterium acnes*). Approximately three decades ago, a bacteriologist, Lane Barksdale, reported the presence of *Corynebacterium acnes* in biopsies from leprosy and tuberculosis patients (3, 4). It is possible that both mycobacteria and propionibacteria have a role in sarcoidosis pathogenesis. More recent studies have noted the presence of *P. acnes* in tuberculosis patients (5). We should be careful not to miss a rare opportunity to understand the role of microbial symbiosis in sarcoidosis pathogenesis.

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