UNDER THE MICROSCOPE

Propionibacterium acnes

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Abstract

Propionibacterium acnes, a common skin organism, is most notably recognized for its role in acne vulgaris. It also causes postoperative and device-related infections and has been associated with a number of other conditions such as sarcoidosis and synovitis, acne, pustulosis, hyperostosis and osteitis (SAPHO), although its precise role as a causative agent remains to be determined. *Propionibacterium acnes* produces a number of virulence factors and is well known for its inflammatory and immunomodulatory properties. Recent publication of the *P. acnes* genome should provide further insights into the pathogenic capabilities of the organism and potentially lead to the development of new therapies.

Introduction

Propionibacterium acnes belongs to the human cutaneous propionibacteria along with *Propionibacterium avidum*, *Propionibacterium granulosum*, *Propionibacterium innocuum* and *Propionibacterium propionicum*. Historically, *P. acnes* has been designated as *Bacillus acnes* and *Corynebacterium acnes* (Marples and McGinley 1974) and *Corynebacterium parvum* (Eady and Ingham 1994).

Propionibacterium acnes is a non-spore-forming, Gram-positive, anaerobic, pleomorphic rod whose end products of fermentation include propionic acid. The organism forms part of the normal flora of the oral cavity, large intestine, the conjunctiva, the external ear canal (Brook and Frazier 1991) and the skin, where it predominates over other constituents of the normal flora in the pilosebaceous follicles (Funke *et al.* 1997). Although it is usually regarded as a strict anaerobe, it can tolerate oxygen up to 100% saturation but grows at reduced rates (Cove *et al.* 1983). *In vitro*, *P. acnes* is capable of surviving for as long as 8 months under anaerobic conditions without subculture, suggesting that it could also survive in human tissues at low oxidation potentials (Csukas *et al.* 2004). In addition, *P. acnes* is slow growing and can resist phagocytosis and persist intracellularly within macrophages (Webster *et al.* 1985). This resistance to phagocytosis may be attributable to the organism's complex cell wall structure, which also has a surface fibrillar layer (Montes and Wilborn 1970).

The subdivision of *P. acnes* into types I and II was first described by Johnson and Cummins (1972) on the basis of cell wall agglutination tests and the organism's cell wall sugars. Type I and II strains can be discriminated biochemically, with type II being unable to ferment sorbitol (Cummins 1975), and by phage typing (Webster and Cummins 1978). More recently immunofluorescence microscopy using specific antisera (McDowell *et al.* 2005) and molecular techniques including *recA* sequence analysis (McDowell *et al.* 2005) and random amplification of polymorphic DNA (Perry *et al.* 2003) have also been used to distinguish between type I and II strains.

Infections and disease associations

Propionibacterium acnes is considered an opportunistic pathogen, causing a range of infections as well as being associated with a number of inflammatory conditions. It is primarily recognized for its role in acne vulgaris where it is thought to contribute to the inflammatory phase of the condition (Leyden 2001). This association is supported by the correlation between antibiotic resistant *P. acnes* and treatment failure (Eady *et al.* 2003). Other conditions where an association with *P. acnes* has been suggested include synovitis, acne, pustulosis, hyperostosis and osteitis (SAPHO) (Schaeverbeke *et al.* 1998) and sarcoidosis, a systemic granulomatous disease of unknown aetiology. *Propionibacterium acnes* DNA has been isolated from lymph nodes of patients with sarcoidosis (Eishi *et al.*

Table 1 Infections where *Propionibacterium acnes* was found to be the causative agent

Infection	Predisposing factor	Reference
Discitis	Surgery	Chia and Nakata (1996) and Harris *et al.* (2005)
Spondylodiscitis	Epidural catheterization	Halkic *et al.* (2001) and Hernandez-Palazon *et al.* (2003)
Central nervous system infections	Neurosurgical procedures	Critchley and Strachan (1996) and Ghalayini *et al.* (2004)
Endocarditis	Prosthetic aortic valve	Gunthard *et al.* (1994)
Osteomyelitis	Lumbar puncture	Abolnik *et al.* (1995)
Endophthalmitis	Postoperative	Benz *et al.* (2004)
Joint infections	Prosthetic hip	Tunney *et al.* (1999)

2002). However, recent findings have shown that *P. acnes* normally resides in peripheral lung tissue and mediastinal lymph nodes and their presence therefore is not specific to sarcoidosis (Ishige *et al.* 2005). Recovery of *P. acnes* from microdiscectomy material removed for the treatment of sciatica has suggested an association between the organism and sciatica (Stirling *et al.* 2001; Vautrin *et al.* 2004). However, other workers have failed to culture *P. acnes* from microdiscectomy material and suggest that such organisms are derived from the skin as contaminants during the surgical procedure (McLorinan *et al.* 2005). *Propionibacterium acnes* infections are predominately associated with a predisposing factor such as surgery, trauma or the presence of a foreign device (Table 1).

Virulence and immunological properties

Pathogenicity of *P. acnes* is mainly centred around the organism's ability to produce bioactive exocellular products and its interactions with the immune system. *Propionibacterium acnes* produces a number of exocellular enzymes (Hoeffler 1977; Holland *et al.* 1981; Ingham *et al.* 1981; Kabongo Muamba 1982) and metabolites that can directly damage host tissue (Allaker *et al.* 1987). Elevated levels of anti-*P. acnes* antibodies have been reported in individuals with acne (Holland *et al.* 1986; Ingham *et al.* 1987; Ashbee *et al.* 1997). *Propionibacterium acnes*-derived components possess chemoattractant properties (Webster and Leyden 1980; Pulverer *et al.* 1988) and the organism itself can activate complement by both the classical and alternative pathway, resulting in the formation of C5-dependant chemotactic factors (Webster *et al.* 1978). Induction of pro-inflammatory cytokines, interleukin (IL)-1α, IL-1β, IL-8 and TNF-α, by *P. acnes* has been reported (Vowels *et al.* 1995). Therefore, although *P. acnes* is usually regarded as a harmless commensal, it possesses many attributes of a disease-causing organism.

Extensive research exists on the modulation of the immune system by bacteria or their products and has shown that *P. acnes* is one of the most potent adjuvants (Roszkowski *et al.* 1990). Pretreatment with heat-killed cells of *P. acnes* has been shown to provide protection against infection and anti-tumour activity in a variety of animal models (Eady and Ingham 1994).

Future prospects

The first genomic sequence for *P. acnes* available to the public was recently published (Bruggemann *et al.* 2004). This information should provide important clues on the pathogenic potential of the organism, the strategies it uses to survive in the environment of the human skin, and potentially new approaches for its control (Bruggemann 2005).

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