Segmented Filamentous Bacteria Interact with Intraepithelial Mononuclear Cells

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Segmented filamentous bacteria (SFB) are found in multiple species and play an important role in the development of mucosal immunity. The mechanism by which the bacteria interact with the immune system has not been well defined. We provide morphologic evidence of direct interaction between SFB and intraepithelial mononuclear cells.

Segmented filamentous bacteria (SFB) are autochthonous bacteria that colonize the small intestines of a wide range of species (4, 8, 17, 18, 20, 21). SFB are generally considered nonpathogenic (13, 18, 20, 21) and host specific (26). The organisms have not been successfully cultured in vitro but have been characterized by 16S rRNA analysis to be closely related to the genus Clostridium (22). As a group, these organisms have been provisionally named Candidatus Arthomitus (23). Intestinal colonization by SFB is influenced by various factors, including diet, weaning, strain, housing, and the immune status of the host.

![FIG. 1. Scanning electron micrographs of ileal tissue with associated SFB. (a) Villi with SFB. Bar = 10 μm. (b) SFB (arrows) attached near M cells (M) of the follicle-associated epithelium. Bar = 10 μm.](http://iai.asm.org/)

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of both the mother and the host (10, 12, 13, 15, 16). SFB attach apically to epithelial cells, with only minor disruption of microvilli and localized actin polymerization at the attachment site (4, 9, 20; M. A. Jepson, M. A. Clark, N. L. Simmons, and B. H. Hirst, abstract from the 649th Meeting of the Biochemical Society 1993, Biochem. Soc. Trans. 22: 91S, 1994).

SFB are suggested to function as an important microbial component of the gastrointestinal ecosystem (4). These organisms may play a role in disease prevention by inhibiting colonization by pathogens such as *Escherichia coli* and *Salmonella enterica* (5, 7). The SFB are most visible soon after weaning and disappear weeks later. The disappearance of SFB coincides with the time of activation of mucosal immunity, suggesting immune-mediated clearance of the organisms at that time (24). SFB colonization in mice increases the number of immunoglobulin A-secreting cells and the levels of immunoglobulin A in both secretions and serum (14, 25, 28). Colonization of mice by SFB is associated with the activation and increased numbers of intraepithelial lymphocytes (25, 27). Furthermore, in germfree mice, SFB colonization is associated with the expression of major histocompatibility complex class II molecules on intestinal epithelial cells (28). SFB are thought to play a significant role in the stimulation of the mucosal immune system (14, 25).

In a separate study of ileal-gut loops prepared from 4- to 5-week-old pigs, SFB colonization in the ileum of one pig was an incidental observation. In this pig, four gut loops had been
prepared from the region containing the continuous ileal Pey-
ner’s patch. Sample preparation for transmission electron mi-
croscopy and scanning electron microscopy was done as pre-
viously described (1, 11). Scanning electron micrographs
showed SFB distributed over the epithelial tissue of the ileum
(Fig. 1a). This colonization was observed in two of the four
sequentially prepared loops. The SFB were distributed on both
the follicle-associated epithelium and the absorptive epithe-
lium. Most of the SFB were located on the upper one-third of
the villi. SFB attached to the apical membrane or along the
lateral borders of epithelial cells (Fig. 1b). The cell types in-
volved included enterocytes, goblet cells, and M cells.

Transmission electron micrographs showed the SFB to be
attached to the apical membranes of epithelial cells. The proxi-
mal bacterial segment attached to and indented the apical cell
membrane (Fig. 2a). In the attachment interface, the proximal
bacterial segment possessed a small protuberance at its base.
The epithelial cell membrane closely paralleled the shape of
the bacteria and contained an adjacent line of intracellular
electron-dense material.

In addition, an SFB was observed to extend from an M cell
into intimate association with an intraepithelial mononuclear
(Fig. 2b and c). In this section, the SFB did not penetrate
the mononuclear cell membrane; however, it did extend the
membrane deeply into the mononuclear cell cytoplasm, to
a point of indentation near the nucleus. The segments of the
SFB farthest into the mononuclear cell were more irregular in
shape and less electron dense than the apical segments.

The SFB morphology and cellular colonization in the pig
ileum were similar to those found in previous work (20). The
SFB were seen in two out of the four ileal loops, suggesting
limited colonization within the region of the continuous ileal
Peyer’s patch. In addition, direct interaction between an SFB
and an intraepithelial mononuclear cell was observed subjacent
to an M cell. The bacterial segments most intimately associated
with the mononuclear cell were morphologically degenerate. We speculate that this intimate interaction may
represent the early processing of the bacteria by the mononu-
clear cell.

M cells are specialized antigen-sampling epithelial cells that
are found over gut-associated lymphoid tissue such as the con-
tinuous ileal Peyer’s patch in pigs (3). Macrophages, dendritic
cells, and lymphocytes are mononuclear cells that can reside
in the basolateral space of the M cell (6, 19). These intra-
epithelial leukocytes receive and process the sampled anti-
gen or bacteria for the induction of immune response or
tolerance (2, 6).

The mechanism of SFB presentation to mucosal immune
cells has not been well defined. Enterocyte phagocytosis
and processing of attached SFB have been suggested to be mech-
anisms of immune cell presentation (29). However, no direct
interactions of SFB with immune cells have been documented.
Our observation of an intimate interaction between SFB and the
host’s intraepithelial mononuclear cells suggests a direct
mechanism of SFB presentation for mucosal immune stimula-
tion.

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