

## CORRESPONDENCE

***Shigella boydii* as Cause of Malacoplakia in a Human Immunodeficiency Virus–Infected Patient**

SIR—We read with great interest the report by Raguin et al. [1] on *Shigella boydii* as a possible causative agent of colonic malacoplakia in an HIV-infected patient. In the absence of positive cultures, *S. boydii* was identified by means of universal bacterial 16S rDNA–based amplification and sequencing. Since malacoplakia is usually caused by *Escherichia coli*, a close relative of shigellae and genetically belonging to the same species (!), despite being classified in 2 separate genera for reasons of different clinical and epidemiological significance, the reliable separation of these 2 organisms would be essential to accepting the conclusion made by the authors. On the basis of the data presented (highest relatedness of the sequence detected to *S. boydii*, with 459 [98%] of 468 nucleotides being identical) and the analysis shown below, this does not seem possible.

When the fragment of the *S. boydii* 16S rRNA gene amplified with primers 91E and 13B [2, 3] is compared with the corresponding sequences deposited in the EMBL/Genebank databases, no differences at all are found between it and several other members of the family Enterobacteriaceae, including *E. coli*, *Escherichia vulneris*, *Salmonella paratyphi* A, *Salmonella weltevreden*, *Shigella sonnei*, *Shigella flexneri*, and *Hafnia alvei*. Above the 98% identity level, there are also other organisms, such as *Klebsiella planticola* and *Citrobacter diversus*. Furthermore, intraspecies variation of 16S sequences has been described for various organisms [4, 5].

This illustrates that several species and genera within the family Enterobacteriaceae are so closely related to each other that their identification solely on the basis of partial sequences of their 16S rRNA genes is certainly not conclusive, even if the amplified fragments are repeatedly sequenced in both directions, thus resulting in absolutely reliable sequence data.

On the basis of the above considerations, we think that it is rather unlikely (though not impossible) that malacoplakia in the patient described was indeed caused by *S. boydii*.

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## Reply

SIR—Altwegg and Hinrikson, in their letter, question the conclusion in our report that *Shigella boydii* may be the causative agent of malacoplakia. We agree that the fragment of the 16S rRNA gene amplified with primers 91E and 13B does not permit sequences of several members of the family Enterobacteriaceae to be distinguished reliably.

At the time of writing our report, the BLAST search version we used (BLASTN 1.4.9 MP 26 h1996) gave the highest score of homology for *S. boydii*, closely followed by *Shigella sonnei*, *Shigella flexneri*, *Hafnia alvei*, and *Escherichia coli*. We agree that the subtle differences given by the alignment search tool should have been interpreted more cautiously. However, since then, we have used the Microseq 16S rRNA Gene Kit (Perkin-Elmer, Applied Biosystems, Foster City, CA) to amplify the first 500 bp in the 5' region of the bacterial 16S rDNA gene, which allows discrimination between *S. boydii* and *E. coli*. The DNA extracted from the malacoplakia tissue was confirmed to contain a 16S rDNA sequence giving the highest genetic relatedness with *S. boydii* 16S sequences and demonstrating 7 bp of difference from *E. coli* 16S rDNA sequences in discriminant codons.

On the basis of these data, we think that it is probable (though not certain) that malacoplakia in the patient described was caused by *S. boydii*.

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