Antimicrobial peptides are important components of natural immunity and have been described for and isolated from plants, insects, and mammals (3). They have been classified in several different families on the basis of their structural features, antimicrobial properties, and expression patterns (2). In mammals, defensins and cathelicidins can be considered the most important antimicrobial peptides, whose main but not only function is to provide a first line of defense against bacterial, fungal, and viral infections, both at epithelial surfaces and in phagocytic cells (4, 5).

Animal models have been used to understand different aspects of innate immune responses in several human diseases (7). Recently, Bals et al. (1) suggested that the rhesus monkey (Macaca mulatta) could be a useful model to study innate immunity in human pathologies. In fact they have found a high homology between β-defensins 1 and 2 and the cathelicidin LL-37/hCAP-18 in Homo sapiens and M. mulatta, which suggests that innate immune responses in nonhuman primates are very similar to those in humans.

We have sequenced the two exons of β-defensin 2 homologous in two different species of the genus Macaca: M. mulatta and M. fascicularis. Genomic DNAs were extracted from hairs by using the Chelex-100 method (8). Primers for PCR (5'-GA CTTTATAGGGTAAAGCGT-3' [forward] and 5'-CTA CGGCTTCTCTCCATTGGG-3' [reverse] for exon 1 and 5'-T GAGTTTGTAGGTCCTTACCGTCT-3' [forward] and 5'-GG AGAGCAGAAAGGGTTTGT-3' [reverse] for exon 2) were designed on the basis of the published human β-defensin 2 sequence (EMBL accession number AF071216). DNA sequencing of both DNA strands was performed using the BigDye Terminator Reaction kit (Applera). Ten wild-caught animals of each species were analyzed. No intraspecific variability in nucleotide sequences was observed.

M. mulatta and M. fascicularis peptides showed the same nucleotide sequences for the coding region of β-defensin 2; conversely, we observed a 90% homology between Macaca (both M. mulatta and M. fascicularis) and the H. sapiens coding regions (19 of 195 sites were found to be variable). This results in 14 (22%) of 65 amino acids being different in the Macaca and human peptides. Most of the amino acid replacements were localized in the active region of the protein (Fig. 1).

Our results and the findings of Bals et al. (1) could be explained by hypothesizing that (i) M. mulatta and M. fascicularis have selected more β-defensins than humans or (ii) other, unknown β-defensins not yet isolated exist in humans. The first hypothesis is supported by the findings of Tang et al. (6) which demonstrated that the rhesus monkey has more α-defensins than humans. In fact seven α-defensins are present in leukocyte granules of M. mulatta, four of which are highly similar to the human neutrophils HNP-1 to HNP-3, while the other three α-defensins are more similar to the human enteric HD-5. At least two β-defensin 2 homologous genes could be present in Macaca species; one a close homologue of the human gene, the other having originated in response to different environmental pathogens.

These findings must be taken into account in considering nonhuman primates as a model for investigating innate immune responses in human diseases.

REFERENCES

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Author’s Reply
The letter from Boniotti et al. reports the identification of genomic sequences from two species of the genus Macaca.
These sequences likely represent the genes of novel antimicrobial peptides. The putative defensin genes of the two species were identical in the coding region, with no intraspecific variability. It would be interesting to measure the expression or to clone the cDNAs of these novel peptides. In comparison to hBD-2 and rhBD-2 (the human and the M. mulatta peptides) the M. mulatta and M. fascicularis peptides described by Boniotto et al. (which are identical) differ in 14 or 15 out of 64 amino acids, respectively. As described in our report, hBD-2 and rhBD-2 differ in 1 out of 64 amino acids (1). These results show that the organization of β-defensins (genomic and functional) is likely more complex than initially thought. Several hypotheses to explain the new findings are discussed in the letter. In my opinion the genomes of humans and animals of the genus Macaca probably contain a large number (4 to 20) of β-defensins genes. For humans, four peptides have been identified and functionally characterized (2–6). Computer-based screening of genomic databases has identified numerous candidate sequences of putative novel β-defensins.

REFERENCES

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