

ROLE OF INTEGRONS IN THE TRANSMISSION OF ANTIBIOTIC RESISTANCE IN THE GENUS *Acinetobacter*

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The dissemination of antibiotic resistance genes among bacteria is an increasing problem, which requires further studies in order to elucidate the mechanisms by which resistance genes are transferred. **Integrons** are genetic elements that possess a specific integration site, *attI*, in which gene cassettes, mostly antibiotic-resistance determinants, can be inserted and accumulated. These elements, therefore, appear to be a kind of naturally occurring cloning and expression vector. Originally described in clinical isolates of many different pathogenic bacteria, integron structures were recently found also in environmental organisms.

The aim of the study was to ascertain the presence and the spread of class 1 integrons (the most frequent class in Gram negative bacteria) **among bacteria of the genus *Acinetobacter***. *Acinetobacter* are ubiquitous organisms, widely distributed in nature (soil, water, activated sludge, etc.) and generally regarded as commensals of human skin and respiratory and genitourinary tracts. During the last 20 years, however, *Acinetobacter*, and particularly *Acinetobacter baumannii*, have gained increasing significance as opportunistic pathogens in hospitalized patients. Treatment of the infections, caused by these organisms, is complicated by their widespread multidrug resistance.

Methods: 122 *Acinetobacter* isolates, identified by ARDRA, were analyzed. 64 were of clinical origin and were collected from 6 different Italian hospitals, between 1989-2000 and 58 were isolated from environmental samples of Friuli-Venezia-Giulia. All isolates were analyzed for the presence of *intI1* (integrase gene). Only those *intI1* positive were amplified with class 1 integron-specific primers and the amplicons obtained were sequenced. The antibiotic resistance profile of all isolates were also investigated.

Results: Class 1 integrons were detected only in 20/40 (50%) clinical isolates of *A. baumannii*. Surprisingly, most (17) of them, although not clonally related (they belonged to 8 different ribotypes), had the same arrangement of cassettes: *aacC1* (gentamicin resistance), *orfx*, *orfx'* (unknown function) and *aadA1* (streptomycin res.). The sequence of this insert has 99% of identity with integrons described in other *Enterobacteriaceae*. This indicates that integrons are stable structure that can be horizontally transmitted not only among *A. baumannii* strains with different genotype but also among strains belonging to different genera. As a consequence, in this bacterial species, transfer of the entire integron could be a more frequent event than single gene mobilization.

A strong correlation between integron carriage and multidrug resistance was also detected even if only few of the resistances observed were directly related with the genetic determinants carried by integrons.

No class 1 integrons were found in isolates from environmental samples. The level of antibiotic resistance in these isolates was much lower than the one of clinical strains and multiresistant isolates were not detected. However, significantly high frequencies of resistance to chloramphenicol (23%), ampicillin (41%), piperacillin (9%), tetracycline (7%), aztreonam (52%) were found.

In conclusion, class 1 integrons were found only in clinical isolates identified as *A. baumannii*, the most relevant pathogen of the genus. This would mean that antibiotic selective pressure can play a significant role in promoting the incorporation and maintenance of gene cassettes in the variable region of integrons and that *A. baumannii* might have acquired integrons from pathogenic *Enterobacteriaceae*. Environmental *Acinetobacter* don't seem to play a significant role as reservoir of resistance genetic determinants for clinical strains. However we can't exclude the presence of integrons of other classes in these strains.