Asia Pacific Journal of Molecular Biology and Biotechnology
Volume 3, No. 4, December, 1995. pp. 356-361.

In Vivo Genetic Stability of *Salmonella typhi* Detected by Ribotyping and Pulsed-Field Gel Electrophoresis

KWAI-LIN THONG[1], SAVITHRI D. PUTHUCHEARY[2], TIKKI PANG[3]*

Centre for Foundation Studies in Science[1], Dept. of Medical Microbiology[2] and Institute of Advanced Studies[3], University of Malaya, Kuala Lumpur, Malaysia.

(Received19 September 1995/Accepted 10 October 1995)

Abstract. Ribotyping, PCR-ribotyping and pulsed-field gel electrophoresis were used to analyze five serial isolates of *Salmonella typhi* obtained from a single patient with relapsing typhoid fever over a 7-week period. The 5 isolates were genetically identical by all three methods thus suggesting relapsing infection with the same strain and implying *in vivo* genomic stability of *S. typhi* even in the presence of selective pressures of antibiotic treatment and host defenses.

INTRODUCTION

The molecular analysis of bacterial pathogens relies to a large extent on the development of molecular approaches which are reproducible and highly discriminatory for differentiating individual strains of these pathogens. These approaches include multilocus enzyme electrophoresis, restriction endonuclease analysis, ribotyping, pulsed-field gel electrophoresis (PFGE), polymerase chain reaction (PCR)-based profiling and nucleotide sequence analysis [1]. Ribotyping and PFGE, in particular, have been widely used recently in molecular epidemiological investigations of infections caused by a large number of bacterial pathogens, including those caused by pathogenic *Salmonella* spp, including *Salmonella typhi*, the causative agent of typhoid fever [2, 3], and *S. enteritidis*, the primary cause of non-typhoidal salmonellosis [4, 5]. However, in addition to investigations of epidemic and nosocomial outbreaks, these methods are also applicable to molecular typing at the level of the individual patient. The use of such typing systems to examine multiple isolates recovered sequentially from an individual patient may help differentiate between relapsing infection with the same strain or reinfection with a new strain [1]. It may also help to define the pathogenesis of the infection and the role of other concomitant factors, e.g. exposure of pathogenic strains to host defenses and antimicrobial agents. It is also of value in assessing the *in vivo* genomic stability of a particular organism. We report here the use of ribotyping, PCR-ribotyping and PFGE to demonstrate *in vivo* genotypic stability of strains of *S. typhi* isolated from a single patient with relapsing typhoid fever.

MATERIALS AND METHODS

A total of 5 isolates of *Salmonella typhi* was obtained from our patient, a 38 year old male admitted to the University Hospital, Kuala Lumpur, Malaysia with a provisional diagnosis of typhoid fever. The first isolate was obtained from blood on April 8 followed by four subsequent isolations from feces on May 6, May 30, May 31 and June 1. A Widal test performed on the patients' sera on April 18 and May 6 was also strongly suggestive of typhoid fever. The patient was initially treated with gentamicin and cefuroxime for 3 days and, when the blood culture was positive for *S. typhi*, treated with chloramphenicol for 2 weeks. The patient was then discharged but re-admitted when he became ill again. On re-admission he was treated with ceftriaxone for 2 days followed by chloramphenicol and ampicillin for 2 weeks. When the stool cultures showed the presence of *S. typhi*, the patient was also given ciprofloxacin. The patient was finally discharged from the hospital on

*Correponding author mailing address: Professor Tikki Pang, Institute of Advanced Studies, University of Malaya, 59100 Kuala Lumpur, Malaysia. Telephone No. : 60 3 759 4437. Fax No. : 60 3 756 8940. e-mail: h1tikkip@cc.um.my