1. INTRODUCTION

The genetic diversity within a bacterial species is determined by the number and size of chromosomal and extrachromosomal elements, rates of nucleotide substitution, recombination, genome rearrangements and gene flow, and both the size and growth of the bacterial population. Most species of bacteria that were initially analyzed, were of a clonal nature.\textsuperscript{77} The structural characteristics of a clonal population are the paucity of genotypes, linkage disequilibrium among gene loci, and recovery of closely related genotypes over large geographic areas and/or over long periods of time. The accumulation of molecular data during the last 15 years and the growing evidence of the occurrence of horizontal gene transfer among bacteria in nature, however, have led to consideration that bacterial populations are not invariably clonal but range from the highly sexual \textit{Neisseria gonorrhoeae} to the almost strictly clonal \textit{Salmonella}.\textsuperscript{80}

The metabolically versatile \textit{Pseudomonas aeruginosa} is present in soil and aquatic habitats, but it is also an important opportunistic pathogen for humans, animals, and plants. Typing of strain collections in single nucleotide polymorphisms (SNPs), DNA fragment length polymorphisms and phenotypic traits indicated that the current \textit{P. aeruginosa} population is in linkage equilibrium and consists of a net of equivalent genotypes (termed clones), whereby a subset of clones is overrepresented due to epidemic spread.\textsuperscript{36,60} Isolates from the
inanimate environment and clinical habitats have been shown to share the same chemotaxonomic profile\cite{23} and repertoire of metabolic and virulence traits.\cite{1} Irrespective of their origin, isolates from disease and environment were similarly proficient in the degradation of environmental pollutants and secretion of virulence factors.\cite{1} In other words, there are no disease- or habitat-associated clones. However, we do observe adaptation of \textit{P. aeruginosa} to a particular niche. Most data exists of how \textit{P. aeruginosa} colonizes and persists in the atypical habitat of the cystic fibrosis (CF) lung where independent of the genetic background of the clone a convergent evolution towards common phenotypes takes place.\cite{89}

This chapter summarizes our current knowledge about the inter- and intraclonal diversity of genotype and phenotype of \textit{P. aeruginosa}.

2. \textbf{INTRA- AND INTERCLONAL GENOME DIVERSITY}

Physical mapping and sequencing and Southern hybridization data indicate that the \textit{P. aeruginosa} genome is made up of a mosaic of a conserved core and variable accessory segments.\cite{20,31,36,66,84} The core genome is characterized by a conserved synteny of genes and a low average nucleotide substitution rate. Clone- or strain-specific genome islands and genome islets define the accessory part of the chromosome and lead to fluctuations in the genome size, which can range from 5.2 to 7 Mbp.\cite{73}

2.1. Clonal Variation of the Core Genome

The complete genome sequence of strain PAO1\cite{85} is the genetic blueprint for \textit{P. aeruginosa}. Genomic DNA hybridization of in total 39 \textit{P. aeruginosa} strains of diverse origin onto PAO1 microarrays\cite{20,95} detected the presence of almost 90\% of the 5570 predicted PAO1 protein coding sequences in all strains. Hence, the core genome is made up of about 5000 highly conserved genes.

Interclonal sequence variation is low in the \textit{P. aeruginosa} core genome. Comparative sequencing of housekeeping genes in strain collections revealed an average rate of sequence polymorphism of 0.3\%, which is about one order of magnitude lower than in comparable housekeeping genes of \textit{Salmonella enterica}.\cite{36} The ratio of non-synonymous to synonymous nucleotide substitutions is about 1:6. Sequence variation within clones is substantially lower than the already low sequence diversity amongst unrelated clones: Within 300 kb of bulk sequence, just a single synonymous nucleotide substitution was detected in one of four analyzed strains.\cite{36,43} In other words, members of a clone are characterized by virtually identical core genome sequence in all segments with low sequence diversity.

Figure 1 shows the comparison of 49 single nucleotide substitutions (SNPs) of \textit{P. aeruginosa} detected in ori\textit{C}, amp\textit{C}, cit\textit{S}, fit\textit{C}, opr\textit{I} with 500 SNPs of \textit{S. enterica} detected in gap\textit{A}, put\textit{P}, and mdh.\cite{37} In contrast to the high GC