

Phylogenetic Analysis of Type I and Type II Polyketide Synthase from Tropical Forest Soil

Mei-Fong Pang, Geok-Yuan Annie Tan, Noorlidah Abdullah,
Choon-Weng Lee and Ching-Ching Ng

Institute of Biological Sciences, Faculty of Science, University of Malaya,
50603 Kuala Lumpur, Malaysia

Abstract: Culture-independent approach was employed to retrieve diverse type I and type II polyketide synthase (PKS) ketosynthase (KS) domains from community DNA extracted from forest topsoil. Type I KS domains detected were from four phyla which comprised Cyanobacteria, Proteobacteria, Actinobacteria, Chloroflexi and uncultured bacteria. The type II KS_α domains were derived from four suborders of actinobacteria in addition to uncultured bacteria. Approximately 25% of the KS domains were recovered from uncultured bacteria and many sequences of type I KS were derived from Myxobacteria. BLASTP results showed that the type I and type II KS domain amino acid sequences were between 52 to 93% identical to the comparative sequences in the GenBank database. Phylogenetic analysis for novelty prediction of KS domains showed 14 and 9 novel clades of type I KS and type II PKS KS_α domains, respectively. These phylogenetically distinct novel clades might represent a new subclass of KS domains. Present data suggests the possibility of further discovery of novel genes encoding bioactive compounds which may have medical and pharmaceutical value.

Key words: Culture-independent, tropical soil, polyketide synthase (PKS), ketosynthase (KS), phylogenetic analysis

INTRODUCTION

It has been estimated that there are approximately 2.6×10^{29} prokaryotes residing in soil (Whitman *et al.*, 1998). Yet, only a small fraction of them (0.1 to 1%) are cultivable with current techniques (Torsvik *et al.*, 1990). Most of the microbial diversity has not been revealed due to the limitation of cultivation (Hugenholtz and Pace, 1996). Since most prokaryotic microbes are known to produce pharmaceutically important secondary metabolites through polyketide synthase (PKS) pathways (Hertweck *et al.*, 2007; Staunton and Weissman, 2001) this massive uncultured community is a large genetic reservoir that contains numerous promising source of novel polyketide chemical structures (Pettit, 2004). Diversity of novel polyketide chemical structure could be utilized to curb the emerging resistance to existing antibiotics among infectious pathogens.

Polyketides are secondary metabolites which possess pharmacologically important activities such as

antimicrobial, antifungal, antiparasitic, antitumor and agrochemical properties (Metsa-Ketela *et al.*, 1999; Staunton and Weissman, 2001). To date, three different classes of PKS genes have been discovered (Shen, 2003). Type I PKS consists of large, multi-domain and highly modular proteins that produce polyketides by successive condensation of simple carboxylic acid units. Type I PKS encodes for macrolides such as erythromycin (antibiotic) and rapamycin (immunosuppressant) which have an indispensable role in medical treatment (Staunton and Weissman, 2001). Type II PKS comprises of aggregates of mono-functional proteins which catalyze formation of compounds through aromatization and cyclization. Doxorubicin (anticancer) and tetracyclines (antibiotic) are among the products synthesized by the type II PKS biosynthesis pathways (Hertweck *et al.*, 2007). Type III PKSs is chalcone synthase-like PKS that is involved in synthesis of chalcones (CHS) and stilbenes in plants and polyhydroxy phenols in bacteria (Hutchinson, 1998). Chalcone and stilbenes are plant-specific PKS which

Corresponding Author: Dr. Ching-Ching Ng, Institute of Biological Sciences, Faculty of Science,
University of Malaysia, 50603 Kuala Lumpur, Malaysia
Tel: +60-(0) 3-79675872 Fax: +60-(0) 3-79675908