Use of Genomic Approaches in Understanding the Role of Actinomycetes as PGP in Grain Legumes

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Mamta Sharma, Avijit Tarafdar, and Raju Ghosh

Abstract

The advancement in molecular technologies has given a breakthrough to explore the untapped and novel microbial isolates for characterization in every aspect as we can consider microbes as an important primary natural store house for key secondary metabolites and enzymes. Actinomycetes are the most fruitful source of microorganisms for all types of bioactive secondary metabolites, including agroactive-antibiotic molecules that are best recognized and most valuable for their role in agriculture and industries. In agriculture, actinomycetes are used as biocontrol agents against some pests and pathogenic organisms as well as plant growth-promoting (PGP) agents for crops. Use of different molecular methods, e.g., metagenomics, metatranscriptomics, genetic fingerprinting, proteogenomics, and metaproteomics, are more significant for classifying and discovering the immense diversity in microbial population and for understanding their interactions with other abiotic and biotic environmental elements. The opportunity of accessing inexpensive sequencing techniques has led to the assemblies of copious genomic data for actinomycetes, such as *Streptomyces* and related species, with the goal of discovering novel bioactive metabolic and their utility as PGP; however, the use of actinomycetes in agriculture using genomic approaches is in its initial stages.

Keywords

Actinomycetes • Plant growth-promotion • Grain legumes • Whole genome sequence • Molecular technologies

16.1 Introduction

The analysis of microbial communities with the recent advances in culture-independent molecular techniques, including sequencing

M. Sharma (✉) • A. Tarafdar • R. Ghosh
International Crops Research Institute for the Semi-Arid Tropics (ICRISAT), Hyderabad, Telengana 502 324, India
e-mail: mamta.sharma@cgiar.org

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technologies and genomics information, has begun a new era of microbial ecology. Multiple techniques in molecular approaches based on direct analysis of lipids, proteins, and nucleic acids from environmental samples have uncovered structural and functional information about microbial communities. Molecular techniques, such as genetic fingerprinting and whole genome sequencing (WGS), are important tools for discovering, characterizing the diversified microbial population, and understanding their chemistry with other abiotic and biotic factors in environs.

Molecular and advanced technologies have a massive role in investigating the knowledge by exploring the actinomycetes across the microbial world. Advancement of WGS has made a scientific breakthrough, which unchains the understanding of latent biochemical and molecular topographies of uncultured microbe present in composite environs. The tactic of WGS of microbes bare the chemistry of the cryptic clusters of biosynthetic-related genes that are sometimes present but hidden, because those are not well recognized for producing any bioactive secondary metabolites (Fraser et al. 2002). In recent days, a total number of six genera of actinomycetes viz. *Corynebacterium*, *Mycobacterium*, *Arthrobacter*, *Frankia*, *Rhodococcus*, and *Streptomyces* have enough information about complete genome sequences to extemporize the core analysis of potential secondary metabolite and gene diversity (James and William 2013). Utilizing inexpensive sequencing techniques has led to the gathering of enormous genome sequencing data for *Streptomyces* and related species (Liu et al. 2013) with the goal of discovering novel bioactive metabolites. This chapter summarizes recent progress in the potential applications of actinomycetes using genomic approaches in agriculture. How they can be combined for a comprehensive evaluation of actinomycetes has been illustrated with example studies.

16.2 Role of Molecular Approaches for Identification of Actinomycetes

For identification and characterization of any biological organism, nucleic acid-based molecular approach is considered the most powerful approach and provides significant information about the organisms and the relationship with others (Kumar et al. 2014a). In past decades, classification and identification of organisms by approach of molecular systematics was based on nucleic acid hybridization studies. Gradual introduction of nucleic acid-based sequencing techniques in molecular systematics has been proved to be authentic (O'Donnell et al. 1993).

Following the polymerase chain reaction (PCR) technology, for better separation of the PCR products in polyacrylamide matrix, urea-formamide denaturing gradient gel electrophoresis (DGGE) (Myers et al. 1985) and temperature gradient gel electrophoresis (TGGE) (Riesner et al. 1989) were well adapted in the laboratory for studying microbial ecology. Later, for getting a sequence-based DNA fingerprint of microbial populations, temperature gradient gels were found to be quite promising (Muyzer 1999). Heuer et al. (1997) used DGGE and TGGE to study the genetic diversity of actinomycetes in different soils and to monitor shifts in their abundances in the potato rhizosphere. They used actinomycetes group-specific primers for the direct amplification of 16S rDNA and an indirect nested PCR approach using a forward actinomycetes group-specific primer and a reverse bacterial primer, followed by PCR with two bacterial primers. Use of DGGE or TGGE of the products obtained with the nested PCR made it possible to estimate the abundance of the actinomycetes populations relative to the abundance of the other bacteria present in the soil.

Sequence of 16S rDNA in systematic as well as phylogenetic studies of actinomycetes and

other bacteria is another most commonly used approach. Primarily, the study of identification and evolution of actinomycetes based on 16S rDNA has been initiated by amplifying the 16S rRNA gene implying PCR strategy and followed by direct sequencing of amplified DNA fragments (Shiva 2001). Generally, thereafter, the obtained sequences are further explored in global database using bioinformatics tools to find out the identity and genetic information of query sequence if available, followed by analysis of phylogenetic correlation which reveals the identification of the actinomycetes up to the genus level and an overview on evolutionary aspect.

In a study by Intra et al. (2011), 16S rRNA gene sequences were used to identify the diversified actinomycetes groups exists in a collection of environmental samples. Detailed comparison of 16S rRNA gene of 30 actinomycetes isolates determined that majority of the isolates (87 %) within the environmental samples belong to the genus *Streptomyces* spp., whereas one each belongs to *Saccharopolyspora* and *Nocardiopsis* and two to *Nocardia*. However, 16S rRNA sequencing does not always give clear resolution to distinguish between closely related genera (Girard et al. 2013). To order the actinomycetes, they presented a novel method based on the conserved sequence of genes *Ssg*A and *Ssg*B proteins. The wide conserve feature between members of the same genus in amino acid (aa) sequence of the *SsgB*, e.g., only one aa variation was found in between all the *Ssg*B orthologues of identified in *Streptomyces*, whereas it has low sequence identity as 40–50 % even between genera of closely related morphologically complex actinomycetes, provides concrete data for better resolution in classification systems. Recently, real-time PCR (RT-PCR) technology is being used for the specific detection and quantification of selected PGP genes of actinomycetes. Quantitative real-time PCR of selected PGP genes of actinomycetes revealed the selective up-regulation of indole acetic acid (IAA)-related and siderophore-related genes by *Streptomyces* sp., CAI-68 and of β-1,3-glucanase genes (Gopalakrishnan et al. 2015).

16.3 Utility of Advanced Genomic Approaches in Actinomycetes

The genomic technologies are promising tools to explore the untapped and novel microbial isolates for characterization in all aspects as we can consider its significance as natural store house of excellent enzymes and bioactive secondary metabolites. Fluorescence-activated cell sorting (FACS) technology is a quick method for separating the cells in a suspension on the basis of fluorescence and cell size. This technology can be performed for isolation of actinomycetes cell from a complex microbial population. Gel MicroDrop technology is an efficient enzyme-fluorescence technology, basically used for detection of positive clones by capturing of emitted fluorescence from catalytic broke down of biotinylated substrate by specific top articular enzymes present in the positive clone (Short et al. 2003).

Recently, high throughput screening (HTS) technique is considered to be rapid and economical for classifying of any microbial population by enzymatic characterization, but it is extended very little for actinomycetes. HTS consists of drop-based microfluid platform and gives an array data of insoluble substrates specific for the desired enzymes (Chang et al. 2013). Compared with all HTS-based methods, currently the proteomics approach is well accepted in the way of discovering new microbial flora and fauna. Wang et al. (2012a) first reported on *Streptomyces* sp. products α-glucosidase inhibitor miglitol using HTS method. They considered 12 actinomycete strains as to be producers of α-glucosidase inhibitors in which strain PW409 showed effective inhibitory and was used for fermentation and separation of bioactive compound using HPLC. In mass spectrometry, two compounds, miglitol and 1-deoxynojirimycin, were identified. The method can be utilized for discovering new α-glucosidase inhibitors or identifying from other inhibitory strains.

However, the common PCR methods used in microbial detection, the amplified DNA fragment, is always not prominent in visibility for

the important microbial species, which are relatively less abundant. Nowadays, two promising and pioneering approaches, preamplification inverse-PCR (PAIPCR) and substrate-induced gene expression screening (SIGEX), are used extensively to overcome this problem in characterization of actinomycetes from metagenomic DNA shuffling in a particular microflora (Kennedy et al. 2010). MALDI-LTQ-Orbitrap is one of the proteomics-based techniques for identifying desired proteins from suspensions and complex matrices. This technique is worked based on the principal of chromatography separations in both media liquid and gas with the coordination of MALDI and ion trap system (Akeroyd et al. 2013). Electrospray ionization mass spectrometry (ESI-MS) is another promising ionization technique that can measure proteins as little as femtomole quantities (Smith et al. 2013). Few in silico techniques, e.g., 3DQSAR, CoMSIA, and CoMFA, are likely to be promising to characterize potent enzymes from database and have the ability to predict superior enzymes and its in silico reaction with substrate and development of microenvironment during reaction (Murumkar et al. 2009).

16.4 Application of Actinomycetes in Agricultural Crops: Genomic Approach

16.4.1 Actinomycetes as Source of Bioactive Compounds

Actinomycetes specifically *Streptomyces* are the most fruitful source for all types of bioactive secondary metabolites. Approximately 60 % of the new insecticides and herbicides reported in the past 5 years originate from *Streptomyces* (Tanaka and Omura 1993; Roshan et al. 2013; Kumar et al. 2014b). It also is estimated that as many as three-quarters of *Streptomycetes* spp. are able to produce antibiotics (Alexander 1977). Actinomycetes produce a variety of secondary metabolites and have a wide range of uses, including antimicrobial, antifungal, herbicidal, antineoplastic, and plant growth-promoting agents. Gopalakrishnan et al. (2011) reported the potential of selected actinomycetes isolates as biological control of *Fusarium* wilt and dry root rot diseases in grain legumes. They reported five most promising antagonistic isolates of *Streptomyces*'s species (CAI-24, CAI-121, CAI-127, KAI-32, and KAI-90) and characterized for the production of siderophore, hydrocyanic acid (HCN), protease, cellulase, IAA, etc. These actinomycetes are likely to be the potential organisms for discovery of novel secondary metabolites for various biocontrol applications.

16.4.2 Actinomycetes as a Source of Nitrogen Fixation

Generally, population of actinomycetes is largely higher in rhizosphere in comparison of non-rhizosphere soils (Miller et al. 1989, 1990). Root colonization of *Streptomyces griseoviridis* in SEM studies showed a higher density in the rhizosphere of lettuce than in non-rhizosphere soil (Kortemaa et al. 1994). A similar result was found when interaction of *Streptomyces lydicus* WYEC 108 and nodules of pea was studied in SEM. *S. lydicus* was found to be colonized at nodulation sites, and then the vegetative hyphae moved onto root hairs and from the external surface of the root cells to the inside of the root cells, intermittently (Tokala et al. 2002). The PCR-DGGE analysis of DNA from colonized nodules showed the presence of a *Streptomyces* band in addition to other bands corresponding to the plant and *Rhizobium*.

Rhizobia with legumes are considered under PGPR genera and play a bigger role in nitrogen fixation. Nitrogen is the most essential nutrient for plant productivity and growth, and it is a vital element for all forms of life. Although 78 % of the atmospheric volume contains dinitrogen they remain unavailable to the plants. Plant growth-promoting actinomycete *Frankia* has the ability to fix atmospheric nitrogen to ammonia

(available form for plants) and provide it to plants by symbiotic association with non-leguminous trees and shrubs (Zahran 2001; Ahemad and Kibret 2014). The nitrogenase (*nif*) genes responsible for nitrogen fixation are found in systems: free living or symbiotic (Reed et al. 2011). The *nif* genes include structural genes responsible for electron donation, iron-molybdenum cofactor biosynthesis, and involved in activation of the Fe-protein, and regulatory genes responsible for the synthesis and function of the enzyme.

16.4.3 Molecular Basis of Nitrogen Fixation

Agrobacterium rhizogenes and *Agrobacterium tumefaciens* are available for studying down-regulation of plant genes by RNAi in some actinorhizal plants (Svistoonoff et al. 2003; Gherbi et al. 2008a, b). In transcriptome analyses, it is found that the common symbiosis (SYM) pathway shared by rhizobium-legume and arbuscular mycorrhizal for nodulation symbiosis is present in *Frankia* (Gherbi et al. 2008a, b; Markmann et al. 2008; Hocher et al. 2011). For the induction of calcium oscillations in this pathway, a receptor, potassium channels, and nuclear pore proteins are required. A putative calcium/calmodulin-dependent protein kinase (CCaMK) also is present and might thus recognize calcium "actinorhizal signatures" (Singh and Parniske 2012). The similar genes linked to a NOD-specific pathway used by legumes for the nodulation process also is present in *Frankia*. This overlapping of legume and actinorhizal root nodule symbiosis RNS supports the hypothesis of a common genetic ancestor with a genetic predisposition for nodulation in the nitrogen-fixing clade (Soltis et al. 1995).

Because traditional approaches are not yet available for studying *Frankia* genetics, most work has proceeded through the cloning of genes via heterologous hybridization to genes from other organisms, most notably those involved in nitrogen metabolism. These genes include the cloning and sequencing of *nif*H (Normand and Bousquet 1989; Normand et al. 1988), *nif* D (Twigg et al. 1990; Normand et al. 1992), part of *nif*K (Twigg et al. 1990), *nif*B, *nif*X, *nifW*, and *nif*Z, open reading frames that correspond to the *Azotobacter vinelandii* orf 3 and *Azorhizobium caulinodans* orf l (Arigoni et al. 1991). At least 20 *nif* genes are involved in N_2 fixation in the well-characterized *Klebsiella pneumoniae*, and many of these genes have homologs in other diazotrophs (Dean and Jacobson 1992).

The nitrogenase and associated proteins are highly conserved in prokaryotes. Nitrogenase of *Frankia* also is O_2 labile, requires Mg ATP and reducing power, and produces NH_4^- and H_2 gas in an ATP-dependent fashion (Benson et al. 1979). There is no alternative N_2 fixing systems akin to the vanadium or iron-based nitrogenases reported from *Frankia*. Because *Frankia* grow and respire slowly, the delivery of substrates to nitrogenase and the maintenance of a low O_2 level in the proximity of nitrogenase are important problems encountered by *Frankia* strains. The structural genes for the Fe protein and the Mo-Fe protein of nitrogenase are encoded by the *nif*H and the *nif*D and *nif*K genes, respectively. Hybridization results have indicated that *nif*HDK in some *Frankia* strains are clustered on the chromosome (Mullin and An 1990), five genes about 4 kbp downstream from *nif*HDK have been sequenced, four of which belong to a single operon consisting of at least orf 3, orf l, *nif*W, and *nif*Z; *nif*B is located immediately downstream from *nif*Z and may be transcribed as part of another operon. The *nif*B, *nif*W, and *nif*Z are all involved in FeMo-cofactor biosynthesis (Dean and Jacobson 1992). Nucleotide and amino acid sequence analyses of *nif*H, *nif*D, and other *nif* genes confirm the similarity of *Frankia* nitrogenase with the classical Mo-Fe protein based systems (Normand and Bousquet 1989; Normand et al. 1988; Simonet et al. 1986). The most common genes present in bacteria for symbiosis and N_2 fixation is as follows (Table 16.1).

Table 16.1 Most common genes present in bacteria and actinomycetes involved in symbiosis and nitrogen fixation

Genes	Function of gene product
Nodulation genes	
*nod*A	Acyltransferase
*nod*B	Chitooligosaccharide deacetylase
*nod*C	N-acetylglucosaminyltransferase
*nod*D	Transcriptional regulator of common nod genes
*nod*IJ	Nod factors transport
*nod*PQ	Synthesis of Nod factors substituent
*nod*X	Synthesis of Nod factors substituent
nof EF	Synthesis of Nod factors substituent
Other nod genes	Several functions in synthesis of Nod factors
nol genes	Several functions in synthesis of Nod factors substituent and secretion
NOE genes	Synthesis of Nod factors substituent
Nitrogen fixation genes	
nif HDK	Nitrogenase
*nif*A	Transcriptional regulator
nif BEN	Biosynthesis of the Fe-Mo cofactor
nif B, *nif* W, and *nif* Z	Fe-Mo cofactor biosynthesis
*fix*ABCX	Electron transport chain to nitrogenase
*fix*NOPQ	Cytochrome oxidase
*fix*LJ	Transcriptional regulators
*fix*K	Transcriptional regulator
*fix*GHIS	Copper uptake and metabolism
*fdx*N	Ferredoxin
Other genes	
exo	Exopolysaccharide production
hup	Hydrogen uptake
gln	Glutamine synthase
dct	Dicarboxylate transport
nfe	Nodulation efficiency and competitiveness
ndv	β-1,2 glucans synthesis
lps	Lipopolysaccharide production

Source: Laranjoa et al. (2014)

16.5 Characterization of Actinomycetes Through Whole Genome Sequencing

Advancement of WGS has unchained the understanding of whole biochemical and molecular potentiality prevailing even in those microbes incompetent in laboratory culture from a composite environment. The WGS of microbes revealed the chemistry of the cryptic clusters of biosynthetic-related genes that are sometimes present but hidden, because those are not well recognized for any secondary metabolites synthesis (Fraser et al. 2002). Currently, six genera of actinomycetes, namely *Frankia*, *Arthrobacter*, *Corynebacterium*, *Mycobacterium, Rhodococcus* and *Streptomyces*, have enough information on whole genome sequences to extemporize the basic analysis of potential secondary metabolite and gene diversity (James and William 2013).

16.5.1 Gene Cluster Diversity Within Actinomycete Groups

The genomes of actinomycetes revealed that they have gene clusters for a high number of natural products, although a lot of these are very complex to tie to products in the laboratory. The evaluations of these gene clusters are more difficult, because the existed domains of the most common biosynthetic machinery, non-ribosomal peptide synthetases (NRPSs) and polyketide synthases (PKSs), are repeated and highly similar. It is predictable that for being diverse lifestyles that habitats use secondary metabolites differently by different genera of actinomycetes.

In many genera, it was found that the siderophores are the most conserved secondary metabolite clusters, whether they are NRPS-independent or NRPS products. The study of Doroghazi and Metcalf (2013) showed that genomes 41 of 102 common actinomycetes contain at minimum one gene cluster for siderophore biosynthesis, which is NRPS-independent (aerobactin-like), whereas 31 genomes of 34 actinomycetes in the group of *Nocardia*, *Mycobacterium*, and *Corynebacterium* do not have this class of siderophores, but except *Corynebacterium kroppenstedtii* all contain the gene cluster for mycolic acid. In general, the more pathogenic genus *Mycobacterium* and *Corynebacterium* contain gene clusters for higher proportions of conserved secondary metabolite, whereas in *Streptomyces* and *Rhodococcus*, the

essentially saprophytic genera are less conserved. This may be due to pathogens that are inhabited in the increased homogeneity of environments compared with free-living bacteria. The pattern of host-association in *Frankia* is different where no overlap secondary metabolic capabilities are present. It is assumed that over the evolutionary period, the location of the gene clusters of natural product will change through horizontal gene transfer and it would make change in the genomes and phylogenetic trees because of genome rearrangements (Fischbach et al. 2008; Osbourn 2010).

Based on genomic data only, *Streptomyces* spp. are the most important actinobacterial groups for secondary metabolites (Table 16.2). *Streptomyces* consists of large numbers of biosynthetic gene clusters related to secondary metabolite with a large variety of classes. The common classes of PKS and NRPS are present in the majority of the *Streptomyces*, followed by terpenoids, aerobactin-like non-NRPS siderophores, and lanthipeptides. Most of the genomes contain the genes for butyrolactone biosynthesis. All *Streptomyces* spp. contain the genes responsible for the biosynthesis of the aerobactin-like siderophore desferrioxamine. Except for *S. griseus*, all *Streptomyces* contain gene cluster for the spore pigment type II PKS, whereas *S. griseus* contains type III PKS for a different spore pigment (Ohnishi et al. 2008). Only half of the strains, including *S. griseus* and *S. coelicolor* A3 (2), contain the gene cluster lanthipeptide *Sap*B that is required for aerial mycelia formation on rich media (Kodani et al. 2004). This genus has very low amount of overlap gene clusters of PKS and

Table 16.2 Recent genome publications for *Streptomyces* species

Species and strain	Motivation for sequencing	References
S. albulus CCRC 11814	Produces ε-poly-L-lysine antibiotic	Dodd et al. (2013)
S. albus J1074	Widely used host for heterologous expression of bioactive natural products; Small genome	Zaburannyi et al. (2014)
S. albulus PD-1	Produces ε-poly-L-lysine and poly-L-diaminopropionic acid antibiotics	Xu et al. (2014b)
S. bottropensis ATCC 25435	Produces bottromycin antibiotics	Zhang et al. (2013)
S. collinus Tu 365	Produces elfamycin-family antibiotic kirromycin	Rückert et al. (2013)
S. exfoliatus DSMZ 41693	Degrades poly3-hydroxyalkanoate	Martínez et al. (2014)
S. fulvissimus DSM 40593	Produces ionophore antibiotic valinomycin	Myronovskyi et al. (2013)
S. gancidicus BKS 13–15	Not known	Kumar et al. (2013)
S. mobaraensis DSM 40847	Industrial producer of transglutaminase	Yang et al. (2013)
S. niveus NCIMB 11891	Produces novobiocin, an aminocoumarin antibiotic	Flinspach et al. (2014)
S. rapamycinicus NRRL 5491	Produces immunosuppressant drug rapamycin	Baranasic et al. (2013)
S. rimosus ATCC 10970	Oxytetracycline	Pethick et al. (2013)
S. roseochromogenes subsp. *oscitans* DS 12.976	Produces clorobiocin, an aminocoumarin antibiotic	Rückert et al. (2014)
Streptomyces sp. Mg1	Causes lysis and degradation of *Bacillus subtilis* cells and colonies. Sequenced using the PacBio platform	Hoefler et al. (2013)
Streptomyces sp. PRh5	An endophyte isolated from wild rice root	Yang et al. (2014)
S. violaceusniger SPC6	Tolerant to multiple stresses. Small genome	Chen et al. (2013)
S. viridochromogenes Tu57	Produces oligosaccharide antibiotic avilamycin	Grüning et al. (2013)
S. viridosporus T7A	Produces oligosaccharide antibiotic avilamycin	Davis et al. (2013)

Source: Harrison and Studholme (2014)

NRPS. Although a large amount of polyketides and non-ribosomal peptides has been discovered already from *Streptomyces*, there are only a few reports for terpenoids in streptomycetes. However, a number of terpene synthases has been discovered in genomes of *Streptomyces* sp., suggesting that a large diverge group of terpenoids has remained to be discovered in members of this genus.

16.6 Genomics and Genetic Information of *Streptomyces*

With the goal of discovering novel bioactive compounds, the huge genomic data of *Streptomyces* and other related species has led to cheap genome sequencing techniques (Liu et al. 2013). However, productive "genome mining" is possible only when the gene clusters clone and express in any heterologous host or to force expression by genetic modification (Gomez-Escribano and Bibb 2014). Therefore, unavoidably there will be a lag between the initial state of genome characterization by sequencing and harder to depict the novel useful products by biochemical investigations. *Streptomyces* PRh5, an endophyte of wild rice, produces nigericin, an antibiotic active antagonized to mycobacteria is recently discovered (Yang et al. 2014). Genetic information of *Streptomyces* species and few other actinomycetes genera are as follows:

Streptomyces sp. strain CT34: total assembly size of the genome of *Streptomyces* sp. strain CT34 is 8,066,430 bp, with coverage of 99.85 %. The genome contains an average GC content of ~71.39 % with 7781 protein coding genes of an average length of 875 bp. The predicted total gene length is about 6,809,991 bp, which makes up 84.42 % of the genome. The analysis of genome data revealed that it comprises 30 gene clusters for secondary metabolites biosynthesis, including four for terpene biosynthesis, three of each for siderophores, PKSs (2T2-PKSs, 1T3-PKS), NRPSs, bacteriocins, and butyrolactones; two for lantipeptides, one of each for mixed lantipeptide/PKS (T1-PKS), mixed PKS (T4-PKS)/PKS (T1-PKS), mixed oligosaccharide/terpene, mixed non-ribosomal peptide synthetase (NRPS)/polyketide synthase (T1-PKS), and ectoine; and four unspecified clusters. A putative gene cluster of 12,108 bp comprises ten ORFs encoding proteins for catalytic activity and auxiliary functions and one ORF for the biosynthesis of prepeptide related to new linaridin RiPP is found to be present in the genome (Zhai et al. 2015).

Streptomyces sp. strain TOR3209: The draft genome sequence of *Streptomyces* sp. TOR3209 is 8,066,796-bp long with an average GC content of 72.59 %. It comprises 4 rRNA genes, 73 tRNA genes, and 7564 protein encoding genes with an average length of 937 bp. The sequence annotation revealed that among all of the genes, 187 genes are associated with transport, biosynthesis, and catabolism of secondary metabolites and 322 genes of unknown function. It is found that among the protein-encoding genes, several genes are involved with the regulation mechanism of rhizosphere microecology, because they take a part in the production of flavonol, flavone, hormones, terpenoid, quinone, antibiotics, and other active substances. In addition, 29 degradation pathways of toxic substances are present in TOR3209 genome. These distinguished features are not present in other microorganisms. The degradation pathways for toxic substances that are difficult to degrade include naphthalene, carbazole, fluorene, anthracene, xylene toluene, trinitrotoluene, atrazine, and ethylbenzene. These pathways may help to resolve toxic substances around crop roots. The genomic information of *Streptomyces* sp. strain TOR3209 has great significance to the research field oriented with the regulation mechanism of rhizosphere microecology (Hu et al. 2012).

Streptomyces sp. strain AW19M42: The total size of the genome is 8,008,851 bp and has a GC content of 70.57 %, similar to that of other sequenced *Streptomyces* isolates. A total of 7727 coding DNA sequences are predicted. In addition, 62 tRNAs and 8 copies of the rRNA operons are identified in the genome of *Streptomyces* sp. strain AW19M42 (Bjerga et al. 2014).

Streptomyces albus strain J1074: The total genome size of *S. albus* strain J1074 is 6,841,649 bp. It is one of the smallest

Streptomyces genomes along with *Streptomyces cattleya* (Zaburannyi et al. 2014). However, the strain contains a mega plasmid *p*SCAT of 1,809,491 bp. Analysis of chromosomal genes revealed that *S. albus* contains highest known GC content ~73.3 % within the Streptomycetes. It is found that *S. albus* have a tendency to reduce the number of orthologous groups of genes. Unlike those of other Streptomycetes genomes, it has the single chromosome includes 66 tRNA genes (41 species) and 7 rRNA operons (16S-23S-5S). The presence of seven rRNA operons may help the strain for its exceptionally fast growth rate and versatility (Klappenbach et al. 2000).

Streptomyces acidiscabies strain 84–104: The size of the draft genome sequence of *S. acidiscabies* is approximately 11,005,945 bp in length (Huguet-Tapia and Loria 2012). The genome encodes 10,070 putative proteins. Reciprocal BLAST analysis with other *Streptomyces* genomes is noted that *S. acidiscabies* 84–104 contains 75 tRNA genes and shares 3006 orthologs with *S. scabies*, *S. coelicolor*, *S. griseous*, *S. avermitilis*, and *S. bingchenggensis*. *S. acidiscabies* and *S. scabies* shares 357 orthologs, including many of which are in asyntenic (Huguet-Tapia et al. 2011).

Streptomyces albus strain NBRC 13014 T: The total size of the assembly of *S. albus* NBRC 13014T genome is 7,594,701 bp, with a GC content of 72.7 %. The genome contains at least one type-II PKS, two NRPS, two hybrid PKS/NRPS, and four type-I PKS gene clusters (Komaki et al. 2015). The type-II PKS gene cluster is required for synthesize of xantholipin-like compounds, because its CLF and KS showed 78 % and 89 % aa sequence identities to XanE and XanF, respectively (Zhang et al. 2012).

Streptomyces auratus strain AGR0001: The genome of *S. auratus* strain AGR0001 contains a linear chromosome of 7,885,420 bp, with average GC content of 71.45 %. The chromosome of *S. auratus* strain AGR0001 comprises 66 tRNA genes, 8 rRNA operons, and 7102 protein-coding genes that encode at least 3935 proteins with assigned putative functions. At least 33 putative gene clusters were identified for the biosynthesis of PKS, NRPS, or terpene in the genome of *S. auratus* strain AGR0001 (Han et al. 2012).

S coelicolor strain A3(2): *S. coelicolor* strain A3(2), a producer of most natural antibiotics, is a representative of the group of soil-dwelling, filamentous bacteria. The linear chromosome of this organism is approximately 8,667,507-bp long, containing the largest number of genes. The genome contains a total number of 7825 predicted protein genes, including more than 20 clusters that are identified as responsible for coding of predicted known secondary metabolites (Bentley et al. 2002).

Streptomyces globisporus strain C-1027: The analysis of draft sequence of whole genome of *S. globisporus* C-1027 revealed that the chromosome is 7,693,617-bp long with GC content of 71.63 %. The chromosome contains 56 tRNA genes, 5 rRNA operons, and at least 7231 putative protein CDSs account for 88.22 % of the genome. A number of clusters related to biosynthesis of varied secondary metabolites, including putative PKS genes, NRPS genes, NRPS-PKS hybrid genes, terpene cyclase genes, and lantibiotic biosynthesis, are found to be present in the genome of *S. globisporus* strain C-1027. The complete genome sequence of *S. globisporus* C-1027 will aid with understanding the biosynthesis-regulatory mechanisms of C-1027 and identifying new natural bioactive compounds by uncovering hidden metabolic pathways (Wang et al. 2012b).

S. griseus strain IFO 13350: The complete genome sequence of *S. griseus* is of 8,545,929 bp in length with no plasmids. The analysis of *S. griseus* chromosome showed that it contains at least 7138 ORFs; of them a total of 4464 ORFs are associated with known or putative functions, and the remaining 2674 ORFs are hypothetical proteins. The chromosome contains 66 tRNA genes (42 species) and 6 rRNA operons (16S-23S-5S). The average GC content of the chromosome is 72.2 %, but the ~300-kb regions at both ends (including the 133-kb TIR sequence) contained lower GC content. The replication origin *oriC* is found to be located at positions of 4,324,631–4,325,203 bp. Nineteen DnaA box-like sequences are predicted to be present

in the middle of the chromosome (52 kb away from the center toward the right end) (Ohnishi et al. 2008).

Streptomyces zinciresistens strain K42: The initial genome sequence data of *S. zinciresistens* strain K42 showed that it comprises 8,228,741 bp with high GC content of 72.46 %. It contained a single plasmid of 30,979 bp. The 5S, 16S, and probably multiple copies of 23SrRNAs, 7307 protein-coding sequences (CDSs), and 69 tRNA genes are annotated. The genome has 2019 proteins with orthologs in *S. coelicolor*, *S. avermitilis*, *S. griseus*, and *S. scabiei*. It has 2520 hypothetical proteins, which may give the high degree genome specificity of strain K42. A total of 61 diverse secondary metabolic genes, of them 31 genes predicted to be involved in biosynthesis of antibiotics could be identified in the genome of K42 (Lin et al. 2011).

Kocuria rhizophila strain DC2201: *K. rhizophila*, a divergent bacterial group of soil actinomycete belongs to the suborder *Micrococcineae*. Until now, a limited amount of genomic information has been available for *K. rhizophila*. Annotation of the whole genome sequence of *K. rhizophila* DC2201 (NBRC 103217) revealed that it contains a single circular chromosome of 2,697,540 bp with high GC content of ~71.16 %. It has 2357 predicted protein-coding genes; most of those (87.7 %) are orthologous to actinobacterial proteins with fairly good conservation of synteny with related actinobacterial genomes. In contrast, the genome seems to encode very few numbers of proteins required for lateral gene transfer, transcriptional regulation, and secondary metabolism (one each of NRPS and type III PKS), indicating the small genome size. The presence of a large number of genes related with membrane transport, especially drug efflux pumps and amino acid transporters, and of possible metabolic pathways for the transformation of phenolic compounds generated after degradation of plant materials, may contribute to the tolerance in various organic compounds and to organism's utilization of root exudates (Takarada et al. 2008).

Amycolatopsis orientalis HCCB10007: The complete genome of *A. orientalis* HCCB10007 contains an 8,948,591-bp circular chromosome and a 33,499-bp dissociated plasmid. In total, 8121 protein-coding sequences are predicted to be present in the genome. In addition, 26 gene clusters related to secondary metabolism, including the 64-kb vancomycin cluster encoded a halogenase, a methyltransferase, and two glycosyltransferases (Xu et al. 2014a).

Rhodococcus imtechensis RKJ300: The genome of *R. imtechensis* RKJ300 is 8,231,486 bp with GC content of 67.22 %. The genome comprises of 8059 predicted coding regions (CDSs), 49 tRNAs, and 5 rRNA genes (Vikram et al. 2012).

16.7 Conclusion

Researchers have great interest in the selection of actinomycetes, because they are importance in sustainable agriculture and are able to antagonize most deleterious phytopathogens. A large number of bioactive compounds have been isolated from different actinomycetes, mostly from *Streptomyces* spp. Different molecular approaches and bioinformatics tools are dynamic for discovering and characterizing the vast actinomycetes diversity. Furthermore, WGS can unzip the chemistry of the cryptic clusters of biosynthetic-related genes that are sometimes present but crypted, because those are not well acknowledged for synthesizing any antimicrobial compounds. In near future, those bioactive products synthesized-related genes may arise as the key of antagonism of major phytopathogens as well as PGP in crops.

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