



Comments on bacterial and fungal interactions in medicine, agriculture and the environment

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Abstract

Bacteria and fungi are associated via interactions dependent on diverse modalities of molecular communications for their development and functionalities. The resultant impact is the discrete contributions to biogeochemical cycles and biotechnological processes. Interactions among bacteria, fungi and other organisms with inter alia the environment in medicine, forestry, agriculture, and food can pose pronounced influence on the colonization, pathogenesis and survival of species. There are several reports of bacterial-fungal interactions which are important in nature but whose significance remains to be established. This article is concerned with a review of some examples, with descriptive analysis related to conceptual and operational difficulties associated with them.

Keywords: soil, mycosphere, phytoremediation, endophytes, biofilm, ecosystem, metals, nanoparticles

Introduction

Bacteria and fungi are liable to constitute an expanse of physical interactions dependent on diverse modalities of molecular communications for their development and functionalities. These bacterial-fungal associations frequently lead to alterations in the pathogenicity or the nutritional impact of one or both associates in plants, animals and Man. The resultant impact is the discrete contributions to biogeochemical cycles and biotechnological processes. On that score bacterial-fungal interactions are of pivotal significance to a plethora of biological questions in agriculture, environment, food production, forestry and medicine. These interactions provide the latitude to enhance research to deal with bacterial-fungal complexes for the encompassing advantage of Mankind; and configure an optimal understanding of the ecological presentation of bacteria and fungi (Frey-Klett et al., 2011); and the understanding of complex microbial

associations encountered in nature are subject to exploitation to discover novel therapeutics (Scherlach et al., 2013; Chukwuma, 2016a).

Bacterial and fungal complexes are located in arenas, such as human buccal cavity (Avula et al., 2009), pulmonary apparatus of cystic fibrosis subjects (Bauernfeind et al., 1987), agricultural and forest environments (Whipps, 2001), and food production with interactions ranging from ostensibly associated polymicrobial populations to highly specified symbiosis between bacterial cells and fungal hyphae (Frey-Klett et al., 2011).

Fungi and bacteria frequently rely on a common substrate, with their spatial proximity in numerous arenas culminating in either antagonistic or synergistic interactions. The antagonism among bacteria and fungi

is due to substrate competition, but the latitude for the establishment of a prior fungal niche invariably precludes viable bacterial inocula (Mille-Lindblom et al., 2006). The established fungi overwhelmed the bacteria even at higher inoculation with augmented substrate concentrations. The ecological functions of bacterial and fungal decomposers depend on the environmental situations. Fungi primarily contribute to terrigenous carbon turnover via carbon provision for the microbial loop, but bacteria are the determinants of the assimilation of available carbon substrate into biomass or recycled into the atmosphere according to phosphate provisions (Fabian et al., 2017). The extant symbiotic/antagonistic associations between diverse soil microorganisms govern their activities which are mutually beneficial, detrimental or neutral. Fungal biomass grows at an accelerated rate greater than bacteria within identical environmental conditions (Li et al., 2011). Even though, the prevalence of metal nanoparticle synthesis by bacteria is higher, the fungal synthesis is more beneficial as the mycelia present a large surface area for interaction. Furthermore, fungi secretion of protein is more abundant than bacterial secretion, thus resulting in accelerated metal salt conversion to metal nanoparticles (Sastry et al., 2003). Due to the toxicity of certain metal ions in numerous microbes, they are prophylactically relevant to inhibit their growth, with an encompassing protocol to regulate metal nanoparticle morphology for application in agriculture, environment and medicine. The objective of this paper is to discuss the beneficial aspects of bacterial-fungal interactions as related to agriculture, environment and medicine.

Soils, bacterial and fungal niches

Bacteria and fungi constitute an excess of 90% of soil microbial biomass, and are the principal protagonists for decomposition of soil organic matter content. As decomposition is conducted by bacteria and/or fungi, it is perspicuous that energy transmission permeates the bacterial or fungal nutrition web with invariably marked impact on the ecosystem at higher trophic levels, nutrient mineralization rates, nutrient channeling in soil, and effect on soil carbon sequestration rate (Rous & Frey, 2015). Bacterial and fungal interactions can pose pronounced influence on the colonization, pathogenesis and survival of both species, whereby bacteria make provision for fungi with ingredients which promote the inducement of determinants of fungal virulence (Wargo & Hogan, 2006). The inextricably complex network of interactions between plant roots, soil resources by means of microbes undergird plants to surmount

difficulties, such as access to water and nutrients or derangements from toxic products and pathogens. The ectomycorrhizal symbiotic influence in temperate and boreal forests is well recognized where fungi colonize plant, water and nutrients in exchange for sugars, including access to minerals (Martin, 2017). It is suggested that ectomycorrhizal fungi and soil organism interactions determine the output of the introduction and survival of inoculated ectomycorrhizal fungi regarding compatibility of an expansive range of soil microflora and plant stimulation efficiency (Bowen & Theodorou, 1979). In probing the function that fungi can perspicuously adapt concerning the provision of optimal niches for soil bacteria, the mycosphere is important due to the restricted or limited milieu of the impact of fungal hyphae on the external soil ambient where hypha-associated bacterial cells inhabit. It is likely that hyphae of both mycorrhizal and saprophytic fungi function in ecological provision of expansive carbon-restricted soil due to their release of carbonaceous compounds proximal to a colonizable surface. Soil bacteria of specific feature are posited as having adapted to such selection pressure, evolving to the magnitude whereby they acquired the potential for thriving in the novel dwelling produced by the emerging fungal hyphae. The mechanisms of interactions and the modalities of genetic adaptation are generally ecologically suitable for mycosphere-adapted bacteria, such as *Burkholderia terrae* BS001 (Haq et al., 2014), where competition for iron is suggested to be a factor (Zhang et al., 2016).

The mycosphere may constitute a gene-transfer zone in which numerous genes and locally adapted ones are exchanged encompassing the microbial milieu. These genetic swaps are suggested to contain plasmids in especially those having expansive host ranges as the foundation. Plasmids may be involved in vital functions as evolutionary enhancers in the mycosphere within a horizontal gene pool resulting in the provision of competitive factors to resident bacteria and fungi. Evidence dictates that mycosphere functions for two main plasmid classes, the IncP-1 and Prom A groups. Data reveal that bacterium-to-fungus gene transfers are demonstrable, and are evolutionarily significant. The latitude for cell-to-cell contact between mycosphere inhabitants provides accelerated recombination frequencies as organisms are locally selected for enhanced fitness in the microhabitat (Zhang et al., 2014).

Globally on cellular levels, bacterial-fungal interaction presents the most common bacterial-eukaryotic interactions with specific responses to diverse Microbe-Associated-Molecular-Patterns, MAMPS on regulatory pathways (Olsson, 2016). Interactions of arbuscular mycorrhizal fungi and specific rhizosphere bacteria improve plant nutrient, such as preponderantly N and P cycling as demonstrated by isotope dilution strategies (Barca et al., 2005). Certain of these interactions improve physicochemical soil attributes and contribute to plant fitness and soil quality as pertinent concerns for sustainable ecosystem functionality, agricultural and forestry development and food production enhancement.

Clinical modalities

Within the complex interplay of health and disease, humans harbor various quantities of microorganisms which include bacteria and fungi. The associations between these taxonomically disparate microorganisms are extremely dynamic and depend on numerous microorganisms and host attributes. Anthropogenic perturbations can result due to imbalance between commensal bacteria and fungi or invasion of host niches by opportunistic organisms, such as bacteria and fungi (Peleg et al., 2010). Understanding interactive mechanisms and antagonistic features between microbes in specific niches can assist to identify, explicate and elucidate novel potentials therapeutic targets to prevent and treat microbial perturbations (Lopez-Medina & Koh, 2016). Approximately 600 bacterial species and an undecipherable number of fungal species reside in human oral cavity (Dupuy et al., 2014; Duran-Pinedo et al., 2014). Oral microbial cells present in organized biofilm conformations on the teeth and non-shedding surfaces. Arranged aggregates are also constituted on mucosal surfaces through discrete cell-to-cell adhesions and during salivary fluid phase (Kolenbrander et al., 2010). This physical proximity enhances metabolic interactions between microbial cells (Kim et al., 2008), and a specific spatial configuration has been demonstrated to facilitate microbial community stability enhancing formation of chemical gradients. Microorganisms in these numerous formations interact via diverse trajectories of metabolic exchanges, such as the cooperativity of bacterial consortia to discharge nutrients from macromolecules in oral fluids (Bradshaw et al., 1994). Advanced throughput sequencing has facilitated information on oral microbiome, with the bacterial component of oral communities have been expansively characterized, but the functionality of the

oral cavity fungal microbiota remains unknown. Bacterial-fungal interactions are liable to effect oral health as demonstrated by the synergistic association of *Candida albicans* and oral streptococci (Diaz et al., 2014). It is pertinent to organize longitudinal clinical approach/research to characterize the bacterial and fungal ingredients of the human oral microbiome in complex interplay of health and disease. These may be extrapolated via employing disease significant modalities to mechanistically test the relationships detected in humans with simultaneous detection of bacterial-fungal interactions which may function in prophylaxis, prevention and therapy regarding oral disorders.

Bacterial-fungal interactions relate the manner whereby bacteria initiate and sustain with fungi via the formation of physical and metabolic interdependent consortia which contain attributes distinct from their single components. Bacterial-fungal interactions have been associated in two aspects of ectosymbionts depicting either negative or positive interactions, resulting in changes of the morphology, reproduction, pathogenicity and symbiosis. Bacterial-fungal interactions and molecular communications were detected via antibiosis, physicochemical environmental modulation, chemotaxis, gene transfer, trophic relatedness (Reddy & Prassand, 2017). The bacterial fungal interactions posed as model systems which are effectively and efficiently employed to understand the basics of host-pathogen interactions and identification of diverse mechanisms of interactions between strains of bacteria and fungi as well as contribute in appropriate management paradigm for an expansive area of microbial defence fortification (Reddy & Prassand, 2017).

Endophytes and biofilms

There is no encompassing agreement available on the specific or precise ecological spectra of diverse categories of endophytes or on the concretization of interactions with plants. This is due to paucity of research on bacterial and fungal endophytes as an integrate strategy in contradistinction to disparate research domains and both taxa. Thus, comprehensive community-stage research on bacterial and fungal interactions and their significance are virtually non-extant. Mixed-community endosphere biofilms portend functionalities to defend endophytes regarding encountered stresses, such as from plant protective assemblage (van Overbeek & Saikkonen, 2016). Transfer from static biofilms to free-living planktonic morphology is suggested to be vital for the

investigation and elucidation of novel habitable niches in plants. Erstwhile recognized characteristics of plant-microbe interactions or antagonistic predilections in endophyte genomes and metagenomes are suggested to display pertinent functionalities in endophyte community modulation (Saikkonen et al., 1998). Also, minimal acid formation is necessary to suppress plant pathogens. Thus, the biofilm production in endophytic ambient ostensibly relates to healthy and improved plant growth. It may not be possible that endophyte interactions occur in nature within the endophytic ambience as a result of plant tissue physical barriers (Bandara et al., 2006). Critical cell density dependent quorum sensing that culminates in biofilm production is not liable to manifest in an endophytic ambient due to restricted arena. Inevitably, *in vitro* formation and beneficial biofilm inocula endophyte application are performed for enhanced agro-ecosystem plant production. It is suggested that the traditional plant inoculation procedure with monocultures or mixed cultures of potent microbes may not result in optimal microbial impact that may be achievable via biofilm production (Bandara et al., 2006).

Metalliferous and toxic environment

Plants and microorganisms co-exist or in competition for survival with a complex interplay of interactions and adaptive tolerance to metalliferous ambient which are exploitable to enhance microbial-augmented phytoremediation (Chukwuma, 2011). Plant root exudates are essential as nutrient and energy sources for soil microbes undergirded with inextricable linkage of communication systems. Certain beneficial bacteria and fungi having attributes of plant growth promoting microorganisms, PGPMs have the potential to mitigate metal phytotoxicity and stimulate plant growth: (i) indirectly via defence mechanism induction to combat phytopathogens; (ii) and/or indirectly via mineral nutrient solubilization, such as nitrogen, phosphate and potassium; (iii) formation of plant growth enhancing compounds, such as phytohormones and; (iv) specific enzyme secretion as per 1-aminocyclopropane-1-carboxylate deaminase. PGPM is capable of altering metal bioavailability in soil via diverse mechanisms, such as acidification, chelation, complexation, precipitation and redox reactions (Ma Y et al., 2016) Applications of advanced strategies can be developed to explicate the biochemical and regulatory mechanisms undergirding plant-microbial interactions (Chukwuma 2016a-c; Chukwuma, 2017), and their functionalities in the processes associated with phytoremediation, for

instance, heavy metals and trace elements, detoxification, transformation, transportation and dissemination (Chukwuma, 2011; Chukwuma, 2014). Soil constitutes one of the principal habitats of fungi and bacteria, with their interactions forming an aspect of a communication network that sustains equilibrium of the microhabitats. Pronounced mediations of these inter- and intra-organismic interactions are organic and inorganic microbial volatile compounds, mVOCs (Effmert et al., 2012). About 300 bacteria and fungi were revealed as VOC precipitations, and circa 800 mVOCs were stored in DOVE-MO database of volatiles via microorganism emissions. The resultant impacts are morphological as well as phenotypical alterations which manifest in the organisms due to available mVOCs. These effects are likely to lead to the elucidation of bioecological importance of the emission of mVOCs in order to explicate volatile-wired interactions beneath the earth (Alharbi et al., 2011; Effmert et al., 2012).

Thus, microbes are relevant in defining our environment, with the attributes to release chemically varied complex volatile compounds of not yet elucidated chemical structures biological and ecological functionalities. There is extant evidence that microbial volatiles are capable of presenting as infochemicals in interactions between microbes and their eukaryotic hosts which are related to impact on quorum sensing, motility, gene expression and antibiotic resistance, especially regarding bacteria (Schmidt et al., 2015). Investigations have shown that inter-kingdom interactions can elicit novel development properties in bacteria, thus inducing *Streptomyces* depart from its conventional natural cycle, such as volatile organic compounds acting as long-range communication signals with the potential to propagate microbial morphological switches (Jones et al., 2017). The basic biological question is the modality of initiating and sustaining of pathogenic associates between bacteria and eukaryotic hosts (Kobayashi & Crouch, 2009) as creative organisms in bacterial-fungal interactions from pathogenesis to symbiosis. In recent decades, it has been revealed that metallic nanoparticles and their syntheses have accelerated in vast dimensions with resultant development of multiple trajectories in the formation of metallic nanoparticles utilizing physicochemical procedures. There are extant constraints and challenges in associated chemical toxicity and high energy production requirements. Live organisms, such as bacteria, fungi and plants have rather been employed in metallic nanoparticle synthesis. The study and application of metal nanoparticles are evident in

several areas, such as biomedicine, agriculture and electronics. Various mechanisms demonstrate the biological synthesis of metal nanoparticles by bacteria, fungi, peptides and plants; but the mechanistic aspects in certain biological arenas require expansive and indepth research (Duran et al., 2011). The “green” method of employing bacteria, fungi and plants for biological nanoparticle production is a strategy that provides the latitude for synthesis in aqueous environments, with requirements for low energy and low pecuniary needs as well as their potential in these approaches in the environment of nanoparticle risk in environment and health (Pantidos & Horsfall, 2014). Currently, the focus has been on the potential of metal nanoparticles as an antimicrobial agent for the inhibition of the growth of pathogenic fungi and other potential uses (Siddiqi & Husen, 2016).

Metal nanoparticles fabrication via biogenic approaches employing plant extract is more environmentally friendly, inexpensive, innocuous and popular since no polluting hazardous residues are evident to cause deleterious impacts to the environment and health (Husen & Siddiqi, 2014). It is well established that nanoparticles are hazardous or beneficial to living systems, depending on their nature, shape and size of the specific metal ion. However, microbes present the natural mechanism for metal ion detoxification via reduction that is achievable extra- or -intra-cellularly by bioaccumulation, biomineralization, biosorption and precipitation (Prabhu & Poulose, 2012; Singh et al., 2015).

Metabolic factors and hormones

Microbe-microbe or microbe-host interactions are strategically relevant in the colonization and establishment of a variety of niches or ambient. These interactions inculcate all ecological dimensions, vis-à-vis physicochemical alterations, metabolic interchange and conversion, signaling, chemotaxis and genetic exchange culminating in genotype selection. Also, the environmental establishment is dependent on species diversity as increased microbial community functional redundancy enhances the community competitive potential lowering the threshold of an invader to establish in the ambient or niche. These relationships are consequent upon co-evolution process that results in the adaptation and specialization with latitude to occupy diverse niches via the reduction of biotic and abiotic stress or in the exchange of growth factors and signaling (Braga et al., 2016). Microbial interactions take place via molecular and genetic information

transfer with numerous mechanisms inculcated in the exchange, such as inter alia secondary metabolites, siderophores, quorum sensing system, biofilm formation and cellular transduction signaling. The pertinent interaction ingredient is each organismal gene expression in relation to abiotic or biotic environmental stimuli indicted for molecular production associated in the interactions. The effect of the multiple interactions is usually associated with host pathogenicity or advantage.

Microbial synthesis of the phytohormone auxin has been established regarding bacterial interactions with plants. Bacterial auxin can induce interference with numerous plant development processes under auxin regulatory mechanisms. As is evident in plants, it is clear that bacterial biosynthesis of auxin occurs via multiple pathways. This is extant evidence that indole-3-acetic acid, IAA is a signaling component in microbes and the principal naturally extant auxin that influences gene expression in certain microbes. Thus, IAA has the attribute as a reciprocal signaling molecule in microorganisms-plant interactions. Additional evident attribute of auxin in Arabidopsis has enhanced further interest (Spnepen & Vanderleyden, 2011). Downregulation of auxin signaling constitutes an aspect of the plant defence system against phytopathogenic bacteria. Exogenous auxin application, such as that produced by the pathogen exacerbates vulnerability to the bacterial pathogen, plants, bacteria and fungi as well as other microbes which produce IAA as the most prevalent plant hormone of the auxin class, and also regulates diverse portions of plant growth and development. Data suggest that IAA regulates physiologic response and gene expression in bacteria, fungi, microalgae and plants. Although, these organisms may have evolved independently, the subsequent evolution of IAA formation culminates in natural selection hypothesis of a predilection of IAA as an expansive physiological code in these microbes and their concomitant interactions (Fu et al., 2015).

Exploration of the complete fungi genome sequences depict that the potency to create secondary metabolites is grossly underestimated (Schroeckh, et al., 2009). It was determined that at the molecular level, a unique bacterial-fungal interaction culminates in particular elicitation of secondary fungal metabolism genes. Dialysis experiments and electron microscopy depicted that intimate association of the bacterial and fungal mycelia is mandatory to activate the specific response. Gene knockout studies indicated that one induced gene cluster encodes for polyketide synthase,

PKS necessary for the archetypal polyketide orsellinic acid biosynthesis, the typical lichen metabolite lecanaric acid, and the cathepsin K inhibitors F-9775A and F-9775B. A phylogenetic analysis indicated that orthologs of this PKS are ubiquitous in all principal fungal groups including lichen mycobionts. These findings elucidate specific interaction evidence between microorganisms of diverse domains, and undergird the hypothesis that not merely diffusible signals but intimate physical interactions are contributory to the communication between microorganisms and elicitation of ostensibly silent or cryptic biosynthesis genes or loci (Schroeckh et al., 2009). Metabolic exchanges abound in microbial communities, but the detection of metabolic cross-feedings face constraints and challenges emanating from inherent dynamic attributes and community complexity. Elucidations of metabolic networks in natural systems pertain ostensibly in the future, but at present, it is partitioned among discrete characterizations of small and mitigated complexity of consortia with focus on specific and unique metabolic dimensions of natural ecosystems. The detection of metabolic interactions necessitates procedural admixture and compliance to inculcate species diversity, similarity and identity, dependencies and features of exchanged metabolites. Multiple combinations of varied procedures extending from metagenomics to mass spectrometry imaging provide solutions to the presenting challenges and constraints with each combination compliantly available to the community (Ponomarova & Patil, 2015).

Discussion and Conclusion

Bacterial-fungal interactions have significant implications on the physiology of the interaction between associates and on the environment. Nutrient turnover is pivotal in bacterial-fungal interactions since both organisms feed by absorption, and invariably compete for resources. In that aspect, bacteria and fungi developed and configured strategies to secrete secondary metabolites and proteins which are toxic to the competitor to protect their nutritional niche. Bacterial presence can precipitate the alteration in gene expression and secondary metabolic production in fungi. Fungi form several relative molecular mass compounds displaying a vast array of biological functionalities. Fungi and prokaryote interactions are ubiquitous in numerous ecosystems, with an expanse of biomolecules regulating these interactions of beneficial medicinal and biotechnological applications. Microfluidic devices have provided the latitude for microscopic research,

long-run and time-lapse studies (Stanley et al., 2014). Elucidation of bacterial-fungal interactions in the rhizosphere is liable to enhance the feasible bacterial application to curb plant fungal pathogens as alternatives to chemicals in sustainable agriculture (Gkarmiri et al., 2015, Chukwuma, 2014), as well as full and proper elucidation of biochemical processes and biosynthetic pathways (Chukwuma 2016b, c; Chukwuma, 2017).

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