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Current Opinion in Microbiology

Extracellular vesicles — new players in cell–cell communication in aquatic environments

Daniella Schatz and Assaf Vardi

Communication between microorganisms in aquatic environments can influence ecosystem function and determine the structure and composition of microbial populations. This microbial cross talk can be mediated by excretion of specialized metabolites or extracellular vesicles (EVs). Recently it has become apparent that cells across all domains of life produce EVs that may convey specific targeted signals that can modulate cell fate, morphology and susceptibility to viruses. The vast majority of knowledge about EVs is derived from studies of mammalian tissues, parasitic host–pathogen interactions and model bacterial systems. Very little is known about the role of EVs in aquatic environments, although they have potential to influence community structure and trophic-level interactions. We propose functions and ecological implications of communication via EVs in aquatic microbial ecosystems.

Address
Department of Plant and Environmental Sciences, Weizmann Institute of Science, Rehovot 7610001, Israel

Corresponding author: Vardi, Assaf (assaf.vardi@weizmann.ac.il)

Current Opinion in Microbiology 2018, **43**:148–154

This review comes from a themed issue on **Environmental microbiology**

Edited by **Alberto Scoma** and **Julia Vorholt**

https://doi.org/10.1016/j.mib.2018.01.014

Introduction

Communication between microorganisms in aquatic environments can influence population composition and ecosystem function, ultimately impacting biogeochemical cycles and even ocean-atmosphere feedback [1–5]. By using communication-conveying signals, microorganisms can acclimate to changing environmental conditions and synchronize population level behaviors such as biofilm formation, defense against pathogens or grazers and quorum sensing responses. The most studied forms of communication are conveyed by specialized metabolites named infochemicals. These are diffusible molecules excreted to the micro-environment surrounding the cells and include quorum sensing and other molecules that can convey signals of cell density, biotic and abiotic stresses. In recent years, extracellular vesicles (EVs) have been discovered as a new mode of communication across all domains of life. EVs are membrane-encapsulated vesicles that are produced and released to the surrounding milieu. There are many types of EVs, defined by their size and mechanism of production. Outer membrane vesicles (OMVs) originate from the cell membrane and are produced by detachment of cell-membrane blebs [6]. Exosomes are produced by eukaryotes following fusion of multivesicular bodies with the cell membrane [7]. In this review we refer all types of vesicles as EVs, and will not discuss the mode of production of the vesicles. EVs are produced by bacteria, archaea and eukaryotes and can act as vectors for pathogenicity, gene transfer and cell–cell communication [7,8]. EVs can contain a wide range of cargo (see Table 1) including signaling metabolites (e.g. acyl-homoserine lactones), toxins, nucleic acids and even ecto-enzymes (lipases, proteases, etc.). The vast majority of our knowledge about EVs and their role is derived from studies of model organisms, mainly cancerous-mammalian tissues, parasitic host–pathogen interactions and lab-based bacterial systems. Very little is known about the role of EVs in aquatic environments, although they have great potential to influence community structure and trophic-level interactions. Recent studies suggest that EVs hold potential in regulating host–virus dynamics [9••] and influencing the partitioning of carbon during interactions of autotrophic and heterotrophic bacteria [10••]. In order to present the possible roles of EVs in aquatic ecosystems we review the roles of EVs and their function in diverse microbial systems (Table 1). We suggest potential functions and ecological implications of communication via EVs in aquatic microbial ecosystems (Figure 1).

Potential roles of EVs in aquatic ecosystems

In aquatic environments, transferring signals between cells by EVs has three main advantages: EVs allow effectors (infochemicals, toxins, proteins, etc.) to be delivered in high local concentrations to the target, that is the cell that receives and responds to the signal conveyed within the EV. Thus, in total, the producing cell has to secrete less effector to reach the target cell. If multiple effectors are needed to generate a response, these can be packaged together into EVs, thus ensuring they all reach the same target cell. Additionally, the EVs protect the effector molecules from degradation in the environment — they will be sequestered away from the harmful activity of nucleases, proteases, etc. The lipid

Table 1

Examples of EVs with functions that are of particular interest in aquatic environments

Species	Class	Function	Cargo[a]	Reference
Prochlorococcus	Cyanobacteria	Possible decoy against phages, vector for HGT	DNA and RNA	[10••]
Pseudomonas aeruginosa	Gammaproteobacteria	Secretion of virulence-associated factors mediated by PQS	Lipopolysaccharides, DNA enzymes (phospholipase C, protease, hemolysin, and alkaline phosphatase); 2-heptyl-3-hydroxy-4-quinolone (pseudomonas quinolone signal, PQS)	[22,23,14]
Pseudomonas syringae	Gammaproteobacteria	Protection against membrane active antibiotics	Phosphatidylethanolamine, Phosphatidylglycerol are main lipid classes, many proteins	[24]
Shewanella putrefaciens	Gammaproteobacteria	Redox reactivity (enzymatic reduction and transformation of heavy metals)	Proteins and cytochromes	[25]
Algoriphagus machipongonensis	Sphingobacteria	Induction of rosette formation in a Choanoflagellate	Sulfonolipids (rosette-inducing factors) and lyso-Phosphatidylethanolamine	[26]
Paracoccus sp.	Alphaproteobacteria	Transfer of hydrophobic signals, cell-to-cell communication	C16-Acyl homoserine lactone	[15•]
Vibrio shilonii	Gammaproteobacteria	Suggested to take part in QS	Acyl homoserine lactone, alkaline phosphatase, chitinase and lipase	[16]
Vibrio tasmaniensis	Gammaproteobacteria	Pathogenicity against oysters	Proteases, lipases, phospholipases, haemolysins and nucleases	[19]
Bacillus subtilis	Bacilli	Exchange of phage receptors (acquisition of sensitivity to phages)	Phage attachment components	[27••]
Bacillus anthracis	Bacilli	Toxicity to host (mammals)	Toxins	[17]
Staphylococcus aureus	Bacilli	Transfer of antibiotic resistance protein to both Gram-positive and Gram-negative bacteria	BlaZ, conferring resistance to antibiotic	[20,21]
Escherichia coli	Gammaproteobacteria	Transfer of DNA to other *E. coli* strains and other bacteria species	DNA	[28]
Escherichia coli	Gammaproteobacteria	Protection against stressors — antimicrobial peptides and bacteriophage	Unknown	[18]
Halorubrum lacusprofundi	Halobacteria	Facilitating plasmid transfer	Cell-encoded plasmid	[29]
Thermococcus sp.	Thermococci	Transfer of plasmid and viral DNA	Plasmid and viral DNA; RNA	[30–33]
Ochromonas danica	Chrysophyceae	Aid in ingestion of bacteria, may have a role in predator–prey interactions	RNA, carbohydrates	[34–36]
Emiliania huxleyi	Prymnesiophyceae	Facilitating viral infection	Small-RNAs, triacylglycerols	[9••]

[a] All EVs contain lipids and proteins. Listed are only those of specific interest or function.

and protein composition of EVs may ensure that the EVs interact only with a subset of cells in the environment, and by that enabling 'targeting' of effector molecules to specific cells in the vicinity of the producing cells. In multicellular organisms, the proteins decorating the membrane of exosomes from cancerous tissues can determine the tropism towards specific tissues and create a premetastatic niche in the target cells [11•]. In aquatic environments, selective targeting may reduce not only the concentration of effector that needs to be secreted, but also the chance of quenching of the signal by bystander cells.

In aqueous environments, the transfer of signals between cells may be hindered by the hydrophobic nature of the signaling molecule. Hydrophobic molecules will need some form of transport, as free diffusivity of these molecules will not take place. To date, mainly hydrophilic molecules have been found to be involved in quorum sensing (QS), although the presence of hydrophobic infochemicals, information conveying molecules, such as long-chain acyl homoserine lactones (AHLs), and 2-heptyl-3-hydroxy-4-quinolone (PQS), has been reported [12–14]. By packing hydrophobic molecules into EVs, the message can be transferred between cells in an aqueous environment. *P. aeruginosa* EVs have been shown to contain the hydrophilic PQS and elicit a QS response [14]. It has also been demonstrated that EVs of the Gram-negative *Paracoccus sp.* contain the hydrophobic AHL *N*-hexadecanoyl-L-homoserine lactone, a C16 highly hydrophobic molecule [15•]. These EVs alone are enough to elicit a QS response in target cells. Interestingly, these