

LUIZ RICARDO OLCHANHESKI

Diversidade e potencial do mobiloma presente ao longo da bacia do Rio Tietê

Tese apresentada ao Programa de Pós-graduação em Microbiologia do Instituto de Ciências Biomédicas da Universidade de São Paulo, para obtenção do Título de Doutor em Ciências.

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RESUMO

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Sistemas de água doce são de importância vital para o sustento da população, além de contribuir com a produção agrícola e processos industriais. Alterações nas características físico-químicas em ambientes de água doce influenciam diretamente na diversidade bacteriana, porém ainda pouco se conhece quanto aos impactos no perfil funcional na comunidade bacteriana. Desta forma, um dos objetivos iniciais deste trabalho foi verificar a correlação dos perfis funcionais em dez amostras metagenômicas sequenciadas em trabalhos anteriores, com diferentes localizações geográficas e características físico-químicas contrastantes. A partir destas análises, foi possível verificar que a localização não está correlacionada com o perfil funcional da comunidade bacteriana. Além disto, a salinidade e a abundância de genes associados ao metabolismo do enxofre são as principais características relacionadas à variação do perfil funcional. Com o objetivo de analisar detalhadamente o perfil do mobiloma por meio de análises de metagenoma plasmidial, foi utilizado como objeto do presente estudo amostras de dois pontos do rio Tietê (TIET02400 e TITR02800). Este rio Tietê percorre 1.136 km no estado de São Paulo (Brasil), passando por diversas áreas preservadas da Mata Atlântica e regiões metropolitanas, como a cidade de São Paulo onde o rio recebe uma grande quantidade de poluentes industriais e esgoto doméstico. Os dois pontos amostrados são contrastantes quando IQA, sendo um classificado como ruim e outro como ótimo. Os genes presentes em plasmídeos no ponto com maior atividade antrópica foram relacionados às funções de transportadores transmembrana, bombas de efluxo, e genes que conferem resistência a compostos xenobióticos e metais pesados, que conferem vantagens adaptativas principalmente na presença de compostos tóxicos. Já no ponto com menor teor de poluentes, os genes de maior abundância estão envolvidos no transporte e assimilação de substâncias encontradas em baixas concentrações, como o fósforo. Os possíveis hospedeiros mais abundantes no ponto com IQA ótimo pertencem ao filo *Cyanobacteria*, o que justifica maior abundância de genes envolvidos com fotossíntese em plasmídeos. Ainda foi estimado a diversidade de genes que conferem resistência a antibióticos em quatro pontos (TIET02400, TIET02500, PATO02900 e TITR02800) contrastantes quando ao IQA. Foi observado maior abundância de genes que conferem resistência a multidrogas no ponto com IQA ótimo, e genes para resistência a sulfonamidas no ponto com IQA péssimo. Foi observado que a presença de metais pesados correlaciona com o aumento de genes que conferem resistência a antibióticos, sugerindo uma situação de co-seleção destes genes. As análises metagenômicas auxiliaram a compreender como as características ambientais podem modular a diversidade funcional na comunidade bacteriana, assim como determinam a pressão de seleção para genes passíveis de serem transferidos lateralmente, por meio de plasmídeos.

Palavras-chave: Metagenômica. Antibióticos. Atividade antrópica. Plasmídeos.

ABSTRACT

OLCHANHESKI, L.R. **Diversity and potential of the mobilome present along the Tietê river basin.** Thesis (Ph. D. thesis in Microbiology) – Instituto de Ciências Biomédicas, Universidade de São Paulo, São Paulo, 2018.

Freshwater systems have vital importance for the livelihood of the population, in addition to contributing to agricultural production and industrial processes. Changes in physical-chemical characteristics in freshwater environments directly influence bacterial diversity, but little is known about the impacts on the functional profile in the bacterial community. Thus, one of the initial objectives of this work was to assess the correlation of the functional profiles in ten samples with different geographic positions and physical-chemical characteristics. From these analyzes, it was possible to verify that the geographical position is not correlated with the functional profile in the bacterial communities. In addition, salinity and genes for sulfur metabolism are the main characteristics that influence the functional profile. With the objective of analyzing the mobilome profile in detail using plasmid metagenome analysis, two points of the Tietê river were used as the object of study. The Tietê river, located in the state of São Paulo (Brazil), runs 1,136 km. Along this route, the river passes through several preserved areas of the Atlantic Forest and metropolitan regions, such as the city of São Paulo where the river receives a large amount of industrial pollutants and domestic sewage. The two points sampled are contrasting when compared to the IQA, one being classified as bad and the other as optimal. The genes present in plasmids at the point with greater anthropic activity were related to the functions of transmembrane transporters, efflux pumps, and genes that confer resistance to xenobiotic compounds and heavy metals, which confer adaptive advantages mainly the presence of toxic compounds. At the point of low pollutants, the genes of greater abundance are involved in the transport and assimilation of substances found in low concentrations, such as phosphorus. Also, with respect to the point with lower anthropogenic activity, the possible hosts more abundant belong to the phylum *Cyanobacteria*, which justifies the presence of more genes aimed at photosynthesis in plasmids. Also, in the Tietê river, it was possible to estimate the diversity of genes that confer resistance to antibiotics in four contrasting points when compared to the IQA. Higher abundance of genes that confer multidrug resistance at point with optimal IQA, and genes for resistance to sulfonamides at the point with poor IQA were observed. It was observed that the presence of heavy metals correlates with the increase of genes that confer resistance to antibiotics, determining a situation of co-selection of these genes. Metagenomic analyzes helped to understand how environmental characteristics modulate functional diversity in the bacterial community, as well as determine the selection pressure for laterally transferable genes, such as plasmids.

Keywords: Metagenomics. Antibiotics. Anthropic activity. Plasmids.

INTRODUÇÃO

A presença de micro-organismos no ambiente é a principal forma de manutenção dos ecossistemas, participando de diversos processos como ciclagem de carbono, fixação biológica de nitrogênio, transformação de compostos xenobióticos, dentre outros. Diversos estudos vêm sendo realizados para entender os impactos ambientais na comunidade microbiana de ambientes de água doce, porém no Brasil, ainda vem sendo negligenciados estes estudos, principalmente no que diz respeito às alterações na diversidade funcional de micro-organismos, os quais podem afetar processos metabólicos, e conseqüentemente a ciclagem dos nutrientes. Com a atividade antrópica, são observadas mudanças da diversidade microbiana nos ecossistemas, e conseqüentemente seu funcionamento. Esta alteração pode acarretar a extinção de espécies capazes de promover a manutenção destes ambientes e o equilíbrio ecológico. À medida que alterações ambientais ocorrem, esta diversidade pode sofrer mudanças, uma vez que a riqueza, abundância e a diversidade são reguladas por fatores físico-químicos, tais como fotoperíodo, temperatura e demanda por nutrientes, além das próprias interações entre as espécies presentes. Essas variações podem ser determinantes para a distribuição de espécies de micro-organismos, as quais podem aumentar o potencial de estabelecimento de espécies exóticas (invasibilidade). Dessa forma, impactos ambientais como descarte de efluentes não tratados contribuem para a rápida alteração desses ecossistemas. Adicionalmente, ocorre um acúmulo de metais tóxicos, prejudicando a qualidade das águas e atividades dependentes do seu uso, desde domésticas e agrícolas até as atividades industriais.

A transferência horizontal de genes vem sendo considerada como sendo uma estratégia importante no âmbito evolutivo. Os principais estudos realizados atualmente sobre mobiloma são desenvolvidos para entender a disseminação de genes de resistência a antibióticos, porém a transferência de genes ocorre em diversas situações no ambiente, muitas vezes como consequência de alterações ambientais específicas, podendo inclusive estar associada à diversidade metabólica encontrada em ambientes específicos. Na transferência de genes, os principais estudos são relacionados às mudanças nos perfis fenotípicos de resistência, porém existem genes de importâncias biotecnológicas que estão presentes nestes

mobilomas e que não têm sido estudados. As condições de ativação e principalmente transferência destes genes passam a ser importantes para um maior entendimento destes processos, incluindo aspectos evolutivos que permitem a estruturação de comunidades microbianas em ambientes impactados ou que passaram por alterações físico-químicas drásticas.

CONCLUSÕES

- A diversidade funcional analisada em ambientes de água doce são selecionadas principalmente pelas características ambientes, independentemente da posição geográfica.
- As pequenas alterações na concentração de salinidade em ambientes de água doce selecionam genes voltados ao metabolismo de sódio e potássio, principalmente.
- A maior parte dos genes considerados acessórios em amostras metagenômicas em ambientes de água doce ainda não são caracterizados, indicando a importância de se explorar o perfil funcional e genes específicos em cada ambiente.
- A diversidade plasmidial em amostras do rio Tietê são selecionadas pelas características ambientais.
- O ponto TIET 02400 (com IQA ruim), apresentou maior abundância de genes relacionados ao transportadores transmembrana, bombas de efluxo, e genes que conferem resistência a compostos xenobióticos e metais pesados se comparado ao ponto TITR 02800 (IQA ótimo), demonstrando adaptações às condições ambientais, provavelmente decorrentes da ação antrópica.
- O plasmidoma do ponto TITR 02800 foi observado maior abundância de genes envolvidos no transporte e assimilação de substâncias observadas em baixas concentrações, como o fósforo.
- Foi observado que os plasmídeos podem afetar o *fitness* ecológico comunidade bacteriana, visto que por meio da transferência lateral de genes envolvidos em processos adaptativos no ambiente e posterior seleção, podem favorecer a adaptação de determinados grupos microbianos.
- Com relação aos genes que conferem resistência a antibióticos, os pontos com IQA ótimo, bom e regular agruparam sendo que apenas o ponto com IQA péssimo ficou separado.

- O ponto com IQA péssimo (TIET 02400) foi o que apresentou maior abundância de genes associados a resistência a antibióticos e maior equitabilidade se comparado aos outros três pontos com qualidade de água melhor.

- O ponto com IQA ótimo (TITR 02800) teve em sua maioria, genes de resistência a antibióticos caracterizados como bombas de efluxo, sugerindo que possa estar ocorrendo co-seleção destas bombas de efluxo pela presença de outros compostos na água.

-Baseado no gradiente na concentração de metais pesados no rio Tietê, foi observada correlação positiva entre a abundância de genes que conferem resistência a sulfonamidas, MLS e aminoglicosídeos e a presença de alumínio, chumbo e cobre.

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