BMC Bioinformatics

BioMed Central

Meeting abstract

Open Access

Bioinformatics determination of ETEC signature genes as potential targets for molecular diagnosis and reverse vaccinology

Heba M Amin[1], Abdel-Gawad M Hashem[2] and Ramy K Aziz*[2]

Address: [1]Department of Microbiology and Immunology, Faculty of Pharmacy, MSA University, Cairo, Egypt and [2]Department of Microbiology and Immunology, Faculty of Pharmacy, Cairo University, Cairo, Egypt

Email: Ramy K Aziz* - ramy.aziz@salmonella.org

* Corresponding author

from UT-ORNL-KBRIN Bioinformatics Summit 2009
Pikeville, TN, USA. 20–22 March 2009

Published: 25 June 2009

BMC Bioinformatics 2009, **10**(Suppl 7):A8 doi:10.1186/1471-2105-10-S7-A8

This abstract is available from: http://www.biomedcentral.com/1471-2105/10/S7/A8

Background

Genomes of the model bacterium, *Escherichia coli*, exhibit high plasticity caused by gene gain/loss via pathoadaptive mutations, genetic rearrangement, and horizontal gene transfer [1,2]. This genetic variability is also translated into a remarkable phenotypic and pathotypic diversity: while some *E. coli* strains normally inhabit the mammalian colon, other pathotypes cause a wide range of intestinal and extraintestinal diseases that include mild intestinal disturbance but also severe urinary tract infections and outbreaks of shigellosis-like dysentery or cholera-like watery diarrhea [1]. In this study, we focus on enterotoxigenic *E. coli* (ETEC), one of the world's deadliest infectious agents, which also represents a serious public health in Egypt's rural areas. Our aim is to integrate multiple bioinformatics tools to determine horizontally transferred, pathotype-specific signature genes as targets for specific, high-throughput molecular diagnostic tools and reverse vaccinology screens.

Methods and results

To estimate the extent of horizontal gene transfer in ETEC, we used a combination of bioinformatics tools, including GC%, comparative genometrics analysis [3], and web-based prediction of pathogenicity islands via IslandPath http://www.pathogenomics.sfu.ca/islandpath[4]. Because *E. coli* strains are typically polylysogenic [5], we used the ACLAME Prophinder tool http://aclame.ulb.ac.be/Tools/Prophinder[6] to predict complete or rudimentary prophages scattered within the ETEC genome. To determine ETEC pathotype-specific genes or signature genes, we used comparative genomic tools available in the National Microbial Pathogen Data Resource (NMPDR) platform http://www.nmpdr.org, including the Signature Genes Tool and the Homolog Spreadsheet Tool [7]. We identified 128 genes that differentiate this pathotype from other *E. coli* strains, based on bidirectional-best-hit signature analysis. We also identified 94 genes that are characteristic to two closely related strains (24377A and 2348/69). Many of the ETEC-specific genes were mapped to prophages, prophage-like elements, and other pathogenicity islands; however, some of these signature genes, e.g., ORFs 21–39 in strain 24377A, seem to be rather lost in other *E. coli* strains (as they are conserved among other enterobacteria, e.g., *Shigella* and *Salmonella*). Our ongoing studies are testing some of these ETEC-specific genes as targets for multiplex PCR amplification to develop a rapid diagnostic typing method. Future studies will analyze the surface-association and antigenicity of these signature gene products as a first step in a reverse vaccinology strategy to develop novel ETEC vaccines.

References

1. Dobrindt U: **(Patho-)Genomics of Escherichia coli.** *Int J Med Microbiol* 2005, **295(6–7):**357-371.
2. Morschhauser J, Kohler G, Ziebuhr W, Blum-Oehler G, Dobrindt U, Hacker J: **Evolution of microbial pathogens.** *Philos Trans R Soc Lond B Biol Sci* 2000, **355(1397):**695-704.
3. Roten CA, Gamba P, Barblan JL, Karamata D: **Comparative Genometrics (CG): a database dedicated to biometric comparisons of whole genomes.** *Nucleic Acids Res* 2002, **30(1):**142-144.

4. Hsiao W, Wan I, Jones SJ, Brinkman FS: **IslandPath: aiding detection of genomic islands in prokaryotes.** *Bioinformatics* 2003, **19(3):**418-420.
5. Canchaya C, Proux C, Fournous G, Bruttin A, Brussow H: **Prophage genomics.** *Microbiol Mol Biol Rev* 2003, **67(2):**238-276. table of contents.
6. Lima-Mendez G, Van Helden J, Toussaint A, Leplae R: **Prophinder: a computational tool for prophage prediction in prokaryotic genomes.** *Bioinformatics* 2008, **24(6):**863-865.
7. McNeil LK, Reich C, Aziz RK, Bartels D, Cohoon M, Disz T, Edwards RA, Gerdes S, Hwang K, Kubal M, *et al.*: **The National Microbial Pathogen Database Resource (NMPDR): a genomics platform based on subsystem annotation.** *Nucleic Acids Res* 2007:D347-353.