Complete Genome Sequence of the Dog Commensal and Human Pathogen Capnocytophaga canimorsus Strain 5

Pablo Manfredi,¹ Marco Pagni,² and Guy R. Cornelis^{1*}

Biozentrum, University of Basel, Basel, Switzerland,¹ and Vital-IT Group, Swiss Institute of Bioinformatics, Lausanne, Switzerland²

Received 21 July 2011/Accepted 25 July 2011

Capnocytophaga canimorsus is a commensal Gram-negative bacterium, originally isolated from a dog's mouth, that causes septicemia in humans. *C. canimorsus* has the unusual ability to feed on host cells, including phagocytes. This capacity depends on surface-exposed glycan-foraging systems. Here we present the first complete genome sequence of a *C. canimorsus* strain (Cc5).

Capnocytophaga canimorsus are commensal Gram-negative bacteria that are present in the mouths of dogs and that cause septicemia in humans who have become infected as a result of contact with a dog (24). Capnocytophaga is exclusively and commonly found in the oral cavities of mammals. This genus belongs to the family Flavobacteriaceae in the group Bacteroidetes (3). These organisms escape the innate immune defenses of the host (19, 22, 23) and have the unusual ability to feed on the glycan moieties of glycoproteins present on the surfaces of mammalian cells, including phagocytes (14). This property is based on a sialidase and specialized complexes of the Sus family, mainly composed of surface-exposed lipoproteins (15, 16, 21). Here, we present the genome sequence of C. canimorsus Cc5, a strain that was isolated from a human septicemia patient (22). It is the first report of a C. canimorsus genome sequence.

Genome sequencing included pair-end reads from 4-kb- and 40-kb-insert libraries, a run of 454 pyrosequencing and a set of Illumina microreads (3.5, 0.5, 34, and $49 \times$ coverage, respectively). 454 reads were condensed into pseudoreads using Newbler and assembled with Sanger data with Phred/Phrap/Consed (6-8). After gap closure, microreads were aligned onto the chromosome to increase coverage using MAQ (12). Coding sequences (CDSs) were predicted with Glimmer 3.02 (5), and start codons were reevaluated considering bacterial frequencies of different start codons, potential signal peptides computed by LipoP (10), and CDS alignments with their best Blast hit against the nonredundant database (1) (http://www.ncbi.nlm.nih.gov/). CDSs were screened with InterProScan (26) and PRIAM (4) for functional annotation. For poorly characterized CDSs, PSI-BLAST (1) was used with uniref90 for matrix computation and Swiss-Prot, TrEMBL (2), or STRING orthologous groups (9) for data retrieval. Noncoding RNAs were inferred from Rfam using INFERNAL (20), RNAMMER (11), and tRNAscan-SE (13). The origin of replication was determined on the basis of the cumulative GC skew and on the occurrence of degenerated DnaA box clusters.

The genome of Cc5 consists of a single circular replicon of 2,571,406 bp with a G+C content of 36.11%, and it contains

2,405 CDSs. This genome size is similar to that of the humanhosted species Capnocytophaga ochracea (NC 013162, 2.6 Mb) (17) but noticeably smaller than that of other members of the Bacteroidetes, such as the free-living species Flavobacterium johnsoniae (6.1 Mb) (18) or the commensal species Bacteroides thetaiotaomicron (6.25 Mb) (25). The Cc5 genome contains 46 tRNAs, three sets of rRNA, an RNase P, two tmRNAs, a TPP riboswitch, and an SRP, and it contains one CRISPR region. It does not encode any type III, IV, or VI secretion system, which are commonly linked to pathogenesis. Consistently with the presence of several Sus-like systems, the Cc5 genome contains 206 lipoprotein genes (8.5% of total CDSs), some potentially acquired from eukaryotes or Gram-positive organisms. This high proportion of lipoprotein genes is unusual among the Eubacteria but typical of the Bacteroidetes. The genome encodes the LolACDE lipoprotein export system but, as for all members of the Bacteroidetes studied to date, lacks a LolB homolog.

Nucleotide sequence accession number. The annotated genome sequence of Cc5 was deposited in GenBank under accession number CP002113.

We thank H. Shin and M. Mally for their early contribution to this project.

This project was supported by the Swiss National Science Foundation (grant 3100A0-128659) and the Novartis Stiftung.

REFERENCES

- 1. Altschul, S. F., et al. 1997. Gapped BLAST and PSI-BLAST: a new gener-
- ation of protein database search programs. Nucleic Acids Res. 25:3389–3402. 2. Boeckmann, B., et al. 2003. The SWISS-PROT protein knowledgebase and
- its supplement TrEMBL in 2003. Nucleic Acids Res. 31:365–370. 3. Brenner, D. J., D. G. Hollis, G. R. Fanning, and R. E. Weaver. 1989. Cap-
- nocytophaga canimorsus sp. nov. (formerly CDC group DF-2), a cause of septicemia following dog bite, and C. cynodegmi sp. nov., a cause of localized wound infection following dog bite. J. Clin. Microbiol. 27:231–235.
- Claudel-Renard, C., C. Chevalet, T. Faraut, and D. Kahn. 2003. Enzymespecific profiles for genome annotation: PRIAM. Nucleic Acids Res. 31: 6633–6639.
- Delcher, A. L., K. A. Bratke, E. C. Powers, and S. L. Salzberg. 2007. Identifying bacterial genes and endosymbiont DNA with Glimmer. Bioinformatics 23:673–679.
- Ewing, B., and P. Green. 1998. Base-calling of automated sequencer traces using phred. II. Error probabilities. Genome Res. 8:186–194.
- Ewing, B., L. Hillier, M. C. Wendl, and P. Green. 1998. Base-calling of automated sequencer traces using phred. I. Accuracy assessment. Genome Res. 8:175–185.
- Gordon, D., C. Abajian, and P. Green. 1998. Consed: a graphical tool for sequence finishing. Genome Res. 8:195–202.
- Jensen, L. J., et al. 2009. STRING 8-a global view on proteins and their functional interactions in 630 organisms. Nucleic Acids Res. 37:D412–D416.

^{*} Corresponding author. Mailing address: Biozentrum, Klingelbergstrasse 50, CH-4056, Basel. Phone: (41) 61 267 21 10. Fax: (41) 61 267 21 18. E-mail: guy.cornelis@unibas.ch.

- Juncker, A. S., et al. 2003. Prediction of lipoprotein signal peptides in Gram-negative bacteria. Protein Sci. 12:1652–1662.
- Lagesen, K., et al. 2007. RNAmmer: consistent and rapid annotation of ribosomal RNA genes. Nucleic Acids Res. 35:3100–3108.
- Li, H., J. Ruan, and R. Durbin. 2008. Mapping short DNA sequencing reads and calling variants using mapping quality scores. Genome Res. 18:1851–1858.
 Lowe, T. M., and S. R. Eddy. 1997. tRNAscan-SE: a program for improved
- Lowe, T. M., and S. R. Eddy. 1997. tRNAscan-SE: a program for improved detection of transfer RNA genes in genomic sequence. Nucleic Acids Res. 25:955–964.
- Mally, M., H. Shin, C. Paroz, R. Landmann, and G. R. Cornelis. 2008. Capnocytophaga canimorsus: a human pathogen feeding at the surface of epithelial cells and phagocytes. PLoS Pathogens 4:e1000164.
- Manfredi, P., et al. 2011. The genome and surface proteome of *Capnocy-tophaga canimorsus* reveal a key role of glycan foraging systems in host glycoproteins deglycosylation. Mol. Microbiol. 81:1050–1060.
- Martens, E. C., N. M. Koropatkin, T. J. Smith, and J. I. Gordon. 2009. Complex glycan catabolism by the human gut microbiota: the *Bacteroidetes* Sus-like paradigm. J. Biol. Chem. 284:24673–24677.
- Mavromatis, K., et al. 2010. Complete genome sequence of Capnocytophaga ochracea type strain (VPI 2845T). Lawrence Berkeley National Laboratory.
- McBride, M. J., et al. 2009. Novel features of the polysaccharide-digesting gliding bacterium *Flavobacterium johnsoniae* as revealed by genome sequence analysis. Applied Environ. Microbiol. **75**:6864–6875.

- Meyer, S., H. Shin, and G. R. Cornelis. 2008. Capnocytophaga canimorsus resists phagocytosis by macrophages and blocks the ability of macrophages to kill other bacteria. Immunobiology 213:805–814.
- Nawrocki, E. P., D. L. Kolbe, and S. R. Eddy. 2009. Infernal 1.0: inference of RNA alignments. Bioinformatics 25:1335–1337.
- Renzi, F., et al. 2011. The N-glycan glycoprotein deglycosylation complex (Gpd) from *Capnocytophaga canimorsus* deglycosylates human IgG. PLoS Pathogens 7:e1002118.
- Shin, H., M. Mally, M. Kuhn, C. Paroz, and G. R. Cornelis. 2007. Escape from immune surveillance by *Capnocytophaga canimorsus*. J. Infect. Dis. 195:375–386.
- Shin, H., et al. 2009. Resistance of *Capnocytophaga canimorsus* to killing by human complement and polymorphonuclear leukocytes. Infect. Immun. 77: 2262–2271.
- Tierney, D. M., L. P. Strauss, and J. L. Sanchez. 2006. *Capnocytophaga canimorsus* mycotic abdominal aortic aneurysm: why the mailman is afraid of dogs. J. Clin. Microbiol. 44:649–651.
- Xu, J., et al. 2003. A genomic view of the human-Bacteroides thetaiotaomicron symbiosis. Science 299:2074–2076.
- Zdobnov, E. M., and R. Apweiler. 2001. InterProScan-an integration platform for the signature-recognition methods in InterPro. Bioinformatics 17: 847–848.