

Microbiological, epidemiological and food safety aspects of *Cronobacter* – an opportunistic foodborne pathogen

Background:

Cronobacter species are opportunistic pathogens that cause serious infections with high-mortality rates, predominantly in pre-term, low-birth weight and/or immune compromised neonates and infants. Clinical manifestations of infection include necrotizing enterocolitis, septicemia, and neonatal meningitis. The mortality rate of *Cronobacter* infection in neonates is 27%–80% and 20 % of the survivors develop neurological disorders. Infections in infants have been epidemiologically often linked to consumption of intrinsically and extrinsically - contaminated batches of reconstituted powdered infant formula (PIF).

WP1: *Cronobacter* as an opportunistic foodborne pathogen - reviews

Microbiological, epidemiological and food safety aspects of *Enterobacter sakazakii*

<https://pubmed.ncbi.nlm.nih.gov/15633700/>

Enterobacter sakazakii: an emerging microbe with implications for infant health

<https://pubmed.ncbi.nlm.nih.gov/17404564/>

Cronobacter spp.- opportunistic foodborne pathogens: an update on evolution, osmotic adaptation and pathogenesis

<https://link.springer.com/content/pdf/10.1007/s40588-018-0089-7.pdf>

WP2: Taxonomy

Cronobacter gen. nov., a new genus to accommodate the biogroups of *Enterobacter sakazakii*, and proposal of *Cronobacter sakazakii* gen. nov. comb. nov., *C. malonaticus* sp. nov., *C. turicensis* sp. nov., *C. muytjensii* sp. nov., *C. dublinensis* sp. nov., *Cronobacter* genomospecies 1, and of three subspecies, *C. dublinensis* sp. nov. subsp. *dublinensis* subsp. nov., *C. dublinensis* sp. nov. subsp. *lausannensis* subsp. nov., and *C. dublinensis* sp. nov. subsp. *lactaridi* subsp. nov.

<https://pubmed.ncbi.nlm.nih.gov/18523192/>

The taxonomy of *Enterobacter sakazakii*: proposal of a new genus *Cronobacter* gen. nov. and descriptions of *Cronobacter sakazakii* comb. nov. *Cronobacter sakazakii* subsp. *sakazakii*, comb. nov., *Cronobacter sakazakii* subsp. *malonaticus* subsp. nov., *Cronobacter turicensis* sp. nov., *Cronobacter muytjensii* sp. nov., *Cronobacter dublinensis* sp. nov. and *Cronobacter* genomospecies 1

<https://bmcecol-evol.biomedcentral.com/articles/10.1186/1471-2148-7-64>

Enterobacter turicensis, sp. nov. and *Enterobacter helveticus*, sp. nov. isolated from fruit powder

<https://pubmed.ncbi.nlm.nih.gov/17392213/>

Enterobacter pulveris, sp. nov. isolated from fruit powder, infant formula and infant formula production environment

<https://pubmed.ncbi.nlm.nih.gov/18175715/>

Re-examination of the taxonomic status of *Enterobacter helveticus*, *Enterobacter pulveris*, and *Enterobacter turicensis* as members of *Cronobacter* and description of *Siccibacter turicensis* com. nov., *Franconibacter helveticus* comb. nov., and *Franconibacter pulveris* com. nov.

<https://pubmed.ncbi.nlm.nih.gov/25028159/>

WP3: Detection, identification and typing methods

16S rRNA gene based analysis of *Enterobacter sakazakii* strains from different sources and development of a PCR assay for identification

<https://bmcmicrobiol.biomedcentral.com/articles/10.1186/1471-2180-4-43>

Comparison of two chromogenic media and evaluation of two molecular based identification systems for *Enterobacter sakazakii* detection

<https://bmcmicrobiol.biomedcentral.com/articles/10.1186/1471-2180-6-15>

Identification of *Cronobacter* spp. (*Enterobacter sakazakii*)

<https://pubmed.ncbi.nlm.nih.gov/17881547/>

Evaluation of an automated repetitive sequence-based PCR system for subtyping *Enterobacter sakazakii*

<https://pubmed.ncbi.nlm.nih.gov/18680935/>

Development of a novel screening method for the isolation of *Cronobacter* spp. (*Enterobacter sakazakii*)

<https://pubmed.ncbi.nlm.nih.gov/18310415/>

Molecular analysis of the *Enterobacter sakazakii* O-antigen gene locus

<https://pubmed.ncbi.nlm.nih.gov/18441119/>

Development of Multiple-Locus Variable Number Tandem Repeat Analysis for the molecular subtyping of *Enterobacter sakazakii*

<https://pubmed.ncbi.nlm.nih.gov/18083860/>

Development and evaluation of *rpoB* based PCR systems to differentiate the six proposed species within the genus *Cronobacter*

<https://pubmed.ncbi.nlm.nih.gov/19467725/>

Improving the enrichment procedure for *Enterobacteriaceae* detection

<https://pubmed.ncbi.nlm.nih.gov/19527830/>

Rapid genus and species specific identification of *Cronobacter* spp. by MALDI-TOF Mass spectrometry

<https://pubmed.ncbi.nlm.nih.gov/20554814/>

Evaluation of three commercially available real-time PCR based systems for detection of *Cronobacter* species

<https://pubmed.ncbi.nlm.nih.gov/21382642/>

Development and validation of a PulseNet standardized protocol for sub-typing isolates of *Cronobacter*

<https://pubmed.ncbi.nlm.nih.gov/22891917/>

Identification of the recently described *Cronobacter condimenti* by a *rpoB* based PCR system

<https://pubmed.ncbi.nlm.nih.gov/22466029/>

Development of a custom-designed, pan genomic DNA microarray to characterize strain-level diversity among *Cronobacter* spp.

<https://pubmed.ncbi.nlm.nih.gov/25984509/>

Determination of single cell lag times of *Cronobacter* spp. strains exposed to different stress conditions: impact on detection

<https://pubmed.ncbi.nlm.nih.gov/27521467/>

WP4: Genome sequences

Complete Genome Sequence of *Cronobacter turicensis* LMG 23827, a foodborne pathogen causing deaths in neonates

<https://pubmed.ncbi.nlm.nih.gov/21037008/>

Genome sequences of two *Enterobacter pulveris* strains 601/05T (= LMG 24057T = DSM 19144T), and 1160/04 (= LMG 24058 = DSM 19146), isolated from fruit powder

<https://pubmed.ncbi.nlm.nih.gov/24309737/>

Genome sequence of an *Enterobacter helveticus* strain, 1159/04 (= LMG 23733), isolated from fruit powder

<https://pubmed.ncbi.nlm.nih.gov/24336376/>

Genome sequence of *Enterobacter turicensis* strain 610/05 (= LMG 23731), isolated from fruit powder

<https://pubmed.ncbi.nlm.nih.gov/24309739/>

Draft genome sequence of *Cronobacter sakazakii* GP 1999, sequence type 145, an epiphytic isolate obtained from the tomato's rhizosphere/rhizosphere continuum

<https://pubmed.ncbi.nlm.nih.gov/28774978/>

Draft genomes of *Cronobacter sakazakii* strains isolated from dried spices bring unique insights into the diversity of plant-associated strains

<https://environmentalmicrobiome.biomedcentral.com/articles/10.1186/s40793-018-0339-6>

Complete genome sequences and genomic characterization of five plasmids harbored by environmentally persistent *C. sakazakii* strains ST83 H322 and ST64 GK1025B obtained from powdered infant formula manufacturing facilities

<https://gutpathogens.biomedcentral.com/articles/10.1186/s13099-022-00500-5>

WP5: Elucidation of phenotypic and physiological features and factors promoting the environmental and PIF associated lifestyle

Biofilm formation, EPS production and cell to cell signalling in various *Enterobacter sakazakii* strains: aspects promoting environmental persistence

<https://pubmed.ncbi.nlm.nih.gov/16300064/>

Cloning and characterization of *Enterobacter sakazakii* pigment genes and in situ spectroscopic analysis of the pigment

<https://pubmed.ncbi.nlm.nih.gov/17069626/>

Molecular characterization of the alpha glucosidase activity in *Enterobacter sakazakii* reveals the presence of a putative gene cluster for palatinose metabolism

<https://pubmed.ncbi.nlm.nih.gov/16563686/>

Cellulose as an extra-cellular matrix component present in *Enterobacter sakazakii* biofilms

<https://pubmed.ncbi.nlm.nih.gov/18236657/>

Proteomic profiling of *Cronobacter turicensis* 3032, a foodborne opportunistic pathogen

<https://pubmed.ncbi.nlm.nih.gov/19609963/>

A gel-free quantitative proteomics approach to investigate temperature adaptation of the food-borne pathogen *Cronobacter turicensis* 3032

<https://pubmed.ncbi.nlm.nih.gov/20718006/>

Genes involved in *Cronobacter sakazakii* biofilm formation

<https://pubmed.ncbi.nlm.nih.gov/20118366/>

Yellow pigmentation in *Cronobacter sakazakii* ES5: Genes involved and influence on persistence and growth under environmental stress

<https://pubmed.ncbi.nlm.nih.gov/20038705/>

Presence of AmpC beta-lactamases, CSA-1, CSA-2, CMA-1, and CMA-2 with an unusual resistance phenotype in *Cronobacter sakazakii* and *Cronobacter malonaticus*

<https://pubmed.ncbi.nlm.nih.gov/24568164/>

Genome-wide survey of efflux pump-coding genes associated with *Cronobacter* survival, osmotic adaptation, and persistence

<https://www.sciencedirect.com/science/article/pii/S221479931830033X>

RNA sequencing based transcriptional overview of xerotolerance in *Cronobacter sakazakii* SP291

<https://pubmed.ncbi.nlm.nih.gov/30446557/>

Comparative genomic characterization of the highly persistent and potentially virulent *Cronobacter sakazakii* ST83, CC65 strain H322 and other ST83 strains

<https://pubmed.ncbi.nlm.nih.gov/28694793/>

The secretion of toxins and other exoproteins of *Cronobacter*: Role in Virulence, Adaption, and Persistence

<https://pubmed.ncbi.nlm.nih.gov/32046365/>

WP6: Pathogenesis studies based on *in vitro* and *in vivo* models**Adhesive properties of *Enterobacter sakazakii* to human epithelial and brain microvascular endothelial cells**

<https://bmcmicrobiol.biomedcentral.com/articles/10.1186/1471-2180-6-58>

Influence of FkpA variants on survival and replication of *Cronobacter* spp. in human macrophages

<https://pubmed.ncbi.nlm.nih.gov/25724920/>

Evaluation of zebrafish as a model to study the pathogenesis of the opportunistic pathogen *Cronobacter turicensis*

<https://pubmed.ncbi.nlm.nih.gov/26060602/>

A *Cronobacter turicensis* O1 antigen specific monoclonal antibody inhibits bacterial motility and entry into epithelial cells

<https://pubmed.ncbi.nlm.nih.gov/25534937/>

Linking genomo- and pathotype: Exploiting the Zebrafish embryo model to investigate the divergent virulence potential among *Cronobacter* spp.

<https://pubmed.ncbi.nlm.nih.gov/27355472/>

Interaction of matrix metalloprotease-9 and Zpx in *Cronobacter turicensis* LMG 23827T mediated infections in the zebrafish model

<https://onlinelibrary.wiley.com/doi/10.1111/cmi.12888>

Characterization of *Cronobacter sakazakii* strains originating from plant derived foods using comparative genomic analysis and zebrafish infectivity studies

<https://doi.org/10.3390/microorganisms10071396>

WP7: Infections in humans

Complete Genome Sequence of *Cronobacter turicensis* LMG 23827, a foodborne pathogen causing deaths in neonates

<https://pubmed.ncbi.nlm.nih.gov/21037008/>

Multicenter Study of *Cronobacter sakazakii* Infections in Humans, Europe, 2017

<https://pubmed.ncbi.nlm.nih.gov/30789137/>