



LOMA LINDA UNIVERSITY

Loma Linda University  
TheScholarsRepository@LLU: Digital  
Archive of Research, Scholarship &  
Creative Works

---

Loma Linda University Electronic Theses, Dissertations & Projects

---

3-2023

## **ABSTRACT: The Role of the Novel Diguanylate Cyclase PG\_0686 in Oxidative Stress Resistance in Porphyromonas gingivalis W83**

Alexia Danielle Ximinies

Follow this and additional works at: <https://scholarsrepository.llu.edu/etd>



Part of the [Microbiology Commons](#), and the [Molecular Genetics Commons](#)

---

### **Recommended Citation**

Ximinies, Alexia Danielle, "ABSTRACT: The Role of the Novel Diguanylate Cyclase PG\_0686 in Oxidative Stress Resistance in Porphyromonas gingivalis W83" (2023). *Loma Linda University Electronic Theses, Dissertations & Projects*. 1830.

<https://scholarsrepository.llu.edu/etd/1830>

This Dissertation is brought to you for free and open access by TheScholarsRepository@LLU: Digital Archive of Research, Scholarship & Creative Works. It has been accepted for inclusion in Loma Linda University Electronic Theses, Dissertations & Projects by an authorized administrator of TheScholarsRepository@LLU: Digital Archive of Research, Scholarship & Creative Works. For more information, please contact [scholarsrepository@llu.edu](mailto:scholarsrepository@llu.edu).

LOMA LINDA UNIVERSITY  
School of Medicine  
in conjunction with the  
Faculty of Graduate Studies

---

The Role of the Novel Diguanylate Cyclase PG\_0686 in Oxidative Stress Resistance in  
*Porphyromonas gingivalis* W83

by

Alexia Danielle Ximinies

---

A Dissertation Submitted in Partial Satisfaction of  
the Requirements for the Degree  
Doctor of Philosophy in Microbiology and Molecular Genetics

---

March 2023

## ABSTRACT OF THE DISSERTATION

The Role of the Novel Diguanylate Cyclase PG\_0686 in Oxidative Stress Resistance in  
*Porphyromonas gingivalis* W83

By

Alexia Danielle Ximinies

Doctor of Philosophy, Graduate Program in Microbiology and Molecular Genetics

Loma Linda University, California USA March 2023

Dr. Hansel M. Fletcher, Chairman

The survival/ adaptation of *Porphyromonas gingivalis* to the inflammatory environment of the periodontal pocket requires an ability to overcome oxidative stress. Several functional classes of genes, depending on the severity and duration of the exposure, were induced in *P. gingivalis* under H<sub>2</sub>O<sub>2</sub>-induced oxidative stress, including the *PG0686* gene which was upregulated ca. 10-fold. In addition, its upregulation was also observed in the presence of oxygen and nitric oxide. This study is aimed to further characterize the function of this gene in response to H<sub>2</sub>O<sub>2</sub>. PG\_0686, annotated as a hypothetical protein of unknown function, is a 60 kDa protein with a diguanylate cyclase (DGC)-like fold and carries other domains including hemerythrin, a PAS10 domain, and Domain of Unknown Function (DUF)-1858. PG\_0686 is missing the classical active site conserved sequence motif (GGD(/E)EF) commonly observed in the DGC of other bacteria. PG\_0686-related proteins are observed in other anaerobic bacterial species. The isogenic mutant *P. gingivalis* FLL361 ( $\Delta$ *PG0686::ermF*) showed increased sensitivity to H<sub>2</sub>O<sub>2</sub> and decreased gingipain activity compared to the parent strain. Transcriptome analysis of *P. gingivalis* FLL361 showed the dysregulation of several gene clusters/operons, known oxidative stress resistance genes and

transcriptional regulators including PG\_2212, CdhR and PG\_1181 that were upregulated under normal anaerobic conditions. The purified recombinant PG\_0686 protein can catalyze c-di-GMP formation from GTP. The intracellular level of c-di-GMP in *P. gingivalis* FLL361 was significantly decreased compared to the parent strain. Collectively, our data suggest a global regulatory property for PG\_0686 that may be part of an unconventional second messenger signaling system in *P. gingivalis*. Moreover, it may coordinately regulate a pathway(s) vital for protection against environmental stress and is significant in the pathogenicity of the *P. gingivalis*, and likely other anaerobes.