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GENETIC VARIABILITY OF PEPTIDYL ARGININE DEIMINASE FROM *PORPHYROMONAS GINGIVALIS* IN PERIODONTITIS PATIENTS

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Introduction & Objective: Periodontitis is a widespread chronic inflammatory disease. Untreated condition leads to progressive destruction of the periodontal tissue and may result in tooth loss. Changes in oral microbiome leading to periodontitis are mainly driven by *Porphyromonas gingivalis*, the pathogen producing numerous virulence factors, including peptidylarginine deiminase (PPAD). PPAD modifies C-terminal arginine to citrulline, causing changes in structure and function of modified proteins, contributing to development periodontitis. The aim of this study was to investigate variability of PPAD in clinical isolates of *P. gingivalis*.

Materials & Methods: Together 23 *P. gingivalis* strains were isolated from patients with periodontitis and the PPAD gene was sequenced and analyzed together with sequences extracted from the GenBank database. Identified differences in the sequence were introduced into PPAD in reference strain ATCC 33277 and expression (mRNA) and PPAD activity were measured in cultures of the mutant. PPAD variants were expressed in *P. gingivalis*, purified and used to compare their enzymatic properties. Clinical parameters of periodontitis severity in patients infected with different *P. gingivalis* strains were determined.

Results: A new form of PPAD with three amino acid substitutions (G231N, E232T, N235D) near the active site was found in approximately 30% of *P. gingivalis* strains. Introduction of those mutations into the PPAD sequence in the ATCC 33277 strain resulted in two-fold increase of PPAD activity in culture, without effect on the level of mRNA expression. Kinetic assessment of the enzymatic reaction revealed that the mutated form of PPAD had higher maximum reaction rate (V_{max}). Patients infected with *P. gingivalis* strains with the super active PPAD variant had more advanced damage of periodontal tissues.

Conclusion: The newly identified form of PPAD shows higher enzymatic activity and its presence in strains of *P. gingivalis* in periodontitis patients correlated with severity of the disease.

BIOGRAPHY

Grzegorz Bereta has completed his MSc in Molecular Biotechnology at Faculty of Biochemistry, Biophysics and Biotechnology, Jagiellonian University, Krakow, Poland and since then he is enrolled on PhD studies at the same faculty. He has authored two publications and two conference reports as well as one book chapter.

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