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Mycoplasma Adaptation to Stress Conditions: Proteome Shift in *Mycoplasma hominis* PG37 in Response to Starvation and Low Temperatures

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Abstract—*Mycoplasma hominis* is a widely spread mycoplasma (class Mollicutes), associated with socially important human diseases and contamination of cell cultures. Controlling infections caused by *M. hominis* depends on determining the molecular mechanisms responsible for the bacterium's survival in unfavorable conditions. A proteome analysis employing 2-DIGE and MALDI TOF/TOF MS was applied to identify, for the first time, 53 proteins of *M. hominis* PG37 whose levels altered in bacteria cultivated in stress conditions (starvation and low temperature). According to the protein classification by functional category (clusters of orthologous groups of proteins, COG), 47 of the 53 mycoplasma proteins identified are involved in fundamental cellular and biochemical processes: translation (12; 22.64%), transcription (2; 3.77%), posttranslational modification (7; 13.20%), cell cycle control (2; 3.77%), energy production and conversion (6; 11.32%), carbohydrate transport and metabolism (3; 5.66%), amino acid transport and metabolism (8; 15.09%), nucleotide transport and metabolism (6; 11.32%), and inorganic ion transport and metabolism (1; 1.89%). For six proteins (11.32%), the function was not determined; 24 proteins (45.28%) were bacterial virulence factors. Those proteins of *M. hominis* PG37 whose expression is modulated in response to unfavorable environmental conditions are components of stress adaptation mechanisms in mycoplasma and potential targets for controlling infections caused by this bacterium.

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INTRODUCTION

Mycoplasma hominis is one of the most common mycoplasma species of the Mollicutes class associated with socially important human diseases and cell culture contamination [1, 2]. *M. hominis* is subject to both vertical (from mother to fetus) and horizontal (contact) transmission [1–4] and can cause both acute and chronic urogenital infections, apparent and unapparent, which lead to pregnancy complications and abnormality or death of the fetus [2–4]. Cell cultures can be contaminated with *M. hominis* via laboratory staff, reagents, equipment, or laboratory vessels, etc. [1], which implies that mycoplasma can survive outside the human body and retain its virulence, i.e., its infectiousness, toxigenicity, and persistence. Relatively recently, it was reported that *M. hominis* can persist in conditions that differ considerably from the bacterium's main environment, e.g., at decreased temperatures or restricted nutrient and energy source supply

(starvation) [5–7]. These data demonstrate that mycoplasma possesses a considerable adaptive potential and a wide range of infection pathways.

Fighting diseases caused by *M. hominis* infection is a serious problem; its solution depends on comprehending the molecular basis of mycoplasma persistence, i.e., the factors determining both susceptibility to *M. hominis* infection, and the bacterium's survival in adverse environments [1, 4, 8]. In 2009, the complete nucleotide sequence of the *M. hominis* PG21 was deciphered [9], providing the basis for identification of stress adaptation-related genes and proteins using postgenomic techniques. However, no such studies have been reported so far. The purpose of the present work was to perform a comparative analysis of *M. hominis* PG37 proteomes expressed in optimal and stress conditions (decreased temperature and starvation).

EXPERIMENTAL

Mycoplasma cultures. This work was performed with *M. hominis* strain PG37 obtained from the microbiological collection of the Gamaleya Institute of Epi-

Abbreviations: UMF—ultramicroform; MV—membrane vesicle; COG—cluster of orthologous groups of proteins; CHAPS—3-[(3-cholamidopropyl)dimethylammonio]-1-propanesulfonate