



Bioinformatic Exploration of Metal-Binding Proteome of Zoonotic Pathogen *Orientia tsutsugamushi*

Dixit Sharma¹, Ankita Sharma¹, Birbal Singh² and Shailender Kumar Verma^{1*}

¹ Centre for Computational Biology and Bioinformatics, School of Life Sciences, Central University of Himachal Pradesh, Kangra, India, ² ICAR-Indian Veterinary Research Institute, Regional Station, Palampur, India

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*Correspondence:

Shailender Kumar Verma
skverma@cuhimachal.ac.in

[†]Present Address:

Department of Biological Chemistry,
John Innes Centre, Norwich,
United Kingdom

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Metal ions are involved in many essential biological processes and are crucial for the survival of all organisms. Identification of metal-binding proteins (MBPs) of human affecting pathogens may provide the blueprint for understanding biological metal usage and their putative roles in pathogenesis. This study is focused on the analysis of MBPs from *Orientia tsutsugamushi* (*Ott*), a causal agent of scrub typhus in humans. A total of 321 proteins were predicted as putative MBPs, based on sequence search and three-dimensional structure analysis. Majority of proteins could bind with magnesium, and the order of metal binding was Mg > Ca > Zn > Mn > Fe > Cd > Ni > Co > Cu, respectively. The predicted MBPs were functionally classified into nine broad classes. Among them, gene expression and regulation, metabolism, cell signaling, and transport classes were dominant. It was noted that the putative MBPs were localized in all subcellular compartments of *Ott*, but majorly found in the cytoplasm. Additionally, it was revealed that out of 321 predicted MBPs 245 proteins were putative bacterial toxins and among them, 98 proteins were nonhomologous to human proteome. Sixty putative MBPs showed the ability to interact with drug or drug-like molecules, which indicate that they may be used as broad-spectrum drug targets. These predicted MBPs from *Ott* could play vital role(s) in various cellular activities and virulence, hence may serve as plausible therapeutic targets to design metal-based drugs to curtail its infection.

Keywords: *Orientia tsutsugamushi*, metal-binding proteins, therapeutic targets, structure modeling, bioinformatics

INTRODUCTION

Orientia tsutsugamushi (*Ott*) is a Gram-negative mite-borne bacterium responsible for life-threatening zoonotic disease, scrub typhus (Walker, 2016; Jain et al., 2018; Jiang et al., 2018). Scrub typhus (mite-borne typhus) represents one of the oldest vector-borne disease which is endemic in Asia Pacific, with some reports from Middle East and South America. One billion people are at risk of attaining the infection and one million people get infected each year globally (Xu et al., 2017). The outbreak of the infection was reported from different Indian provinces and is related to various complications with 30% fatality rate or even higher (Mahajan et al., 2010; Khan et al., 2017; Xu et al., 2017; Jain et al., 2018). There are certain antibiotics for the treatment of disease, but resistance to these antibiotics by strains of *Ott* has been reported and reviewed earlier (Watt et al., 1996; Mathai et al., 2003; Kelly et al., 2017). According