Ain Shams University
Faculty of Science
Department of Biochemistry

Development of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) candidate vaccine

THESIS

Submitted for the Degree of PhD in Science
(Biochemistry)

By

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(M.Sc. Biochemistry / 2012)

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APPROVAL SHEET

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This thesis has not been previously submitted for any degree at this or at any university.

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DEDICATION

I dedicate this work with all my deepest love and appreciation to all my family especially my awesome father, my lovely mother, my sisters, my father in law, my mother in law, my aunts, my uncles, my brothers in law, my sisters in law and my lovely wife for their love, patience, care, help and permanent encouragements during my study and for helping me throughout my life.

"Praise to Allah for choosing you to be my family"

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ABSTRACT

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) represents a global human health threat since its first zoonotic transmission to humans. Since 2012, a total of 2229 human confirmed infections with MERS-CoV were documented (791 fatalities; case-fatality rate=36%) in 27 countries. Herein, an active surveillance of MERS-CoV in Egypt among local and imported camels was conducted to demonstrate the prevalence situation and to characterize MERS-CoVs in Egypt. Subsequently, a well-characterized MERS-CoV isolate was used to develop vaccines via three different approaches; (1) DNA vaccines (encode structural proteins spike S, envelope E, membrane M and nucleocapsid N); (2) outer-membrane vesicles (OMVs)-based preparations expressing receptor-binding domain (RBD) of MERS-CoV spike protein; (3) a novel recombinant chimeric influenza A H1N1 pandemic (A/California/04/2009) (5+3) as a vector to express an immunogenic short peptide residue of MERS-CoV spike protein to elucidate immunity against MERS-CoV and H1N1pdm09. This study included the molecular characterization and serological analysis of 5693 samples. Interestingly, collected samples from camels have showed relatively high seropositivity for sera samples (71.2%). Nevertheless, for other types of collected samples which were tested by RT-PCR, the positivity rate was low and variable: nasal (15.4%), rectal (15.8%), milk (6.4%) and urine (0%). The imported camels showed higher percent in sera and viral prevalence than local one. The full genome sequences of Egyptian MERS-CoVs are grouped with a novel clade C out of clades A and B. Interestingly, the results of developed vaccine trials showed that BALB/c mice vaccinated with pcDNA3.1-S and pcDNA3.1-N gave potent neutralizing antibodies (nAbs) against MERS-CoV. The novel recombinant OMV-H1-RBD and the two chimeric rescued inactivated rgH1N1-peptide-MERS-CoVs stimulated a protective nAbs against H1N1pdm09 and MERS-CoV in vaccinated mice. This study is providing evidences that camels are the main reservoirs for MERS-CoV and surveillance in African exporting countries is urgently required. Also to control MERS-CoV, DNA vaccines of S and N encoded protein are highly recommended. The novel recombinant OMVs vaccine and two chimeric influenza virus with immunogenic peptide of MERS-CoV is can serve as effective bivalent vaccine to combat both H1N1pdm09 and MERS-CoV infections.

Keywords: MERS-CoV, surveillance, vaccine, and Egypt.

CONTENTS