JOURNAL OF EXTRACELLULAR VESICLES
2019, VOL. 8, 1578116
https://doi.org/10.1080/20013078.2019.1578116

Taylor & Francis
Taylor & Francis Group

RESEARCH ARTICLE

OPEN ACCESS

Exploration of extracellular vesicles from *Ascaris suum* provides evidence of parasite–host cross talk

Eline P. Hansen[a], Bastian Fromm [b,c], Sidsel D. Andersen[d], Antonio Marcilla [e,f], Kasper L. Andersen[a], Anne Borup[d], Andrew R. Williams[a], Aaron R. Jex[g,h], Robin B. Gasser[g], Neil D. Young[g], Ross S. Hall[g], Allan Stensballe[i,j], Vladimir Ovchinnikov[k], Yan Yan[l], Merete Fredholm[a], Stig M. Thamsborg[a] and Peter Nejsum [d,a]

[a]Department of Veterinary and Animal Sciences, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark; [b]Department of Tumor Biology, Institute for Cancer Research, The Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway; [c]Science for Life Laboratory, Department of Molecular Biosciences, The Wenner-Gren Institute, Stockholm University, Stockholm, Sweden; [d]Department of Clinical Medicine, Faculty of Health, Aarhus University, Aarhus, Denmark; [e]Departament de Farmàcia Ii Tecnologia Farmacéutica i Parasitologia, Universitat de València, València, Spain; [f]Joint Unit on Endocrinology, Nutrition and Clinical Dietetics, Instituto de Investigación Sanitaria-La Fe Valencia, València, Spain; [g]Population Health and Immunity Division, The Walter and Eliza Hall Institute, Melbourne, Australia; [h]Faculty of Veterinary and Agricultural Sciences, The University of Melbourne, Melbourne, Australia; [i]Department of Health Science and Technology, Aalborg University, Aalborg, Denmark; [j]Clinical Cancer Research Center, Aalborg University Hospital, Aalborg, Denmark; [k]Department of Human and Animal Genetics, The Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russian Federation; [l]Interdisciplinary Nanoscience Center (iNANO), Aarhus University, Aarhus, Denmark

ABSTRACT

The prevalent porcine helminth, *Ascaris suum*, compromises pig health and reduces farm productivity worldwide. The closely related human parasite, *A. lumbricoides*, infects more than 800 million people representing a disease burden of 1.31 million disability-adjusted life years. The infections are often chronic in nature, and the parasites have a profound ability to modulate their hosts' immune responses. This study provides the first in-depth characterisation of extracellular vesicles (EVs) from different developmental stages and body parts of *A. suum* and proposes the role of these vesicles in the host–parasite interplay. The release of EVs from the third- (L3) and fourth-stage (L4) larvae and adults was demonstrated by transmission electron microscopy (TEM), and sequencing of EV-derived RNA identified a number of microRNAs (miRNAs) and transcripts of potential host immune targets, such as IL-13, IL-25 and IL-33, were identified. Furthermore, proteomics of EVs identified several proteins with immunomodulatory properties and other proteins previously shown to be associated with parasite EVs. Taken together, these results suggest that *A. suum* EVs and their cargo may play a role in host–parasite interactions. This knowledge may pave the way to novel strategies for helminth infection control and knowledge of their immune modulatory potential.

ARTICLE HISTORY
Received 16 April 2018
Revised 18 January 2019
Accepted 29 January 2019

KEYWORDS
Ascaris suum; host–parasite interactions; extracellular vesicles; immunity; miRNA; proteomics

Introduction

The large roundworm, *Ascaris suum*, is one of the most important and prevalent parasitic nematodes of pigs. Although mostly subclinical, infections are associated with production losses due to impaired nutrient utilisation and reduced weight gain, but pigs may also be affected by a high worm burden [1]. In addition, *A. suum* infection may increase the pathogenicity of bacterial co-infections and compromise vaccine efficacy [2]. *A. lumbricoides* is highly prevalent in humans and 819 million people are estimated to be infected [3]. Due to the high genetic relatedness between *A. suum* and *A. lumbricoides* and the pronounced similarities in host physiology, *A. suum* infections in pigs can be used as model system for studying *A. lumbricoides* infections in humans [4].

Helminths, including *Ascaris* spp., induce a Th2-type immune response in their host, characterized by an increased production of eosinophils as well as an elevated secretion of IL-4 and IL-13 by T helper cells [5], and IL-25 and IL-33 by intestinal epithelial cells [6]. An increased level of IL-10 has also been observed in the intestine, where it acts as regulator of inflammation [7]. In addition, a strong suppression of both Th1 and Th17 immune function is a typical outcome of helminth infections [8] and T cell function is impaired in mice by *A. suum* products [9]. Dendritic cells (DCs) play an important role in the initiation of immune

CONTACT Peter Nejsum pn@clin.au.dk Department of Clinical Medicine, Aarhus University, Palle Juul-Jensens Boulevard 99, Aarhus N 8200, Denmark

Supplementary data for this article can be accessed here