CHAPTER ONE: INTRODUCTION

1.1 Background

One of the ways through which cells communicate is through the release of extracellular vesicles (EVs) into their environment. *Plasmodium falciparum* derived extracellular vesicles (PfEVs) mediate cell-cell communication within the parasite population, and with the host [1, 2]. PfEVs contain both parasite proteins and RNA and can transfer these to recipient cells. Several groups have shown that PfEVs have the potency to activate cells of the immune system and endothelium. Interestingly, when added to parasite cultures, PfEVs promote the formation of sexual stages that are transmitted from humans to the mosquito vector [1, 3-5]. However, the key parasite transcripts and pathways that are selectively included in PfEVs are poorly understood.

1.2 Research questions

1) Do the breadth and quantity of the parasite RNA content of EVs secreted by *P. falciparum* change over the intraerythrocytic life cycle?

2) Does the parasite RNA profile of *Pf*EVs secreted by two *P. falciparum* Kenyan clinical isolates differ to those secreted by NF54, a long-term adapted laboratory parasite line?

1.3 Objectives

1.3.1 General objective

To generate a dense map of *Pf*EV-RNA content across the intraerythrocytic life cycle, and establish the difference of this content between *P. falciparum* NF54 strain and two Kenyan clinical isolates.

1.3.2 Specific objectives

1) To determine the parasite RNA contained in *Pf*EVs released during the asexual life cycle of *P. falciparum*.

2) To determine whether the parasite RNA selectively included into *Pf*EVs secreted by two *P. falciparum* clinical isolates differs to *P. falciparum* NF54 strain.

1.4 Significance of the study

Specific transcripts could potentially be selectively packaged into PfEVs and transferred to recipient cells to impact function. However, this has not been determined before, and to the best of my knowledge, this is the first study to explore such a possibility. Analysing the content of PfEVs will help us understand their role in host-parasite interaction, and could guide novel malaria interventions.