BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
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NAME	POSITION TITLE
Blackman, Michael John	Senior Research Scientist
eRA COMMONS USER NAME	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Leeds, U.K.	B.Sc. (Hons)	1981	Microbiology
University of Warwick, U.K.	M.Sc. (Dist)	1985	Immunology
National Institute for Medical Research, U.K.	Ph.D.	1991	Biochemistry
National Institute for Medical Research, U.K.	Postdoctoral	1991-1993	Parasitology

A. Positions and Honors. List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

Positions and Employment

1981-1985 Research Officer, Dept. of Biological Sciences, University of Warwick, U.K.
1985-1988 Research Officer, MRC Laboratories, The Gambia, West Africa.
1988-1991 Research Officer/Graduate Student, Division of Parasitology, National Institute for Medical Research, London, U.K.
1991-1993 Postdoctoral Fellow, Division of Parasitology, National Institute for Medical Research, London, U.K.
1993-2000 Career Track Scientist, Division of Parasitology, National Institute for Medical Research, London, U.K.
2000-present Senior Research Scientist and Program Leader, Division of Parasitology, National Institute for Medical Research, London, U.K.

Other Experience, Honors and Professional Memberships

1998-present Member, Biochemical Society.
2000-present Editorial Board Member: Current Drug Targets.
2004-present Executive Committee member, European Union Framework 6 *BioMalPar* Network of Excellence.
2003-present Honorary Reader of University College, London (Dept of Medical Microbiology)

B. Selected peer-reviewed publications (selected from a total of 72 peer-reviewed publications)

Withers-Martinez C, Haire LF, Hackett F, Walker PA, Howell SA, Smerdon SJ, Dodson GG, **Blackman MJ** (2008). Malarial EBA-175 region VI crystallographic structure reveals a KIX-like binding interface. J. Mol Biol 375:773-781.

Yeoh S, O'Donnell RA, Koussis K, Dluzewski AR, Ansell KH, Osborne SA, Hackett F, Withers-Martinez C, Mitchell GH, Bannister LH, Bryans JS, Kettleborough CA, **Blackman MJ** (2007) Subcellular discharge of a serine protease mediates release of invasive malaria parasites from host erythrocytes. Cell 131: 1072-1083.

Blumenschein, TM, Friedrich N, Childs RA, Saouros S, Carpenter EP, Campanero-Rhodes MA, Simpson, P, Chai W, Koutroukides T, **Blackman MJ**, Feizi T, Soldati-Favre D, Matthews S (2007). Atomic resolution insight into host cell recognition by Toxoplasma gondii. EMBO J 26:2808-2820.

Collins CR, Withers-Martinez C, Bentley GA, Batchelor AH, Thomas AW, **Blackman MJ** (2007). Fine Mapping of an Epitope Recognized by an Invasion-inhibitory Monoclonal Antibody on the Malaria Vaccine Candidate Apical Membrane Antigen 1. J Biol Chem 282: 7431-7441.

O'Donnell RA, Hackett F., Howell SA, Treeck M, Struck N, Krnajski Z, Withers-Martinez C, Gilberger TW, **Blackman MJ** (2006). Intramembrane proteolysis mediates shedding of a key adhesin during erythrocyte invasion by the malaria parasite. J Cell Biol 174: 1023-1033.

Harris PK, Yeoh S, Dluzewski AR, O'Donnell RA, Withers-Martinez C, Hackett F, Bannister LH, Mitchell GH, **Blackman MJ** (2005) Molecular Identification of a malaria merozoite surface sheddase. PLoS Pathogens 1: 241-251.

O'Donnell RA, **Blackman MJ** (2005) The role of malaria merozoite proteases in red blood cell invasion. Curr Opin Microbiol 8: 422-427.

Howell SA, Hackett F, Jongco AM, Withers-Martinez C, Kim K, Carruthers VB, **Blackman MJ** (2005) Distinct mechanisms govern proteolytic shedding of a key invasion protein in apicomplexan pathogens. Mol Microbiol 57: 1342-1356.

Polson HE, **Blackman MJ** (2005) A role for poly(dA)poly(dT) tracts in directing activity of the Plasmodium falciparum calmodulin gene promoter. Mol Biochem Parasitol 141: 179-189.

Pizarro JC, Normand BV, Chesne-Seck ML, Collins CR, Withers-Martinez C, Hackett F, **Blackman MJ**, Faber BW, Remarque EJ, Kocken CH, Thomas AW, Bentley GA (2005) Crystal structure of the malaria vaccine candidate apical membrane antigen 1. Science 308: 408-411.

Carruthers VB, **Blackman MJ** (2005) A new release on life: emerging concepts in proteolysis and parasite invasion. Mol Microbiol 55: 1617-1630.

Zhou XW, **Blackman MJ**, Howell SA, Carruthers VB (2004) Proteomic analysis of cleavage events reveals a dynamic two-step mechanism for proteolysis of a key parasite adhesive complex. Mol Cell Proteomics 3: 565-576.

Blackman MJ (2004) Proteases in host cell invasion by the malaria parasite. Cell Microbiol 6: 893-903.

Withers-Martinez C, Jean L, **Blackman MJ** (2004) Subtilisin-like proteases of the malaria parasite. Mol Microbiol 53: 55-63.

Fleck SL, Birdsall B, Babon J, Dluzewski AR, Martin SR, Morgan WD, Angov E, Kettleborough CA, Feeney J, **Blackman MJ**, Holder AA (2003) Suramin and suramin analogues inhibit merozoite surface protein-1 secondary processing and erythrocyte invasion by the malaria parasite Plasmodium falciparum. J Biol Chem 278: 47670-47677.

Miller SA, Thathy V, Ajioka JW, **Blackman MJ**, Kim K (2003) TgSUB2 is a Toxoplasma gondii rhoptry organelle processing proteinase. Mol Microbiol 49: 883-894.

Bannister LH, Hopkins JM, Dluzewski AR, Margos G, Williams IT, **Blackman MJ**, Kocken CH, Thomas AW, Mitchell GH (2003) Plasmodium falciparum apical membrane antigen 1 (PfAMA-1) is translocated within micronemes along subpellicular microtubules during merozoite development. J Cell Sci 116: 3825-3834.

Howell SA, Wells I, Fleck SL, Kettleborough C, Collins CR, **Blackman MJ** (2003) A single malaria merozoite serine protease mediates shedding of multiple surface proteins by juxtamembrane cleavage. J Biol Chem 278: 23890-23898.

Jean L, Hackett F, Martin SR, **Blackman MJ** (2003) Functional characterisation of the propeptide of Plasmodium falciparum subtilisin-like protease-1. J Biol Chem 278: 28572-28579.

Blackman MJ, Corrie JE, Croney JC, Kelly G, Eccleston JF, Jameson DM (2002) Structural and biochemical characterization of a fluorogenic rhodamine-labeled malarial protease substrate. Biochemistry 41: 12244-12252.

Withers-Martinez C, Saldanha JW, Ely B, Hackett F, O'Connor T, **Blackman MJ** (2002) Expression of recombinant Plasmodium falciparum subtilisin-like protease-1 in insect cells: Characterization, comparison with the parasite protease, and homology modelling. J Biol Chem 277: 29698-29709.

Kocken CH, Withers-Martinez C, Dubbeld MA, Van Der Wel A, Hackett F, **Blackman MJ**, Thomas AW (2002) High-Level Expression of the Malaria Blood-Stage Vaccine Candidate Plasmodium falciparum Apical Membrane Antigen 1 and Induction of Antibodies That Inhibit Erythrocyte Invasion. Infect Immun 70: 4471-4476.

Howell SA, Withers-Martinez C, Kocken CH, Thomas AW, **Blackman MJ** (2001) Proteolytic processing and primary structure of Plasmodium falciparum apical membrane antigen-1. J Biol Chem 276: 31311-31320.

C. Research Support.

1. Role: PI UK Medical Research Council core support (2000-present)
"Proteases and proteolytic processing in erythrocyte invasion by the malaria parasite."
2. Role: PI MRC Technology Pilot Development Gap Award "PfSUB-2, a serine protease of the malaria merozoite; expression, structural determination and development as drug target". Feb 2003 – Feb 2005.
3. Role: PI Wellcome Trust Travelling Fellowship grant to Dr Rebecca O'Donnell. "Functional analysis of subtilisin-like proteases of the malaria merozoite". June 2003 -June 2005.
4. Role: PI European Union Framework 6 Network of Excellence (NoE) grant "Biology and Pathology of the Malaria Parasite (*BioMalPar*)". Contract no. 503578. April 2004 - April 2009.
5. Role: PI MRC Technology Development Gap Award, "Inhibitors of a malarial serine protease". Start date Feb 2005 – Feb 2007.

C. Research interests.

Malaria is directly responsible for an estimated 2-3 million deaths per annum, imposing an immense economic burden on much of the developing world. There is no malaria vaccine, and resistance against mainstay antimalarial drugs is widespread, resulting in an increasing threat to travellers.

Malaria is caused by an obligate intracellular parasite, which invades and replicates within red blood cells. We are interested in the molecular mechanisms by which the invasive blood-stage form of the parasite, the merozoite, modifies, exits (a process called egress) and enters its host red cell.

Blood stages of the most virulent species of the malaria parasite, *Plasmodium falciparum*, can be cultured in vitro, and our work uses classical biochemical approaches, transgenesis and microscopy to study invasion and egress in this system. A major element of our work makes use of heterologous expression systems for structural and enzymological studies.

At or around egress and invasion, several essential parasite proteins are dramatically restructured as a result of proteolytic activity. A subtilisin-like parasite protease called PfSUB1 plays a role in release of the parasite from its host cell. At invasion, several merozoite surface proteins known to play a key role in invasion are precisely cleaved by another parasite subtilisin-like protease called PfSUB2 and shed from the merozoite surface. Our investigations of these proteases are focused on determining their structure, their fine substrate specificity and their precise function in the parasite as well as the identification of selective low molecular weight inhibitors of the enzymes that have potential for development as antimalarial drugs. In addition we have found that members of a different family of serine proteases called rhomboids, first discovered in Drosophila, also play an important role in invasion. We are engaged in active collaborations with other groups interested in the role of serine proteases in host cell invasion by related Apicomplexan parasites, including the pathogen *Toxoplasma gondii.* Our research focuses on the physiological significance of these proteolytic processing events, and the structural and functional characterization of the enzymes involved in these and other important protease-mediated processes during invasion. A better understanding of these will help to lay the groundwork for development of new, much needed drugs or vaccines which target processes and molecules involved in this critical step in the parasite's life cycle.

D. Short biography.

Mike Blackman was born in Stockport in the UK, and obtained a BSc in Microbiology from the University of Leeds in 1981. He worked on interferon gamma in Alan Morris' group at the University of Warwick, where he obtained an MSc by research in 1985. That same year he took up a post as a research officer in the Medical Research Council's unit in The Gambia, West Africa, where he worked on the role of antibodies in protection against malaria. It was here that he developed his interest in malaria and in particular the mechanistic basis of host cell invasion by the malaria parasite. Mike returned to the UK in 1988 to study for a PhD in Tony Holder's lab at NIMR. Following this he stayed at NIMR, taking up a career track appointment and then being awarded tenure in 2000. He also holds a position as Honorary Reader in the Department of Medical Microbiology of

University College London. His current research interests focus on the role of proteases in host cell invasion by the malaria parasite and other apicomplexan parasites.
