

# Eva-Maria Frickel, PhD

---

Host-*Toxoplasma* Interaction Laboratory, The Francis Crick Institute, London, UK  
<http://www.crick.ac.uk/research/a-z-researchers/researchers-d-h/eva-frickel/>  
[www.frickellab.com](http://www.frickellab.com)  
[eva.frickel@crick.ac.uk](mailto:eva.frickel@crick.ac.uk)

## **Research Interest Keywords**

Host-pathogen interaction, *Toxoplasma gondii*, *Salmonella typhimurium*, ubiquitin, guanylate binding proteins, host cell death pathways, gamma interferon, stem-cell derived macrophages, artificial intelligence-driven image analysis

## **Education and Research Experience**

since 7/2011	<b>Group Leader</b> Division of Parasitology MRC National Institute of Medical Research, London, UK Has become: The Francis Crick Institute (current lab size: 3 postdocs, 3 PhD students)
2/2011-6/2011	<b>Visiting Scientist</b> University of Georgia, Athens, Georgia, USA and Hospital San Martin, Provincia Buenos Aires, Argentina Supervisors: Prof. Rick Tarleton and Dr. Susana Laucella (Parasitology and Human Immunology)
11/2005-11/2010	<b>Postdoctoral Research Fellow</b> Whitehead Institute, USA Supervisor: Prof. Hidde Ploegh (Immunology, Parasitology and Cell Biology)
6/2004-5/2005	<b>Postdoctoral Research Associate</b> ETH Zurich, Switzerland Supervisor: Prof. Ari Helenius (Cell Biology)
10/2000-4/2004	<b>Ph.D. student</b> ETH Zurich, Switzerland Thesis Advisor: Prof. Ari Helenius (Biochemistry and Biophysics)
6/2000-9/2000	<b>Research assistant</b> University of Auckland, New Zealand Supervisor: Prof. Peter Metcalf (Protein Crystallography)
8/2000	<b>MSc in Chemistry/Biochemistry</b> Uppsala University, Sweden Thesis Advisor: Prof. Bengt Mannervik (Enzyme Kinetics)
7/1997	<b>BSc in Chemistry</b> Freiburg University, Germany

## **Honours and Funding History**

2017	Boehringer Ingelheim Fellowship awarded to PhD student Daniel Fisch
2011-2016	Career Development Award, Wellcome Trust
2012	Boehringer Ingelheim Fellowship awarded to PhD student Clemence Foltz
2011	Travel grant from the Journal "Disease Models and Mechanisms"
2010	Wellcome Beit Prize Fellowship for top interview at Wellcome Trust
2006	Postdoctoral Research Grant from the Human Frontiers Science Foundation
2006	EMBO postdoctoral long-term fellowship (declined)
2005	Postdoctoral Research Grant from the Swiss National Science Foundation

- 2004 Postdoctoral research grant from UBS
- 2004 Travel award from the ETH Zurich for the Calreticulin meeting in Zermatt, Switzerland
- 2003 Travel award from Keystone to attend the conference “Conformational Diseases of the Secretary Pathway” in Taos, NM, USA
- 2001-2004 Ph.D. studentship grant from the ETH Zurich (TH grant)

### **Teaching Experience**

#### ***London, UK***

- 2014-2017 Yearly 1.5h lecture on “Immunity to *Toxoplasma gondii*” for MSc students at The London School of Hygiene and Tropical Medicine
- 2016-2018 2h tutorial for the Infection and Immunology Graduate Program at the Laboratory for Molecular Cell Biology, University College London

#### ***Whitehead Institute/MIT, USA***

- 2007 Set-up and co-taught an Advanced undergraduate seminar (“Chronic Infection and Inflammation: What are the Consequences on Your Health?”) for MIT Biology
- 2007-2010 Thesis Supervisor for three MSc students and one undergraduate trainee (9 and 6 months each, respectively)

#### ***ETH Zurich, Switzerland***

- 2004 Teaching Assistant, Advanced Biochemistry Course for third-year students
- 2001-2003 Teaching Assistant, Basic Biochemistry Lab Course for first-year students
- 2002 Responsible Leader for Enzyme Kinetics, Basic Biochemistry Lab Course
- 2000-2004 Thesis Supervisor for two MSc students and one technician trainee

### **Training and Recruitment**

- Panel member for NIMR/Crick PhD selection in 2012, 2013, 2016, 2018
- 2011-ongoing Member of 4 thesis committees

### **Public Engagement**

- 2016/2017 Participant in the exhibit “How do we look?” at the Francis Crick Insititute.
- 2016 Speaker at the “Pint of Science” event
- 2012-ongoing Science ambassador for Reagent High School, Camden
- 2015 “Meet a Nobel Scientist” Member of panel in a discussion with students
- 2014 NIMR Centenary Day talk
- 2013/2014 NIMR Schools day talk
- 2013/2014 St Paul School talk
- 2013 National Institute of Medical Research (NIMR) Open Day talk

### **Conference Organisation**

- Co-organizer of the 1<sup>st</sup> UK Toxo Day in Liverpool, UK, November 12-13, 2014
- Co-organizer of the 2<sup>nd</sup> D-BIOL PhD Summer School (Molecular Mechanism of Disease and Drug Development), Les Côtes, Switzerland, September 11-14, 2002

### **External Reviewer**

Journals: Autophagy, Journal of Experimental Medicine, Nature Immunology, Parasite Immunology, PLoS One, Scientific Reports

Granting agencies: Wellcome Trust, Medical Research Council, French National Research Council (ANR), European Research Council

Interviewer on Grant panels: Wellcome Trust Post-doc fellowships, UCL Excellence Fellow (starting PI grant)

### **Selected peer-reviewed publications (EM Frickel and lab members in bold)**

Total citations: 1605; h index: 16

**Foltz C, Napolitano A, Khan R, Clough B, Hirst EM, Frickel E-M** (2017) TRIM21 is critical for survival of *Toxoplasma gondii* infection and localises to GBP-positive parasite vacuoles. *Sci Rep.* 7 (1), 5209.

**Clough B, Wright JD, Pereira PM, Hirst EM, Johnston AC, Henriques R & Frickel E-M** (2016) K63-linked

ubiquitination targets *Toxoplasma gondii* for endo-lysosomal destruction in IFN $\gamma$ -stimulated human cells. *PLoS Pathog.* 12: e1006027.

**Johnston AC**, Piro A, **Clough B**, **Siew M**, Virreira Winter S, Coers J and **Frickel E-M** (2016) Human GBP1 does not localise to pathogen vacuoles but restricts *Toxoplasma gondii*. *Cell. Microbiol.* 18 (8), 1056-1064.

Haldar AK, Piro AS, Finethy R, Espenschied ST, Brown HE, Giebel AM, **Frickel E-M**, Nelson DE & Coers J (2016) Chlamydia trachomatis is resistant to inclusion ubiquitination and associated host defense in gamma interferon-primed human epithelial cells. *MBio* 7: e01417–16.

Swee LK, Tan ZW\*, **Sanecka A\***, **Yoshida N**, Patel H, Grotenbreg G, **Frickel E-M\*\*** & Ploegh HL\*\* (2016) Peripheral self-reactivity regulates antigen-specific CD8 T-cell responses and cell division under physiological conditions. *Open Biol* 6: 160293.

\*shared authorship, \*\*co-corresponding author

**Sanecka A**, **Yoshida N**, Dougan S K, Jackson J, Shastri N, Ploegh H, Blanchard N, **Frickel E-M**. (2016) Transnuclear CD8 T cells specific for the immunodominant epitope Gra6 lower acute phase *Toxoplasma gondii* burden. *Immunology*, Jul 5.

Haldar AK, **Foltz C**, Finethy R, Piro AS, Feeley EM, Pilla-Moffett DM, Komatsu M, **Frickel E-M** & Coers J (2015) Ubiquitin systems mark pathogen-containing vacuoles as targets for host defense by guanylate binding proteins. *Proc. Natl. Acad. Sci. U.S.A.* 112: E5628–37

Jensen KDC, Camejo A, Melo MB, Cordeiro C, Julien L, Grotenbreg GM, **Frickel E-M**, Ploegh HL, Young L & Saeij JPJ (2015) *Toxoplasma gondii* superinfection and virulence during secondary infection correlate with the exact ROP5/ROP18 allelic combination. *MBio* 6: e02280–14

Ohshima J, Sasai M, Liu J, Yamashita K, Ma JS, Lee Y, Bando H, Howard JC, Ebisu S, Hayashi M, Takeda K, Standley DM, **Frickel E-M** & Yamamoto M (2015) RabGDI $\alpha$  is a negative regulator of interferon- $\gamma$ -inducible GTPase-dependent cell-autonomous immunity to *Toxoplasma gondii*. *Proc. Natl. Acad. Sci. U.S.A.*

Niedelman W, Sprokholt JK, **Clough B**, **Frickel E-M** & Saeij JPJ (2013) Cell death of gamma interferon-stimulated human fibroblasts upon *Toxoplasma gondii* infection induces early parasite egress and limits parasite replication. *Infection and Immunity* 81: 4341–4349

Virreira Winter S, Niedelman W, Jensen KD, Rosowski EE, Julien L, Spooner E, Caradonna K, Burleigh BA, Saeij JP, Ploegh HL, **Frickel E-M** (2011) Determinants of GBP recruitment to *Toxoplasma gondii* vacuoles and the parasitic factors that control it. *PLoS One*; 6(9).

Kirak, O., **Frickel, E-M**, Grotenbreg, G.M., Suh, H., Jaenisch, R. and Ploegh, H.L. (2010) Transnuclear mice with predefined T cell receptor specificities against *Toxoplasma gondii* obtained via SCNT. *Science*. 328: 243-248.

Wilson DC, Grotenbreg GM, Liu K, Zhao Y, **Frickel E-M**, Gubbels, M.J., Ploegh, H.L., Yap, G.S. (2010) Differential regulation of effector- and central-memory responses to *Toxoplasma gondii* infection by IL-12 revealed by tracking of Tgd057-specific CD8+ T Cells. *PLoS Pathog* 6(3).

**Frickel E-M**, Sahoo N, Hopp J, Gubbels MJ, Craver MPJ, Knoll LK, Ploegh HL and Grotenbreg GM (2008) Parasite stage-specific recognition of endogenous *Toxoplasma gondii* derived CD8+ T cell epitopes. *J Infect Dis* 198, 1625-33.

**Frickel, E-M**, Quesada, V, Muething, L, Gubbels, M J, Spooner, E, Ploegh, H, and Artavanis-Tsakonas, K (2007). Apicomplexan UCHL3 retains dual specificity for ubiquitin and Nedd8 throughout evolution. *Cell Microbiol* 9, 1601-1610.

Kulp, M S, **Frickel, E-M**, Ellgaard, L, and Weissman, J S (2006). Domain architecture of protein-disulfide isomerase facilitates its dual role as an oxidase and an isomerase in Ero1p-mediated disulfide formation. *J Biol Chem* 281, 876-884.

**Frickel, E-M**, Frei, P, Bouvier, M, Stafford, W F, Helenius, A, Glockshuber, R, and Ellgaard, L (2004). ERp57 is a multifunctional thiol-disulfide oxidoreductase. *J Biol Chem* 279 18277-18287.

**Frickel, E-M**, Riek, R, Jelesarov, I, Helenius, A, Wuthrich, K, and Ellgaard, L (2002). TROSY-NMR reveals interaction between ERp57 and the tip of the calreticulin P-domain. *Proc Natl Acad Sci U S A* 99 1954-1959.

**Frickel, E-M**, Jemth, P, Widersten, M, and Mannervik, B (2001). Yeast glyoxalase I is a monomeric enzyme with two active sites. *J Biol Chem* 276, 1845-1849

### **Selected reviews**

Saeij, JP\*\*, **Frickel, E-M\*\*** (2017) Exposing *Toxoplasma gondii* hiding inside the vacuole: as role for GBPs, autophagy and host cell death. *Current Opinion in Microbiology* 40, 72-80.

\*\*co-corresponding author

**Clough B, Frickel E-M** (2017) The *Toxoplasma* Parasitophorous Vacuole: an evolving host-parasite frontier. *Trends Parasitol* 33:473-88.

Yoshida N, EM **Frickel E-M\*\***, S Mostowy S\*\* (2017) Macrophage-microbe interactions: lessons from the zebrafish model. *Frontiers in Immunology* 8:1703.

\*\*co-corresponding author

**Sanecka A, Frickel E-M** (2012) Use and abuse of dendritic cells by *Toxoplasma gondii*. *Virulence* 3:678-89.

### **Deposited preprints**

**Sanecka A, Yoshida N**, Kolawole EM, Patel H, Evavold BD, **Frickel E-M**. TCR-MHC Interaction Strength Defines Trafficking and Resident Memory Status of CD8 T cells in the Brain. *bioRxiv*, 263152

**A Napolitano**, van der Veen AG, **Bunyan M**, Borg A, Kjaer S, Beling A, Knobloch, KP, Snijders, A, **Frickel E-M**. Free ISG15 as a dimer generates IL-1b-producing CD8a+ dendritic cells at the site of infection. *bioRxiv*, 111658

### **Selected oral conference presentations**

28/6/2017 Biology of Parasitism course, Invited Lecturer, Woods Hole, USA

“Sensing and destructing *Toxoplasma* in Mouse and Man”

6/4/2017 Society of Microbiology Meeting, Edinburgh, UK

“Border control: *Toxoplasma gondii* and the human host cell”

8/9/2015 Cold Spring Harbor Microbial Pathogenesis & Host Response Meeting, USA

“TRIM21 regulates cytoplasmic non-cell autonomous immune defence to *Toxoplasma gondii*”

19/6/2015 International *Toxoplasma* Conference, Gettysburg, USA

“Non-cell autonomous resistance to *Toxoplasma gondii* is mediated by TRIM21-dependent ubiquitination of GBP1-positive parasitophorous vacuoles”

21/4/2015 Woods Hole Immunoparasitology Conference, Cape Cod, USA

“The formation and maintenance of brain resident memory CD8 T cells is dependent on the affinity of TCR-MHC interaction”

Presenter: Anna Sanecka (post-doc in Frickel lab), only students and post-docs present at this meeting

10/9/2014 The Inflammation and Disease conference, Manchester, UK

“Do different T cell receptor sequences dictate the phenotype of memory CD8 T cells in the *Toxoplasma gondii*-infected brain?”