Francesco Flandi

PhD Student in Cellular and Molecular Biology
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Research Profile

PhD student specializing in host-pathogen interactions between *Streptococcus pneumoniae*, hypervirulent *Klebsiella pneumoniae*, and tissue-resident macrophages, focusing on how these cells clear encapsulated pathogens. Skilled in primary macrophage culture from human, porcine, and murine spleen and liver, *ex vivo* organ perfusion models (human spleen and liver), advanced microscopy (confocal, time-lapse, whole-slide scanning immunohistochemistry, 3D reconstruction, LiveCyte), ELISA, quantitative image analysis with Fiji/ImageJ and mechanistic studies of cellular responses to bacterial infection in host-specific niches. Additional experience in bacterial genetics, biofilm assays, and antibiotic susceptibility testing. Limited but certified exposure to *in vivo* mouse infection models.

Education

PhD in Cellular and Molecular Biology – University of Bologna, Italy (in progress, thesis submitted, PhD title expected Mar-Apr 2026).

- Supervisor: Prof. Marco Rinaldo Oggioni.
- Thesis: Mechanisms of host-species-specific tissue macrophages immunity to *Streptococcus pneumoniae* and *Klebsiella pneumoniae* infections.

Master's Degree in Molecular and Industrial Biotechnology (Laurea Magistrale, equivalent to MSc) – University of Bologna, Italy, Sept 2019 – Mar 2022.

- Thesis: Study of the hypothetical role of the endo-α-N-1,3-acetylgalactosaminidase of *Streptococcus pneumoniae* in cellular auto-aggregation and biofilm formation.
- Supervisor: Prof. Marco Rinaldo Oggioni.
- Grade: 110/110 cum laude (with prize).

Bachelor's Degree in Biotechnology (Laurea Triennale, equivalent to BSc) – University of Bologna, Italy, Oct 2016 – Oct 2019.

- Thesis: Nanomechanical characterization of microglia cells by atomic force microscopy (AFM).
- Supervisor: Prof. Giampaolo Zuccheri.
- Grade: 107/110.

Research Skills

Bacterial manipulation

- Manipulation of class II pathogenic bacteria.
- Generation of *K. pneumoniae* capsule mutants (*rmpA* gene).
- Testing bacterial survival of hypervirulent *K. pneumoniae* to porcine serum.
- Genetic manipulation of *S. pneumoniae* and generation of deletion mutants by Gibson Assembly.
- *In vitro* biofilm formation assays with *S. pneumoniae*.
- Antibiotic susceptibility testing of *S. epidermidis* (MICs, MBCs, Killing and growth curves).
- Testing oxidative and metals stress responses in *K. pneumoniae*, *S. epidermidis*, *S. aureus* and *E. Coli*.
- Bacterial DNA extraction and sample preparation for sequencing.
- *E. coli* cloning and *S. epidermidis* transformation.

Human organ perfusions

- Developed *ex vivo* perfusion and infection models of human spleen and liver with *S. pneumoniae* and hypervirulent *K. pneumoniae*, and data analysis.
- Cryosectioning of frozen human spleen and liver samples.
- Immunohistochemistry and whole slide scanning microscopy of frozen human spleen and liver samples.
- Extraction of high-quality RNA from frozen human spleen and liver tissue slices for spatial transcriptomic analysis, with support in RNA integrity and quality assessment.
- ELISA assays for cytokine and immune mediator quantification during organ infections.
- **Clinical Trial, UK:** Ashley Dennison, University Hospitals of Leicester, HPB surgical team – human spleen (REC 18/EM/0057, NCT04620824). Operator in infection and *ex vivo* studies.
- **Clinical trial, Italy:** Matteo Ravaioli, University of Bologna, IRCCS Sant'Orsola transplant team – human liver and spleen (CE668/2023/Sper/AOUBo). Operator in infection and *ex vivo* studies.
- NIHR Certificate of Achievement in Good Clinical Practice (GCP).

Primary cell culture and cell line

- Isolation and culture of primary macrophages from human, porcine, and murine spleen and liver tissues.
- *In vitro* phagocytosis, adhesion and invasion assays of primary macrophage cell cultures with *S. pneumoniae* and hypervirulent *K. pneumoniae* and data analysis.
- Receptor-blocking assays to assess how inhibition of macrophage receptors affects bacterial uptake in primary human, porcine, and murine splenic and hepatic macrophages.
- Immunohistochemistry of infected primary human, porcine, and murine splenic and hepatic macrophages.
- Sample preparation of primary cells for Flow Cytometry and data analysis.
- Culturing and maintaining murine macrophage cell lines (RAW 264.7, J774A.1), human monocytic cell line (THP-1), and human promyelocytic cell line (HL60).
- *In vitro* phagocytosis, adhesion, and invasion assays with *S. pneumoniae*, hypervirulent *K. pneumoniae*, and *S. epidermidis*, including quantitative data analysis.

Microscopy and image data analysis

- Confocal and time-lapse fluorescence microscopy to study bacterial uptake and clearance.
- Confocal z-stack and 3D reconstruction of tissue sections and primary cells using Huygens Essential deconvolution and Imaris 3D rendering software, to analyse high resolution host-pathogen interactions.
- High-content time-lapse to study cellular morphological and kinetical changes during host-pathogen interaction using the LiveCyte system.
- Microscopy image analysis for determining host-pathogen interaction using Fiji/ImageJ.

Animal experiments

- Italian certificate for *in vivo* mouse experiments and experience in assisting murine *in vivo* infections.

Research Experiences

- **Postgraduate Researcher**, University of Leicester, UK , Jan–Oct 2024.
- **Research Collaborator**, University of Bologna, Italy, Mar–Oct 2022.
- **Visiting MSc Student**, University of Leicester, UK, Nov 2021.
- **MSc Internship**, University of Bologna, Italy, Apr 2021–Mar 2022.
- **BSc Internship**, University of Bologna, Italy, Mar–Jul 2019.

Publications

- Alnabati N*, Flandi F*, AlSaoudi T, Cattabriga G, Richardson T, Ghezzi D, Hames RG, Isherwood J, Kanani T, Jasiunaite Z, Tang S, Germinario G, Radi G, Rizzo F, Schilcher K, Bayliss CD, Parolin C, Fedi S, Chung WY, Garcea G, Giampieri E, Castellani G, Straatman K, Bruno S, Trappetti C, Ravaioli M, Dennison AR, Martinez-Pomares L, Oggioni MR. (2025). The Mannose Receptor on Sinusoidal Lining Cells Mediates Two-Step Bacterial Clearance in the Human Spleen. Nature Communications, under review. *These two authors contributed equally to this work.
- Flandi F, Bracchi C, Cattabriga G, Mojsilovic T, Alnabati N, Ventura A, Richardson T, Germinario G, Radi G, Menozzi I, Mazzera L, Angelone S, Prosperi A, Radice M, Harada S, Ardanuy C, Brisse S, Anjum M, Williamson S, Trappetti C, Wanford JJ, Pongolini S, Oun MA, Ravaioli M, Scaltriti E, Oggioni MR. (2025). Host-species specific disease potential of *Klebsiella pneumoniae* in swine and humans driven by toxicity to splenic macrophages. Manuscript in preparation.
- Kanani T, Alnabati N, Flandi F, Cattabriga G, Tang S, AlSaoudi T, Richardson T, Ghezzi D, Isherwood J, Chung WY, Issa E, Malde D, Garcea G, Germinario G, Radi G, Rizzo F, Fedi S, Parolin C, Caprini M, West K, Magnani F, Giampieri E, Castellani G, Giancristofaro S, Camilli R, Petersen FC, Yesilkaya H, Haigh R, Schilcher K, Straatman K, Bruno S, Trappetti C, Ravaioli M, Martinez-Pomares L, Dennison A, and Oggioni MR. (2025). Human Kupffer Cells Exhibit Capsule-Independent Bactericidal Activity in Segmental Liver Perfusion and Primary Culture Models. In submission. **Personal contribution:** acquisition, analysis and interpreted the microbiological and microscopy data, developed the primary cell cultures, and contributed to the paper draft.

- Stawarska O, Nair AR, Green L, Gazioglu O, Flandi F, Lam MMC, Holt KE, Yesilkaya H, Oggioni MR, Bengoechea JA, Odendall C, McCarthy AJ, and Wanford JJ. (2025). Simple Sequence Repeats Mediate Phase Variation of the Mucoid Phenotype in Hypervirulent *Klebsiella pneumoniae*. Nature Microbiology, under review.

Oral presentations – International and National Conferences

- Flandi F, Alnabati N, Cattabriga G, Richardson T, Ghezzi D, Alsaoudi T, Martinez-Pomares L, Dennison A, and Oggioni MR. Title: Human spleen macrophages clear the pneumococcus by apoptosis. FEMS Micro 2025, Milan (Italy).
- Flandi F, Alnabati N, Cattabriga G, Richardson T, Ghezzi D, Alsaoudi T, Martinez-Pomares L, Dennison A, and Oggioni MR. Title: Human spleen macrophages clear the pneumococcus by apoptosis and not by phagolysosome. Italian Society of Microbiology (SIM), 2024, Pavia (Italy).
- Flandi F, Cattabriga G, Alnabati N, Ghezzi D, Alsaoudi T, Giampieri E, Martinez-Pomares L, Dennison A, and Oggioni MR. Title: *Ex vivo* human spleen perfusion as a model to study the bacteria-macrophages interaction. Cortona Prokaryotes 2024, Cortona (Italy).
- Seminar given at the University of Bologna, 2024. Title: The management of infection by innate immunity differs between mice and humans.

Poster presentations – International and National Conferences

- Flandi F, Alnabati N, Cattabriga G, Richardson T, Ghezzi D, Alsaoudi T, Martinez-Pomares L, Dennison A, and Oggioni MR. Title: *S. pneumoniae* clearance by human spleen macrophages is complemented through apoptosis activation. Italian Society of Microbiology (SIM), 2025, Catania (Italy) (19-22 September).
- Flandi F, Alnabati N, Cattabriga G, Richardson T, Ghezzi D, Alsaoudi T, Martinez-Pomares L, Dennison A, and Oggioni MR. Title: Discrepancies between humans and mice in innate cellular immunity against *Streptococcus pneumoniae*. 17th European Meeting on the Molecular Biology of the Pneumococcus, 2025, Azores (Portugal).
- Flandi F, Alnabati N, Cattabriga G, Richardson T, Ghezzi D, Tang S, Giampieri E, Alsaoudi T, Martinez-Pomares L, Dennison A, and Oggioni MR. Title: *In vitro* and *ex vivo* models to study macrophage phagocytosis. IUMS 2024, Florence (Italy).
- Flandi F, Alnabati N, Cattabriga G, Richardson T, Ghezzi D, Alsaoudi T, Martinez-Pomares L, Dennison A, and Oggioni MR. Title: *Ex vivo* human spleen perfusion as a model to study the bacteria-macrophages interaction. Italian Society of Microbiology (SIM), 2024, Pavia (Italy).
- Flandi F, Alnabati N, Cattabriga G, Richardson T, Ghezzi D, Tang S, Giampieri E, Alsaoudi T, Martinez-Pomares L, Dennison A, and Oggioni MR. Title: Dynamics of macrophage phagocytosis: *in vitro* and *ex vivo* models. Annual Conference 2024 Microbiology Society, Edinburgh (UK).
- Flandi F, Hames R, Ghezzi D, Iacono L, and Oggioni MR. Title: Dynamics of macrophages phagocytosis. 34th Società Italiana di Microbiologia Generale e Biotecnologie Microbiche (SIMGBM) Congress, 2023, Cagliari (Italy).
- Flandi F, Hames R, Parolin C, and Oggioni MR. Title: Time-lapse of pneumococcal phagocytosis. 16th European Meeting on the Molecular Biology of the Pneumococcus, 2023, Crete (Greece)
- Flandi F, Alonzi V, Poletti A, Bowen F, Okoliegbe I, Bonvicini F, Gentilomi GA, Hijazi K, and Oggioni MR. Title: The role of the fosfomycin resistance *fosB* gene in *Staphylococcus epidermidis*. Microbiology Society Annual Conference 2023. Abstract.

Awards

- **Best Oral Presentation**, Italian Society of Microbiology (SIM), 2024.
- **Best Poster**, Italian Society of Microbiology (SIM), 2024.
- **Best Poster**, EuroPneumo 2023.

Grants

- ESCMID Attendance Grant 2025.
- Microbiology Society Events Grant 2024.
- FEMS Meeting Attendance Grant 2023.
- HORIZON-MSCA Staff Exchanges 2022. Secondee Staff.

Workshops

- ESCMID Postgraduate Course "Experimental Models of Brain Infections: New developments from basic to translational research", 2025, Nice (France).
- FISV Postgraduate Course "Advanced Technologies in Single Cell Omics", 2025, Milan (Italy).

Teaching & Mentoring

- **Teaching Labs** for Microbial Biotechnologies, Master in Molecular and Industrial Biotechnology, University of Bologna, 2022–2023, 2024-2025.
- **Thesis co-supervisor:** "Effect of glucose on the antibiotic activity of fosfomycin against *Staphylococcus epidermidis*".
- **Thesis co-supervisor:** "Searching for paralog genes in *Staphylococcus epidermidis* that may have evolved antibiotic resistance as indicators of environmental selective pressures".

Professional Memberships

- European Society of Clinical Microbiology and Infectious Diseases (ESCMID), 2025-Now.
- Microbiology Society, 2022-2024.