Doctoral School of Information and Biomedical Technologies Polish Academy of Sciences (TIB PAN)

SUBJECT: Analysis of host-pathogen interactions of *L. monocytogenes* at the single-cell level

DISCIPLINE: Biomedical Engineering and Medical Sciences

SUPERVISOR: Prof. dr hab. inż. Paweł Paszek, <u>ppaszek@ippt.pan.pl</u> Laboratory of Modelling in Biology and Medicine Department of Biosystems and Soft Matter Institute of Fundamental Technical Problems, Polish Academy of Sciences ul. Pawińskiego 5B, Warsaw

DESCRIPTION: The dynamic and stochastic nature of host cell and pathogen interactions ultimately decide the fate of the whole organism; however, the underlying mechanisms are masked in typical population-level analyses. In this project, we will use live-cell imaging and gene expression approaches to mechanistically understand invasion strategies of *Listeria monocytogenes*, an important food-borne pathogen of humans. We will employ an in vitro model system of infection of macrophages, which is a critical step controlling the overall infection outcome. We will monitor activation of a critical PrfA virulence system in single pathogen cells to quantitatively understand its regulation upon infection of macrophages, phagosome escape and replication. To understand how the host regulates the antibacterial effector responses to kill bacteria we will visualize the activation of the NF-kappaB and STAT signalling, the main antibacterial defence systems against infection. We will use mathematical modelling to predict and manipulate the course of infection. Together, these single cell approaches will provide new insights into mechanisms that control infection of *L. monocytogenes*. We welcome candidates with experimental and/or mathematical/engineering background.

BIBLIOGRAPHY:

- 1. Moran, J., Feltham, L., Bagnall, J., Goldrick, M.C., Lord, E.A., Nettleton, C., Spiller, D.G., Roberts, I., and Paszek, P. Single-cell imaging reveals non-cooperative and cooperative infection strategies of Listeria monocytogenes in macrophages. (2023) Frontiers immunology, in press. 10.3389/fimmu.2023.1235675
- 2. Alachkar N, Norton D, Wolkensdorfer Z, Muldoon M, Paszek P. Variability of the innate immune response is globally constrained by transcriptional bursting. (2023) *Frontiers in Molecular Biosciences*. 2023;10. doi: 10.3389/fmolb.2023.1176107
- 3. Kalliara E, Kardyńska M, Bagnall J, Spiller DG, Muller W, Ruckerl D, Biswas SK, Śmieja J, Paszek P, Post- transcriptional regulatory feedback encodes JAK-STAT signal memory of interferon stimulation, (2022) *Frontiers in Immunology*:13, 10.3389/fimmu.2022.947213
- 4. Bagnall J., Rowe W, Alachkar N, Roberts R, England H, Clark C, Platt M, Jackson D, Muldoon M, Paszek P, Gene-specific linear trends constrain transcriptional variability of the toll-like receptor signalling, 2020, *Cell Systems*, 11, 1-15
- 5. Bagnall, J., Boddington, C., England, H., Brignall, R., Downton, P., Alsoufi, Z., Boyd, J., Rowe, W., Bennett, A., Walker, C., Adamson, A., Patel, N., O'Cualain, R., Spiller, D., Jackson, D., Muller, W., Muldoon, M., White, M. & Paszek, P. "A quantitative analysis of competitive cytokine signaling predicts tissue thresholds for the propagation of macrophage activation", *Science Signalling* 11(540),eaaf3998
- 6. Adamson A, Boddington C, Rowe W, Bagnall JS, Downton P, Lam C, Schmidt L, Harper CV, Spiller DG, Rand DA, Jackson DJ, White MRH and Paszek P. "Signal transduction controls heterogeneous NF-кВ dynamics and target gene expression through cytokine-specific refractory states", *Nature Communications* 2016 7:12057