BIOENGINEERING, BIOMEDICAL, AND MATERIALS FRONTIERS

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Publications

1. Mohiuddin, S.G., Kavousi, P. and Orman, M.A., 2020. Flow-cytometry analysis reveals persister resuscitation characteristics. BMC microbiology, 20(1), pp.1-13.

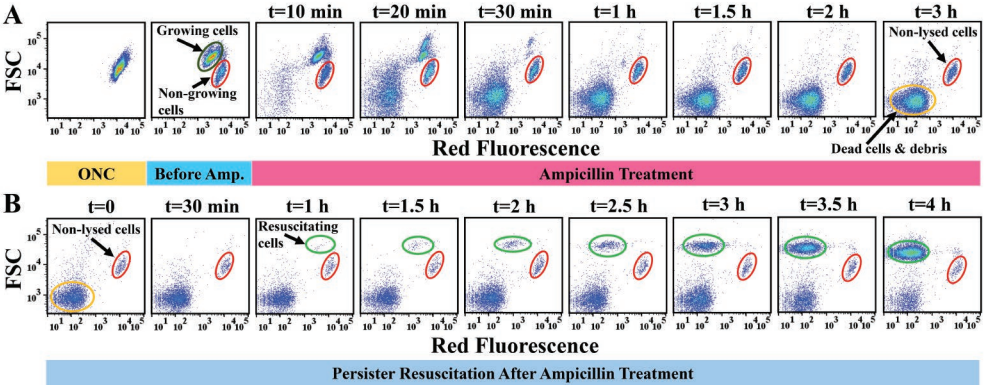
2. Mohiuddin, S.G., Hoang, T., Saba, A., Karki, P. and Orman, M.A., 2020. Identifying Metabolic Inhibitors to Reduce Bacterial Persistence. Frontiers in Microbiology, 11, p.472.

3. Karki, P., Mohiuddin, S.G., Kavousi, P. and Orman, M.A., 2020. Investigating the Effects of Osmolytes and Environmental pH on Bacterial Persisters. Antimicrobial Agents and Chemotherapy, 64(5).

4. Orman, M.A. and Brynildsen, M.P., 2015. Inhibition of stationary phase respiration impairs persister formation in E. coli. Nature communications, 6(1), pp.1-13.

Dr. Orman received his Ph.D. in 2011 from Rutgers University and completed his postdoctoral studies at Princeton University and the Memorial Sloan Kettering Cancer Center. He received the K22 Career Transition Award from the National Institute of Allergy and Infectious Diseases (NIAID) in 2018. In 2020, he was awarded an R01 grant from NIAID at NIH. He was awarded the NSF CAREER in 2021. Dr. Orman's research group focuses on persister cells that are observed in both bacterial and cancer cell populations. Persister cells are phenotypic variants that are highly tolerant to treatment where the tolerance is reversible under certain conditions.

PERSISTER CELLS



The figure above shows monitoring of persister cell resuscitation by flow cytometry. (A) E.coli cells were treated with antibiotics (i.e. ampicillin) for 3 hours in the presence of the inducer for the fluorescent protein (i.e. mCherry) expression. Cells during the treatment were collected at designated time points and analyzed by a flow cytometer. The growing cells (highlighted with a dark-green circle) lost their membrane integrity and mCherry in the presence of ampicillin. However, non-growing cells (highlighted with red circles) remain intact, as ampicillin cannot lyse these cells. (B) After 3-hour ampicillin treatment, the cells were collected and washed to remove the antibiotic and the inducer. The cells were then resuspended into fresh liquid medium and cultured. Samples were collected at designated time points and analyzed with a flow cytometer to monitor the resuscitating cells. Upon resuscitation in the absence of the inducer, the flow cytometry analysis reveals ongoing cell division as dilution of mCherry protein (highlighted with light green circles)

Persister cell phenotypes generally exist in a transient, growth-inhibited state. They can be formed stochastically or induced by environmental factors. They are thought to underlie the propensity of recurrent diseases to relapse. However, very little is known about the physiology of these rare sub-populations. More importantly, deeper understanding of the molecular make-up of these phenotypic variants will facilitate the development of therapeutics. Therefore, a major goal of Dr. Orman's research is to study their physiology: the metabolite, RNA, protein, and regulatory content that allow them to tolerate extraordinary concentrations of drugs.

Dr. Orman's group uses advanced technologies, including flow cytometry, microscopy, gene-expression reporters, chemical screening and high-throughput metabolomics, to understand the molecular mechanisms of persistence and to establish the feasibility of therapeutically targeting the metabolism of persister cells to reduce recurrence risk and treatment resistance.

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