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CIRCULATING NEUTROPHILS FROM PATIENTS WITH CHRONIC URINARY TRACT INFECTION SHOW AN ALTERED IMMUNE RESPONSE TOWARDS BACTERIAL STIMULATION

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One-third of acute urinary tract infections (UTIs) develop into recurrent or chronic disease. The primary immune responders in UTI are neutrophils [1]. Aberrant neutrophil responses may play a role in incomplete disease resolution in chronic UTI. In this study, blood samples were collected from six healthy females and chronic UTI patients. Isolated neutrophils were resuspended in three urine media – artificial urine 'AUR', sterile-filtered pooled control urine 'CUR' or patient urine 'PUR'. The cells were infected with two urinary isolates of Escherichia coli – one from a healthy individual to represent bladder-resident commensal strain 'CEC' and another from a chronic UTI patient to represent uropathogenic strain 'PEC'. Both neutrophils and bacteria were stained with Hoechst and propidium iodide. Timelapse live-imaging was performed at 5-minute intervals for 15 hours at 37oC. From the images, percentage of dead neutrophils were plotted over time in six conditions (AUR x CEC, AUR x PEC, CUR x CEC, CUR x PEC, PUR x CEC, PUR x PEC) (Figure 1). In AUR, patient neutrophils reached half-maximal death significantly earlier than control neutrophils. Neutrophils in CUR were significantly more active with instances of phagocytosis and release of neutrophil extracellular traps (NETs). This potentially explains their earlier and faster rate of death as they underwent phagocytosis-induced cell death and NETosis [2]. However, patient neutrophils showed a delayed response in CUR. In PUR, both neutrophil populations remained relatively inactive yet survived for the longest. Patient neutrophils achieved more than 80% death in all conditions while in control neutrophils, this was 30% to 70% in AUR and PUR (Figure 2). This study suggests a marked difference in the immune response between healthy individuals and chronic UTI patients, influenced by types of urine media and bacteria. Future works to better understand the underlying mechanisms include neutrophil functional assays and urine/bacteria characterisation.

References:

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[2] Kobayashi SD, Malachowa N, DeLeo FR. Influence of microbes on neutrophil life and death. (2017) Front Cell Infect Microbiol 7, 159.