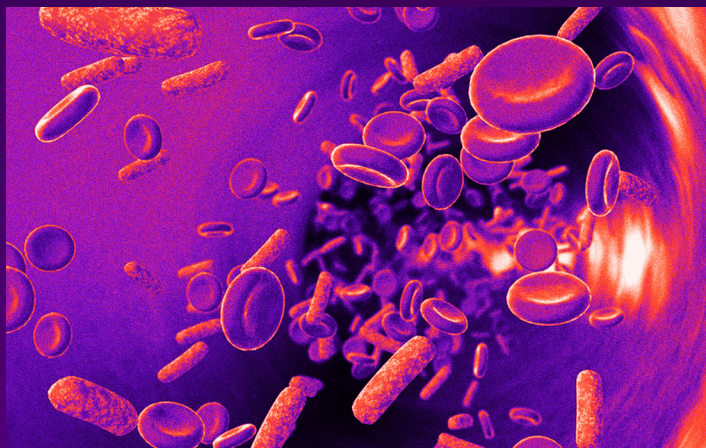


ARTIFICIAL INTELLIGENCE IN EARLY SEPSIS DETECTION

ZAHRA TAUSEEF



Sepsis is caused by an unusually severe immunological response in patients with infectious disease(s). Septic shock, a severe complication of sepsis, is responsible for nearly 1/3 of in-hospital deaths in the US.¹ Unfortunately, the speed at which the condition escalates and manifests (i.e. through flu-like symptoms) makes timely treatment difficult. Recently, an algorithm developed by researchers at Johns Hopkins University (JHU) has proven to bypass this issue.²

The Targeted Real-Time Early Warning System (TREWS) is a program that scans electronic patient health records for factors that increase the risk of developing sepsis, such as age and medical history. The program combines this information with current vital signs and lab tests to create a score indicating which patients are likely to develop septic shock.³ In 2012, JHU implemented the TREWS system in five affiliated sites where it was used in >760,000 patient encounters, over 17,000 of which developed sepsis.⁴ In 2022, two clinical cohort analyses corroborated these results, confirming TREWS led to earlier diagnoses and reduced mortality in sepsis patients by approximately 18%.^{4,5}

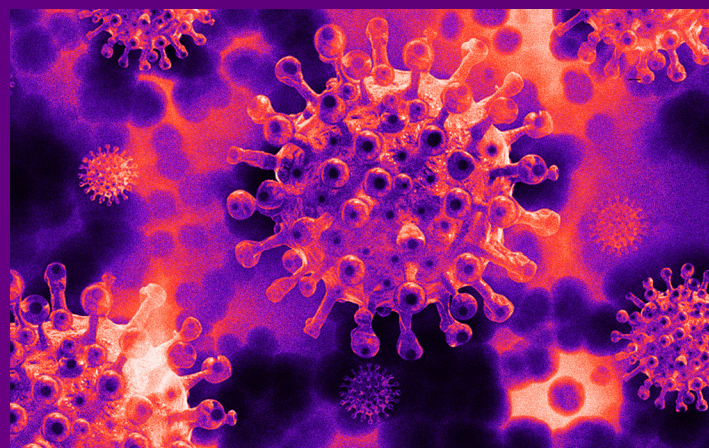
Despite its positive reception, there are still several drawbacks to the widespread adoption of TREWS.⁶ Notably, the program must be revised to accommodate the differences between electronic systems used by medical facilities.³ Limitations aside, TREWS is just one of the many recent advances in the intersection between emergency medicine and artificial intelligence. With continued development, TREWS and other predictive algorithms may drastically improve patient outcomes.

GLUCOCORTICOIDS & COVID-19: THE IMPLICATIONS OF GLUCOCORTICOID TREATMENT FOR COVID-19

JACQUELINE CHEN

Glucocorticoids are stress response hormones that play a key role in physiological processes like metabolic homeostasis, cognition, cell proliferation, and reproduction. More importantly, glucocorticoids are one of the most commonly prescribed drugs due to their anti-inflammatory and immunosuppressive properties. In response to severe cases of COVID-19, glucocorticoids have emerged as a powerful and effective intervention for physicians to treat acute lung injury.² However, there are multiple side effects associated with long-term usage of glucocorticoids, especially when administered in high doses. These adverse events range in severity, from fluid retention and weight gain to muscle atrophy, hypertension, and neuropsychiatric disorders.¹ In some COVID-19 patients, glucocorticoids can lead to an increase in adverse outcomes. A study by Keller et al. reports that glucocorticoid usage increases the odds of mortality or mechanical ventilation in patients with C-reactive protein (CRP) levels <10 mg/dL by almost three times. In contrast, it decreases the odds in patients with CRP levels ≥20 mg/dL (OR: 0.23).³ Because CRP levels are markedly elevated in cytokine storm syndrome, a hyperinflammatory condition that occurs in some COVID-19 patients, studying the outcomes associated with glucocorticoid use and CRP levels is clinically important. Thus, patients with lower CRP levels may experience more harm than benefit associated with glucocorticoid treatment.³

In contrast, Liu et al. found that there was no significant difference in virus clearance between COVID-19 patients with pneumonia administered low (≤2 mg/kg/day) and high (>2 mg/kg/day) doses of glucocorticoids.³ A study conducted by Yang and Yu suggests that glucocorticoids are most beneficial for short-term use in patients with severe COVID-19, and advises against chronic glucocorticoid exposure.¹ Future research should focus on the associated adverse effects of glucocorticoid usage to treat COVID-19.

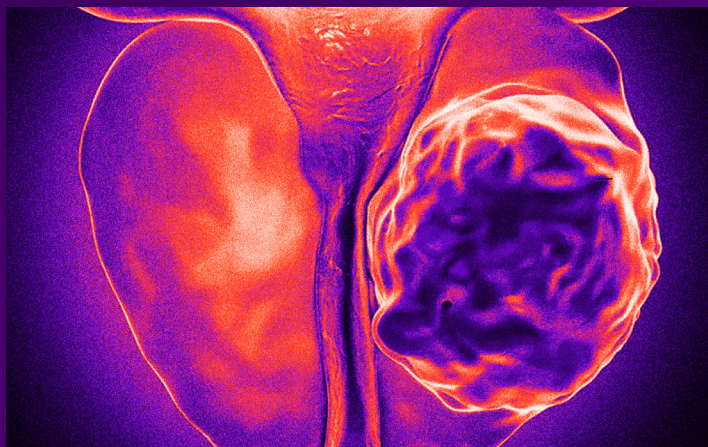


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A NOVEL INTERVENTION FOR ADVANCED PROSTATE CANCER

FAN ZE (ALEX) WANG



In 2022, the United States recorded 268,490 new cases and 34,500 deaths from prostate cancer.¹ Metastatic castration-resistant prostate cancer (mCRPC) is an advanced form of metastasized prostate cancer that grows with low levels of testosterone in the body. mCRPCs are almost always incurable, thus physicians currently pursue therapies that postpone or delay disease progression rather than cure it.²

Recently, researchers have developed lutetium-177-PSMA-617 (177Lu-PSMA-617) as a potential therapy for mCRPCs. This treatment targets the prostate-specific membrane antigen (PSMA), a transmembrane glutamate carboxypeptidase highly expressed on prostate cancer cells, while preserving normal surrounding tissues.³ Metastatic tumors often present with PSMA-positive markers. High PSMA expression has been associated with poor disease prognosis and reduced survival.⁴ In combination with standard therapy, 177Lu-PSMA-617 selectively emits beta-particle radiation to PSMA-positive cells and has been correlated with improved response rates, reduced pain, and low toxicity in patients with mCRPC.⁴

Clinical trials of 177Lu-PSMA-617 were performed on 831 randomized patients from June 2018 to October 2019. Compared to the overall survival period of standard care (11.3 months), 177Lu-PSMA-617 combined with standard care prolonged overall survival to 15.3 months. However, the prevalence of severe and undesirable adverse effects was higher with 177Lu-PSMA-617 than without (52.7% vs. 38.0%, respectively).⁴ Overall, the efficacy of 177Lu-PSMA-617 shows promise as a potential treatment for PSMA-positive mCRPCs. Further clinical trials could improve 177Lu-PSMA-617 into a reliable therapy to what would otherwise be an incurable and fatal form of prostate cancer.

CAR T-CELL THERAPY FOR NOVEL TREATMENT OF RELAPSED ACUTE MYELOID LEUKEMIA

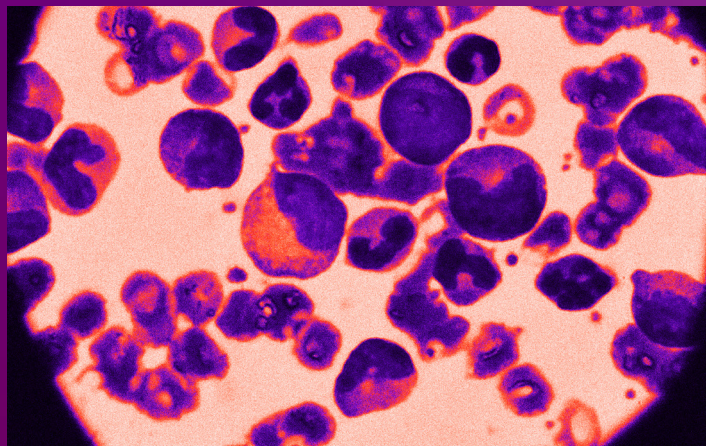
AUDREY DONG

Acute myeloid leukemia (AML) is a cancer characterized by uncontrolled production of immature blast cells in peripheral blood and bone marrow. AML accounts for 80% of all leukemia cases in adults and relapse occurs in 40–50% of patients. Currently, allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the most prevalent therapy for relapsed patients, however it has poor prognosis as 40% of those patients relapse again after HSCT.¹

A novel alternative for relapsed AML cases is chimeric antigen receptor (CAR) T-cell immunotherapy.² T-cells are a subset of immune cells that can recognize and target specific foreign particles. T-cells are extracted from the patient and genetically altered to produce CARs that recognize and destroy cancer cells before being re-infused into the patient. Two distinct phases of the treatment may be identified. First, initial infusion is characterized by the onset of CD8+ cells, or killer T-cells, dominating immune cell response to destroy cancerous cells.³ Then, CD4+ cells subvert dominance to control long-term remission by suppressing further cancer cell growth.³

Recent clinical trials at the University of Pennsylvania tested interleukin-3 receptor alpha chain (CD123)-specific CAR T-cells on relapsed AML.⁴ CD123 is prevalent in AML blasts and leukemia stem cells, with significantly higher levels in leukemia blasts than normal myeloid progenitors. By engineering CD123-CAR T-cells to target CD123 AML cells, clinical results reported strong anti-tumor cytotoxicity and long-term memory T-cell proliferation. As such, CD123-CAR T-cells show a promising future for relapsed AML patients.⁵

Currently, the application of CAR T-cell immunotherapy is being expanded, as oncologists explore its effects on solid malignancies, such as prostate tumors and brain cancer glioblastomas.⁶



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