Immune system simulation shows need for multi-target treatments for sepsis

February 15 2018

Using a computational model of the human immune system, scientists have shown that efforts to combat sepsis might be more effective if they targeted multiple steps in the molecular processes that drive the illness. This finding is presented in *PLOS Computational Biology*.

Sepsis is a dysregulation of the body's normal inflammatory response to injury and infection. People with sepsis may receive oxygen and intravenous fluids, as well as antibiotics to fight the underlying infection, but the condition kills 28 to 50 percent of affected patients. So far, drugs developed to attack the molecular processes that underpin sepsis have not shown clinical success.

To explore the molecular challenges of sepsis treatment, Chase Cockrell and Gary An of the University of Chicago employed a computational model of the human immune system, which they had previously developed specifically to investigate systemic inflammation. The model simulates how immune system cells and signaling molecules behave during sepsis, as well as the effects of disrupting various parts of these processes.

Using their model, the researchers showed that disrupting a single signaling process at a single point (or just a few points) in time would not be adequate to treat sepsis. This may explain why previous attempts that employed such a strategy have not been effective. Instead, the simulation showed, successful treatment would require drugs that frequently target multiple immune system processes.

The model also showed that a "one-size-fits-all" multi-target approach would still be inadequate, and true "precision medicine" would require a treatment to adapt itself based on each patient's individual response. The researchers concluded that computational modeling is necessary to generate the amount of data required by machine-learning algorithms to aid development of effective sepsis drugs.

"This project provides a reality check on how people are currently thinking about trying to treat sepsis at a drug-design level," Cockrell says. "It will hopefully help focus research into those areas that will actually provide a path towards effective therapy, such as high-resolution diagnostics and sampling, and realizing that there is no 'one-size-fits-all' answer."

More information: Cockrell RC, An G (2018) Examining the controllability of sepsis using genetic algorithms on an agent-based model of systemic inflammation. *PLoS Comput Biol* 14(2): e1005876. doi.org/10.1371/journal.pcbi.1005876

Provided by Public Library of Science