PreCyte identifies patients at risk for postoperative complications

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Objective of the technology

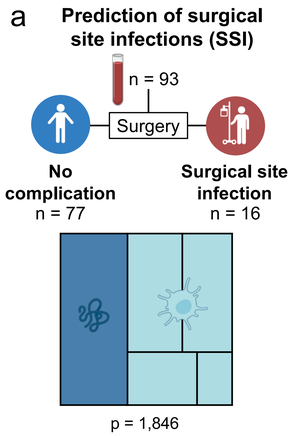


Figure 1. **PreCyte blood kit**

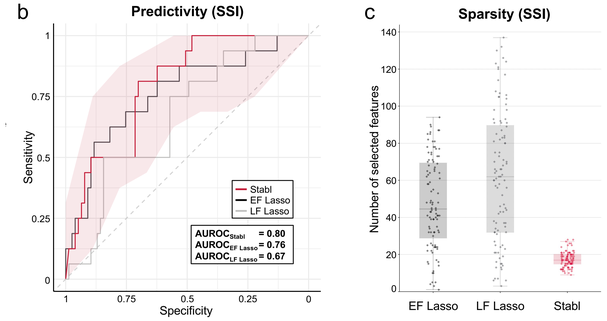
PreCyte predicts patient risk for postoperative complications, allowing for personalized surgical decisions and improved patient outcomes. The technology uses a standard blood draw to provide real-time information for clinicians to tailor their treatment protocols to individual immunological needs. With a 30% complication rate for major surgeries, PreCyte's risk prediction has the potential to reduce patient morbidity and healthcare costs.

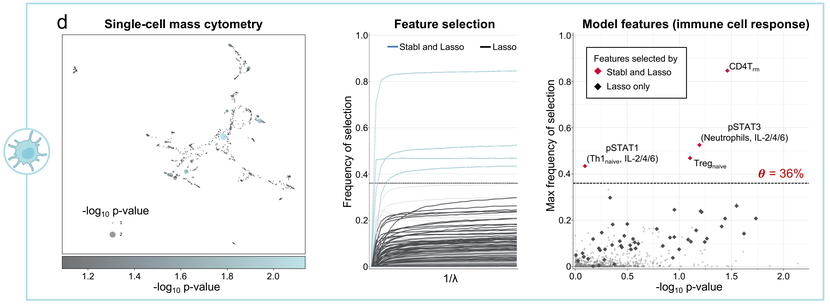
Technology and Method

In a previous study of 43 patients, application of Stabl a novel machine learning analysis to the three existing omic datasets demonstrated the algorithm's performance in the context of biomarker discovery studies with a known biological signal. To complete its systematic evaluation, Stabl was applied to our newly generated multi-omic clinical study performing an unbiased biomarker discovery task to predict which patients will develop a postoperative surgical site infection (SSI) from analysis of pre-operative blood samples (Fig.2a). A cohort of 274 patients undergoing major abdominal surgery were enrolled and preoperative blood samples were collected. Using a matched, nested case-control design, 93 patients were selected from the larger cohort to minimize the effect of clinical or demographic confounders. These samples were analyzed using single-cell mass cytometry and plasma proteomics approach.



Results





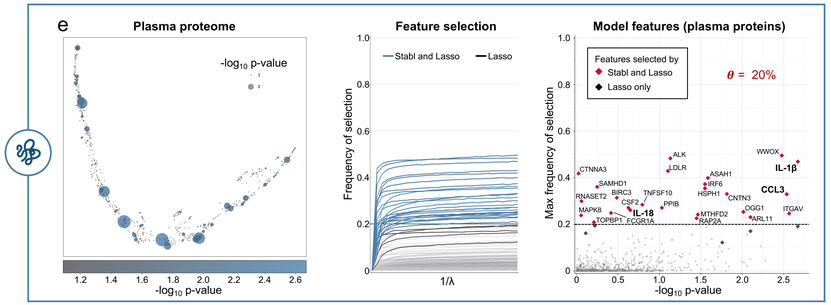


Figure 2. Stabl performance in selecting candidate biomarkers for the prediction of SSI.
2a. Among the 93 patients analysed, 16 suffered from SSI and 77 did not. **2b.** Stabl merged all omic datasets into a final model that accurately classified patients with and without SSI (AUROCStabl = 0.80 [0.69, 0.89]). When compared to early and late fusion Lasso, Stabl had comparable predictive performance yet superior sparsity (**2c.**)
2d.e. Stabl selected four mass cytometry and 25 plasma proteomic features that were combined into a biologically interpretable immune signature predictive of SSI. Examination of Stabl features revealed cell-type specific immune signaling responses associated with SSI that resonated with circulating inflammatory mediators. Notably, the STAT3 signaling response to IL-6 in neutrophils was increased before surgery in patients predisposed to SSI. Correspondingly, patients with SSI had elevated plasma levels of IL-1β and IL-18, two potent inducers of IL-6 production in response to inflammatory stress. CCL3 coordinates recruitment and activation of neutrophils, and the canonical stress response protein HSPH1. These findings are consistent with previous studies showing that heightened innate immune cell responses to inflammatory stress, such as surgical trauma can result in diminished defensive response to bacterial pathogens thus increasing a patient's susceptibility to infection.

Conclusions

These new findings emphasize the potential of STABL to discover predictive biomarkers that link multiple omics data layers with high biological plausibility and provide an avenue for efficient diagnostic and therapeutic development. Informative features of the SSI classification are readily interpretable biologically and the model points at coordinated bulk and single-cell proteomic features that are consistent with previously unrecognized innate immune system mechanisms, conducive to infection after surgery. To confirm these results, we are running a larger prospective clinical trial of 240 patients in five hospitals, with expected results by the end of 2023.