Antibioprophylaxie et infection post-opératoire

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An Immune Signature of Surgical Site Infections (SSI), a Retrospective Study with a Novel Machine Learning Pipeline for Biomarker Identification

J. Hedou*(1), F.Verdonk(2), A.Cambriel(2), G.Bellan(3), B.Gaudilliere(4)

(1) Anesthesia, Stanford School of Medicine, California, United States , (2) Anesthésie-Réanimation, AP-HP, Saint Antoine, Paris, France , (3) Biostatistics, SurgeCare, SAS, Paris, France , (4) Anesthesia, Stanford School of Medicine, Palo alto, ca, United States

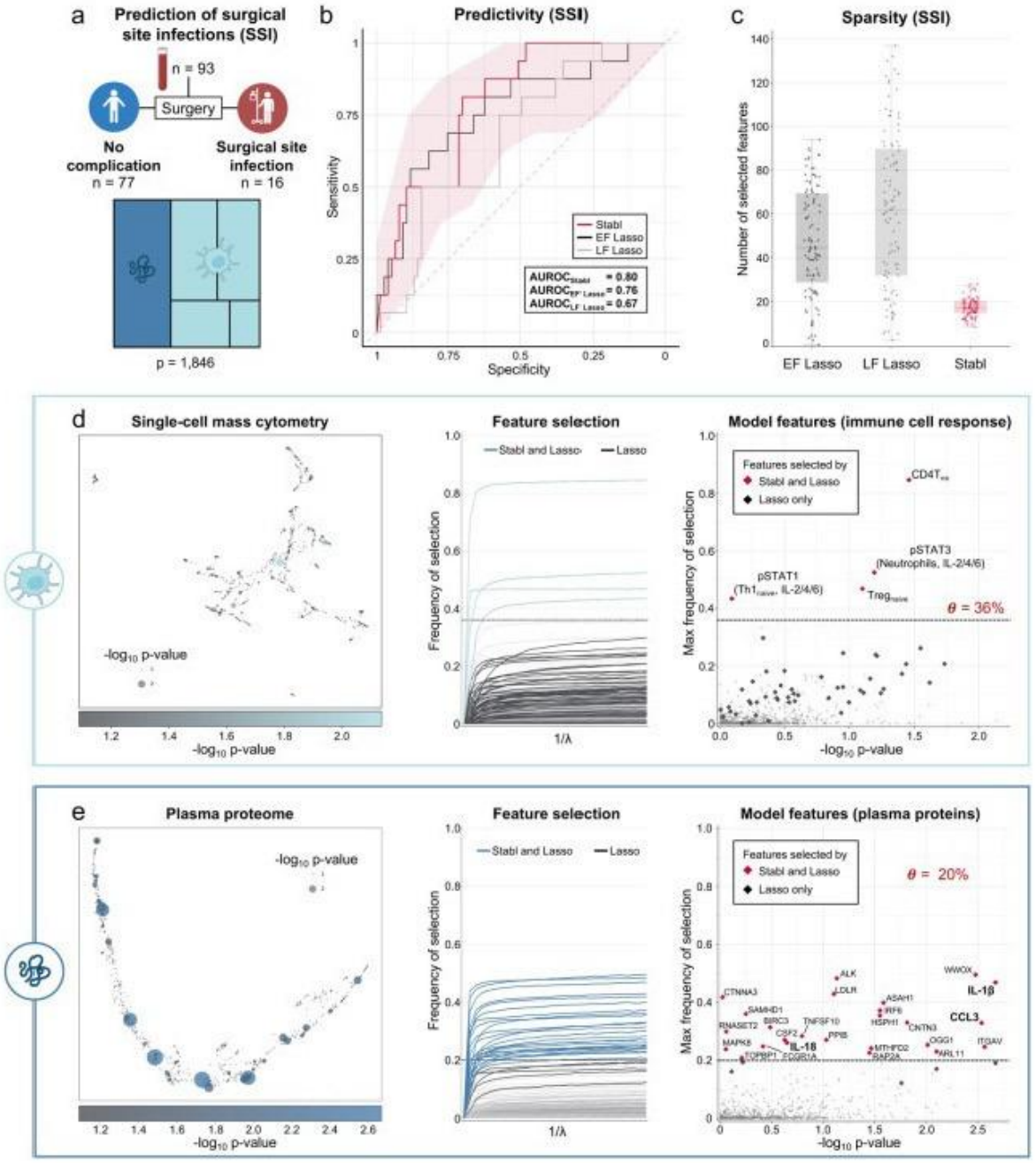
**Auteur présenté comme orateur*

Position du problème et objectif(s) de l'étude:
Surgical Site Infections are devastating, costly, and common surgical complications after surgery. Existing risk prediction tools perform poorly. In a prospective study of 43 patients, our group previously identified strong immune correlates of SSI in blood samples collected after surgery. Here we performed a retrospective study in 96 patients undergoing abdominal surgery to identify pre-operative immune responses predictive of SSI by analyzing peripheral blood samples collected before surgery.

Matériel et méthodes:
Blood samples collected before surgery were analyzed using a combined single-cell (mass cytometry)and plasma proteomic (SomaScan) approach. Samples were selected from a larger cohort using a frequency-matching procedure to minimize the effect of confounders on identified immunological biomarkers. The analysis combines two omics datasets, a plasma proteomic dataset and a mass cytometry dataset containing four omicssublayers. STABL, a novel machine learning analysis for omics data, is applied to obtain a unique set of predictive features.

Résultats & Discussion:
STABL identifies a model of SSI with good predictive performance (AUC = 0.74), improving current clinical scales performance. Notably, patients at risk for SSI showed increased MyD88 signaling in response to LPS in myeloid cell subsets such as granulocytes. Thisresonates with the proteomic dataset features, including increased levels of pro inflammatory cytokinesIL-1b and CCL3 or the stressresponse protein HSPH1. While IL-1b and HSPH1 represent classic mediators of the acute response to inflammation and are released, among others, by activated neutrophils, CCL3 mediates the initial recruitment of neutrophils to sites of inflammation.

Conclusion:
These new findings emphasize the potential of STABL to discover predictive biomarkersthat 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.



Candidate biomarker identification using Stabl for analysis of a newly generated multi-omic clinical dataset a. Clinical case study 4: Prediction of postoperative surgical site infections (SSI) from the combined plasma proteomic and single cell mass cytometry assessment of pre-operative blood samples in patients undergoing abdominal surgery. **b.** Predictivity performances (AUROC) for Stabl, early fusion (EF) and late fusion (LF) Lasso. **c.** Sparsity performances (number of features selected across cross-validation iterations, $median_{Stabl}$ = 17.0, IQR = [15.0,20.0], $median_{EF}$ = 44.5, IQR = [29.0,69.3], p-value < 1e-16, $median_{LF}$ = 62.0, IQR = [32.0,89.5], p-value < 1e-16. **d-e.** UMAP (left panel), stability paths (middle panel), and volcano plots (right panels) visualization of the single-cell mass cytometry (**d**) and plasma proteomics (**e**) datasets. The data-driven reliability threshold θ is computed for individual omic datasets and indicated by a dotted line on the volcano plots.

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