Understanding Immune Response using Statistical and Machine Learning Approaches

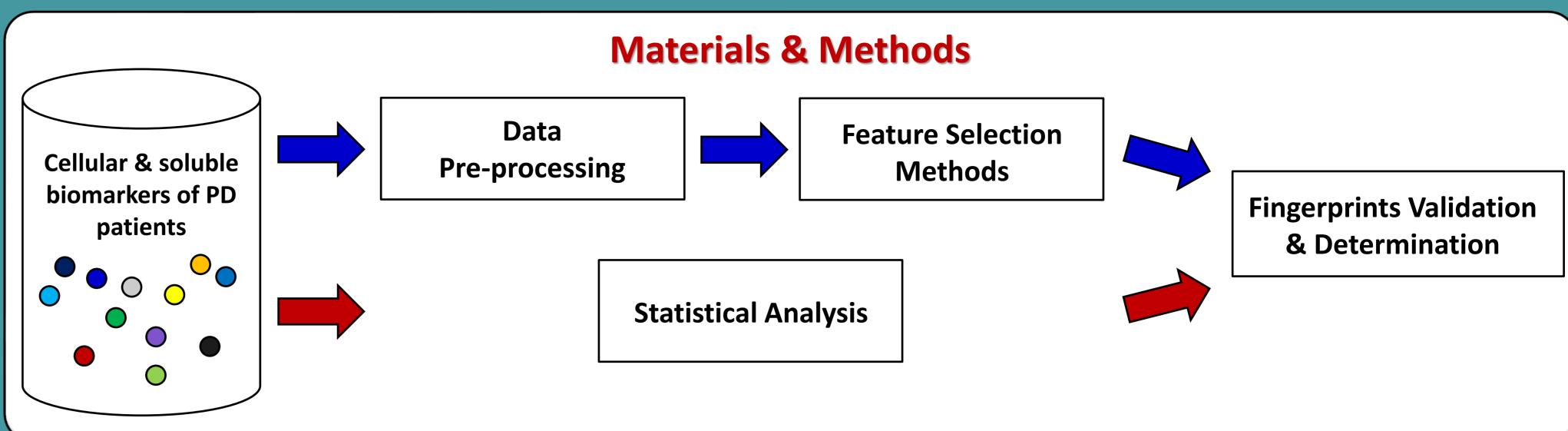
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Introduction

The unequivocal evidence that the immune system distinguishes between different types of organisms and mounts appropriate responses has been missing. This research used a systematic approach applying machine learning algorithms to define pathogen-specific local immune fingerprints and statistical analyses for validation in a total of 83 peritoneal dialysis (PD) patients on the day of presentation with acute peritonitis, based on a broad range of cellular and soluble biomarkers.



Correlation analysis of local biomarkers in peritoneal dialysis patients on the day of presentation with acute peritonitis

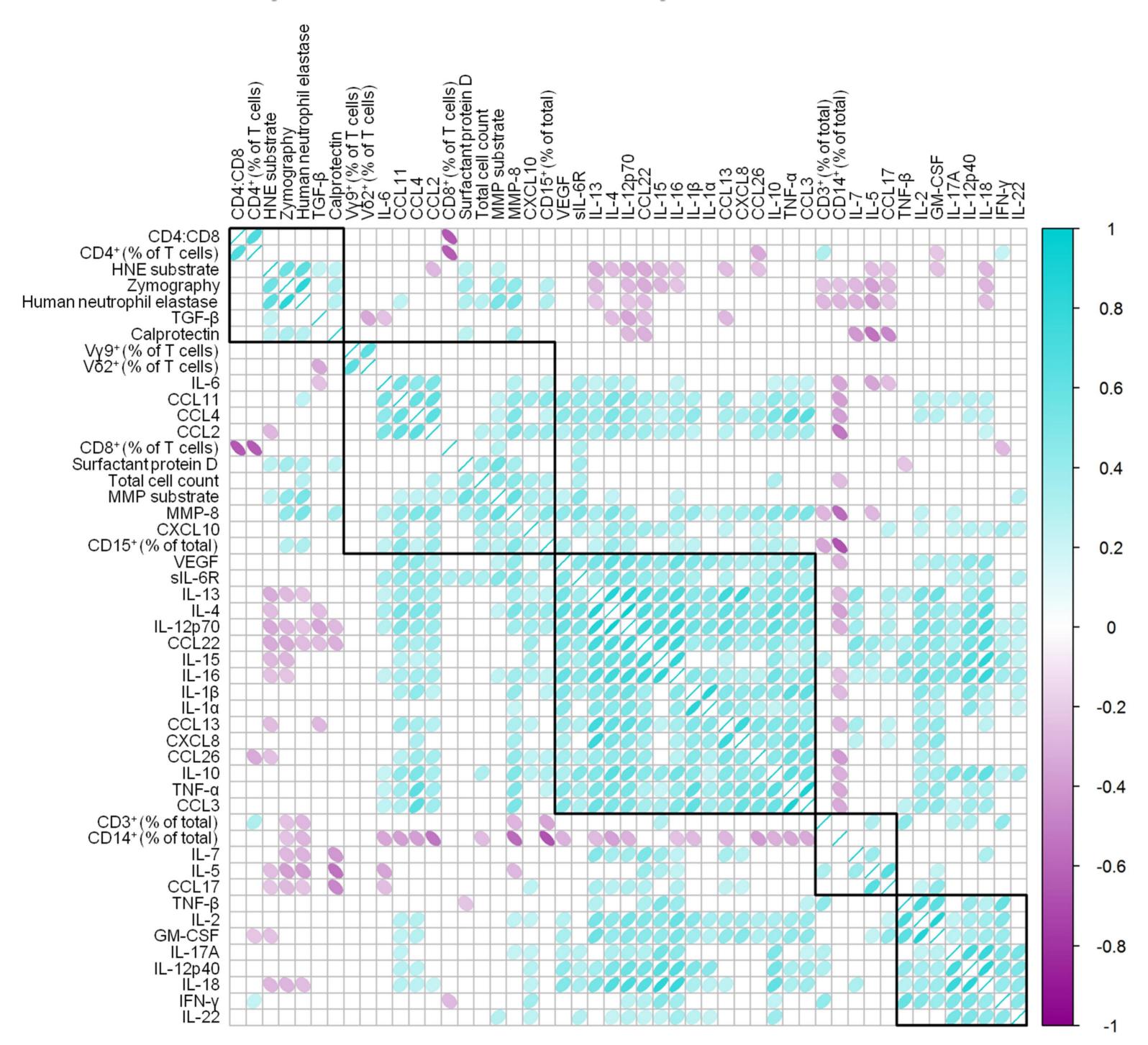


Fig.1: Correlation analysis of local biomarkers in a total of 83 peritoneal dialysis patients on the day of presentation with acute peritonitis. Ellipses depict the correlation coefficients for each pair of biomarkers in the corresponding cell of the matrix, with the direction of the dip and the colour of the shading representing positive and negative correlations, respectively. Only pairs with significant correlations (p<0.05) are shown.

Summary No growth: $8 - IL-1\beta$ 9 - Total cell count 10 - MMP-8 11 - CD14+ cells **All Gram-positives:** 12 - CCL4 2 - IL-12p406 – IL-17A 7 - IFN-yTechnique $8 - IL-1\beta$ failure: 9 – Total cell count 10 - MMP-8 16 - sIL-6R 20 - Calprotectin 3 4 (3) (2) 22 21 - CD4:CD8 22 – TGF-β **Gram-negatives:** 13 1 – Vδ2+ T-cells 15 2 – IL-12p40 **Coagulase-negative** 3 – Vγ9⁺ T-cells Staphylococcus: Non-streptococcal 4 – VEGF 5 – TNF-α **Gram-positives:** 9 - Total cell count 18 13 – IL-15 6 – IL-17A 15 – IL-16 7 – IFN-γ 16 – sIL-6R 9 - Total cell count 17 – MMP substrate 13 – IL-15 14 - CCL3 Streptococcus, **Enterococcus:** $8 - IL-1\beta$ 13 – IL-15 17 – MMP substrate 18 – TNF-β

19 – Zymography

Fig.3: Summary of disease-specific immune fingerprints in patients presenting with acute peritonitis. Shown are the top biomarkers associated with the type of causative organism as indicated, or with the risk of technique failure over the next 90 days.

The results demonstrate the power of advanced machine learning models to analyse complex biomedical datasets, highlight key pathways involved in pathogen-specific responses. This research not only defines pathogen-specific local immune fingerprints in acute infections but may also help understand other biological using systems machine learning algorithm.

Feature selection methods define local fingerprints associated with Gramnegative infections and the validation

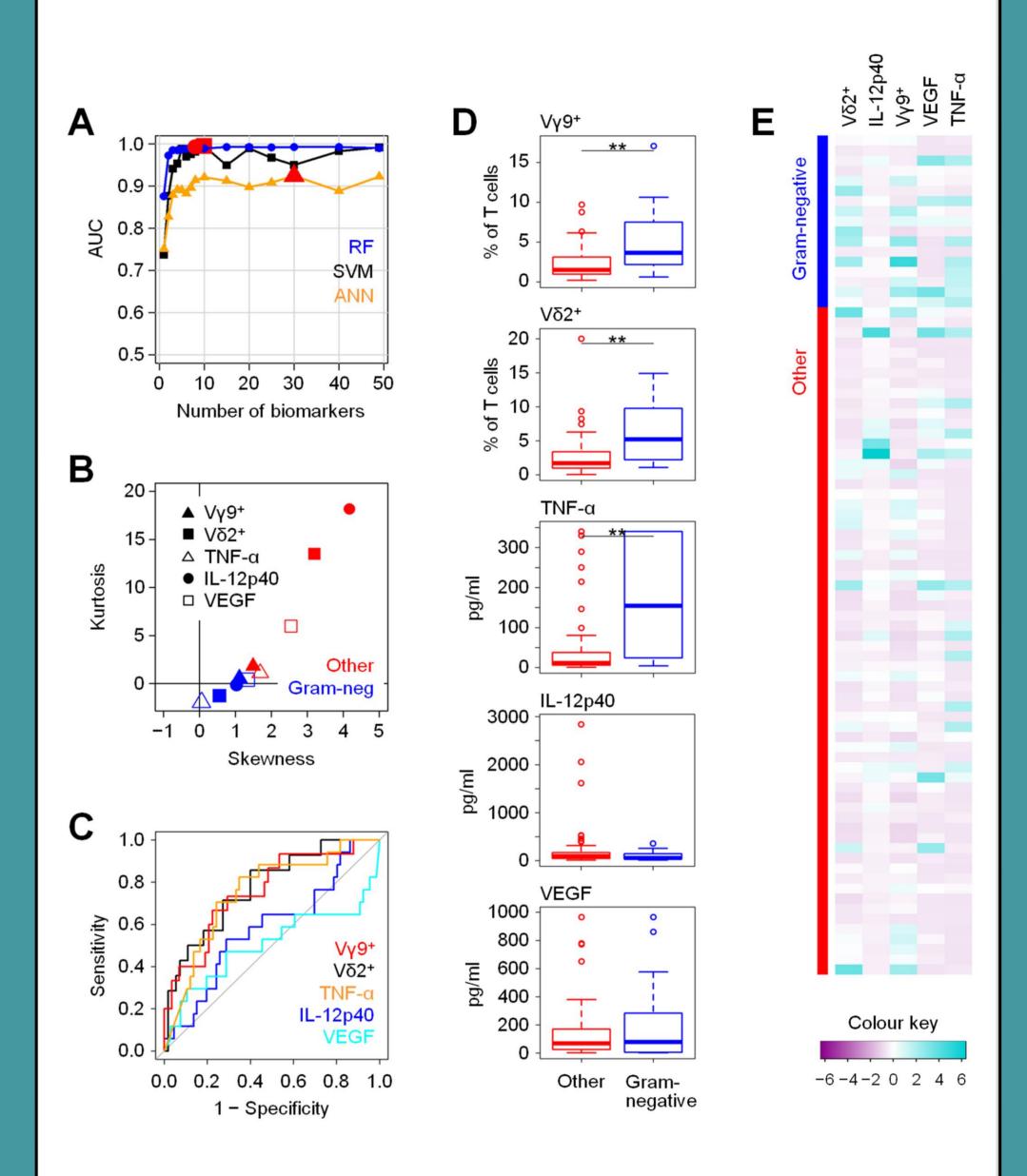


Fig.2: Identification of local immune fingerprints associated with peritonitis caused by Gram-negative bacteria (Gram-negative infections, n=17; all other episodes of peritonitis, n=66). (A) Performance of RF (Random Forest), SVM (Support Vector Machine) and ANN (Artificial Neural Network) based feature elimination models, shown as AUC depending on the number of biomarkers. Red symbols depict the maximum AUC for each model. (B) Kurtosis and skewness of the top 5 biomarkers selected by RFbased feature elimination. (C) ROC analysis showing specificity and sensitivity of the top 5 biomarkers. (D) Tukey plots of the top 5 biomarkers in patients of the two groups, as assessed by Mann-Whitney tests. (E) Heatmap showing the top 5 biomarkers across all patients presenting with acute peritonitis.

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