

Unveiling Immune Heterogeneity in JIA: A Multiplex Cytokine and Principal Component Analysis (PCA) Approach

Ludwig Fuhrmann^{1*}, Niklas Wiemers^{2*}, Anja Grahnert³, Boris Huegle^{4,6}, Christine S Falk⁵, Maik Friedrich³, Nadine Fischer⁶, Johannes-Peter Haas^{6#}, Christian Klemann^{1#}

¹Department of Pediatric Immunology, Rheumatology and Infectiology, University Hospital Leipzig, Germany; ²Clinic and Polyclinic for Neurology, Leipzig, Germany; ³Institute of Clinical Immunology, Medical Faculty Leipzig, Germany; ⁴Rheumatology Center Rhineland Palatinate, Hospital for Pediatric Rheumatology, Bad Kreuznach, Germany; ⁵Institute of Transplant Immunology, Hannover Medical School, Germany; ⁶German Centre for Pediatric and Adolescent Rheumatology, Garmisch-Partenkirchen, Germany; * / # both authors contributed equally

Background

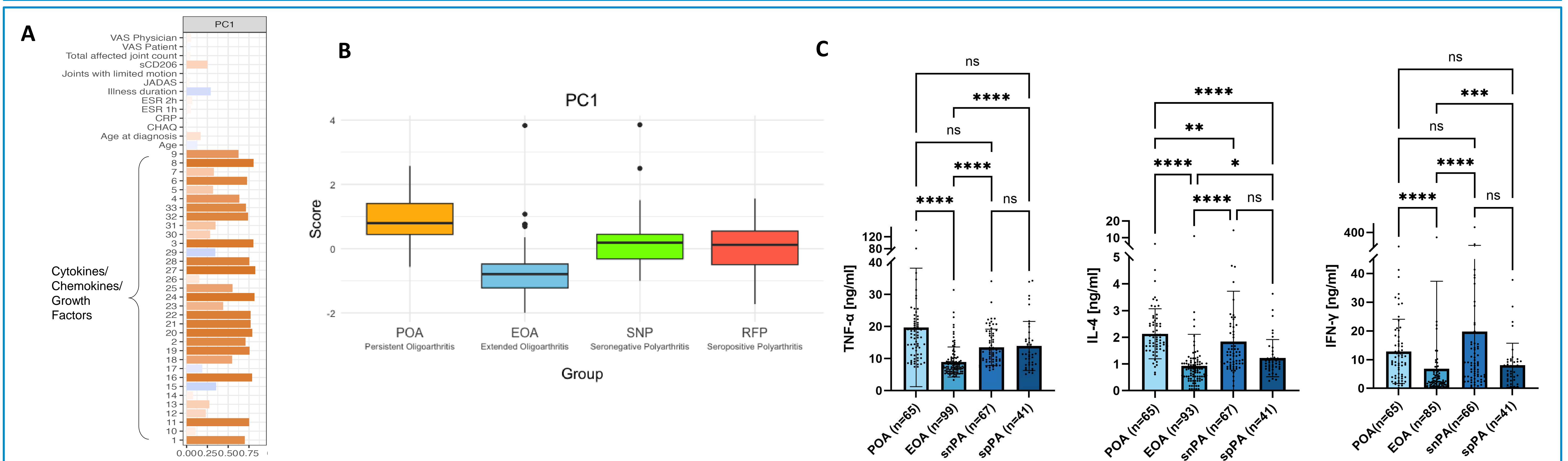
Juvenile idiopathic arthritis (JIA) comprises heterogeneous subtypes characterized by varying immunopathological mechanisms. A deeper understanding of cytokine profiles among JIA subtypes can aid to detect critical courses earlier in order to refine therapeutic approaches. **This study utilized multiplex cytokine analysis to explore cytokine biomarkers in four distinct JIA subtypes and applied principal component analysis (PCA) for data reduction and pattern identification.**

Conclusion

We identified significant ($p < 0.001$) differences between the examined rheumatic subtypes based on the 7 principal components (PCs). Our analysis demonstrated that the subgroups differ in their biomarker and clinical profiles, with particularly pronounced differences between the Persistent Oligoarthritis and Extended Oligoarthritis groups.

Current research: Retrospective analysis of therapeutic interventions in our JIA cohort ($n=289$) and their potential effects on biomarker profiles.

Results Principal Component 1



Analytical Approach

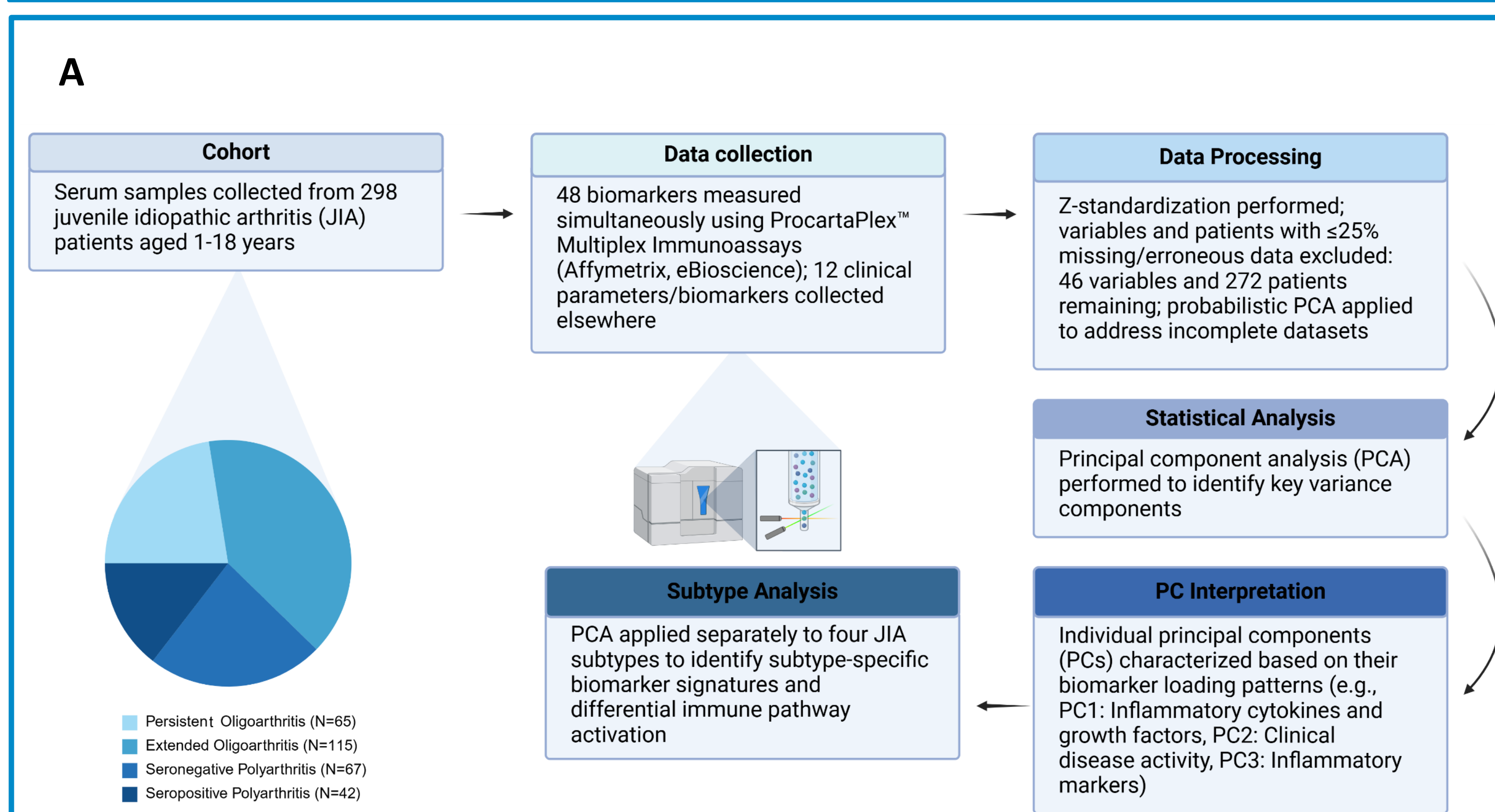


Fig. 1: Methods and analytical workflow for Juvenile Idiopathic Arthritis subtype biomarker profiling.

PCA: Method Overview

Principal component analysis (PCA) reduces data dimensionality by transforming correlated variables into uncorrelated principal components (PCs). In our analysis:

- Measured biomarkers (manifest variables) were projected into multidimensional space (dimensions equal to number of variables [46])
- Orthogonal axes (PCs = latent variables) were identified that capture maximum variance patterns
- Loading values show correlation between biomarkers and PCs; high loading biomarkers strongly define a PC's biological meaning

This method reduced 46 biomarkers from 272 patients to 7 PCs, explaining 65% of the total variance in our dataset.

PCA: Principle of Dimensionality Reduction

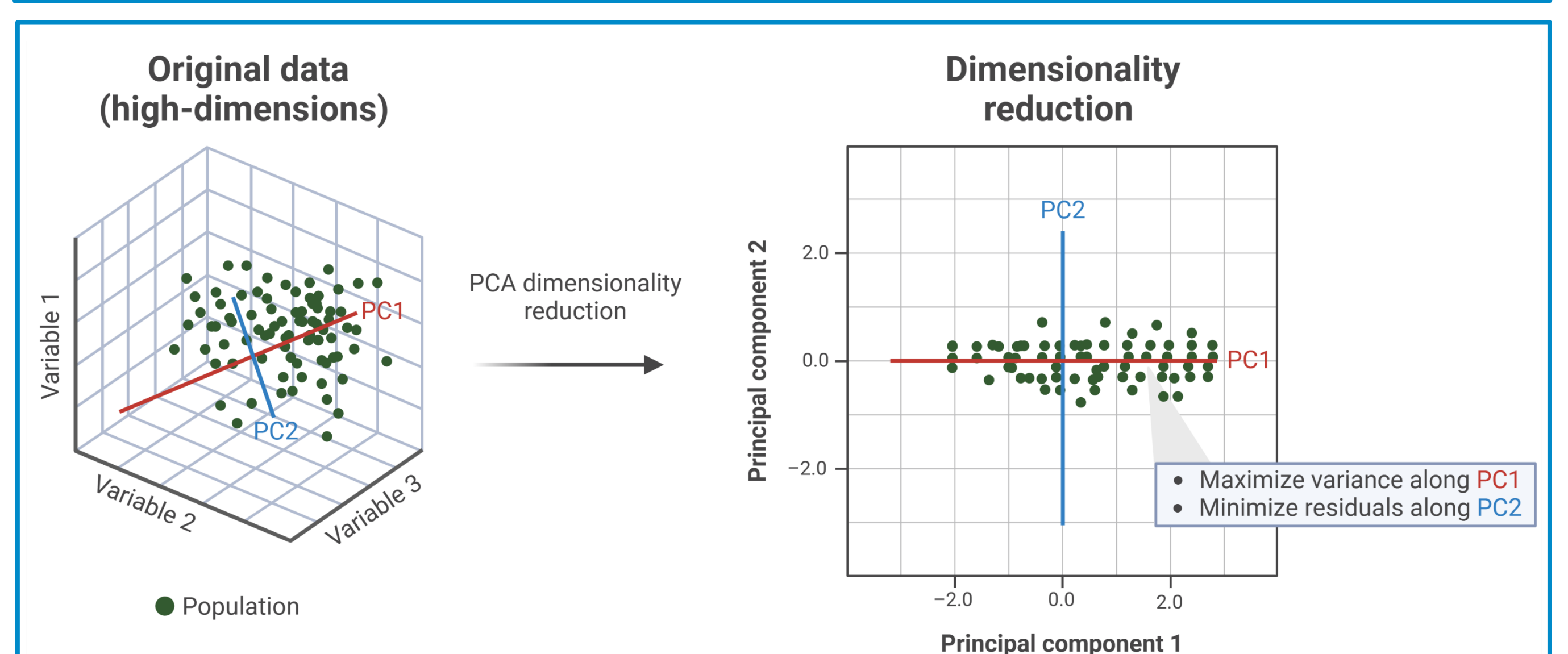


Fig. 2: Schematic representation of dimensionality reduction using Principal Component Analysis (PCA). For clarity, only three example variables and two principal components (PCs) are shown. The green dots represent the biomarker profiles of individual patients.

Correlation matrix

