

# Histological and Complement Biomarker Correlations in C3 Glomerulopathy

Jillian Hall<sup>1</sup>, Monica Hall<sup>1,2</sup>, Patrick D. Walker<sup>3</sup>, Richard J. H. Smith<sup>1,2</sup>, Carla M. Nester<sup>1,2</sup>

<sup>1</sup>Molecular Otolaryngology and Renal Research Laboratories, <sup>2</sup>University of Iowa Hospitals and Clinics, <sup>3</sup>Arkana Laboratories

## Background

C3 Glomerulopathy (C3G) is characterized by complement dysregulation and resulting C3 deposition in glomeruli. We reviewed the characteristics of the baseline kidney biopsy in a cohort of patients with C3G to determine if biopsy features of activity and chronicity correlate with complement biomarkers and clinical parameters at presentation.

## Methods

Patient data from the University of Iowa's C3G Natural History Study were used. Criteria for entry included baseline native biopsy diagnosis of C3G and complement biomarkers within one year of diagnostic biopsy. Patients with a history of dialysis, transplant, or anti-complement therapy were excluded. Significance was assessed using Pearson correlation coefficients with two-tailed p values (95% confidence). Significance was adjusted using a Bonferroni correction; p-values less than 2.9e-3 were considered significant.

## References

1. Kidney Int. 2018 Apr;93(4):977-985
2. Clin J Am Soc Nephrol. 2022 Jul;17(7):994-1007
3. Am J Kidney Dis. 2021 May;77(5):684-695.e1.

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Iowa Hospital



Figure 1: Significance of Chronicity Score Correlation with Complement Biomarkers:

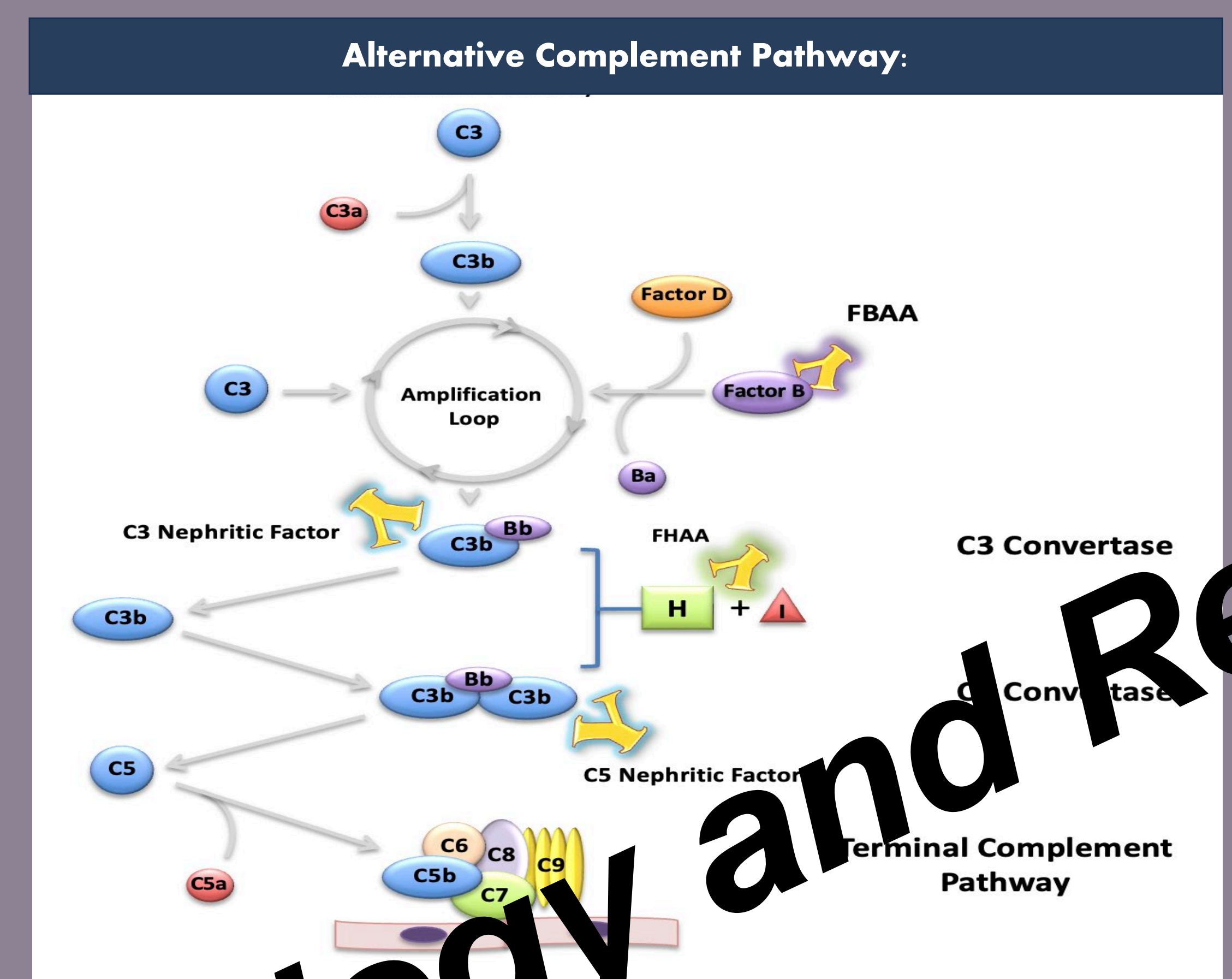
Marker:	p-value:
APFA%	0.002
CFB Autoantibody (AU)	0.902
C3 Nef: C3CSA%	0.766
C5 Nef: C3CSAP%	0.013
C4 Nef: %	0.257
C3 (g/L)	0.024
C4 (g/L)	0.762
C5 (mg/dL)	0.019
Factor B (mg/dL)	0.87
Ba (mg/L)	1.74E-09
Bb (mg/L)	0.027
Properdin (mg/L)	0.16
sC5b-9 (mg/L)	0.26
Factor H (mg/L)	0.369
Factor I (mg/L)	0.368
sCr (mg/dL)	4.67E-16
GFR (mL/min/1.73m2)	2.52E-10
UPC (mg/mg)	0.8

Figure 2: Significance of Activity Score Correlation with Complement Biomarkers:

Marker:	p-value:
APFA%	0.251
CFB Autoantibody (AU)	0.471
C3 Nef: C3CSA%	0.244
C5 Nef: C3CSAP%	0.011
C4 Nef: %	0.441
C3 (g/L)	0.15
C4 (g/L)	0.41
C5 (mg/dL)	0.15
Factor B (mg/dL)	0.297
Ba (mg/L)	0.534
Bb (mg/L)	0.901
Properdin (mg/L)	0.02
sC5b-9 (mg/L)	0.009
Factor H (mg/L)	0.369
Factor I (mg/L)	0.368
sCr (mg/dL)	0.551
GFR (mL/min/1.73m2)	0.944
UPC (mg/mg)	0.239

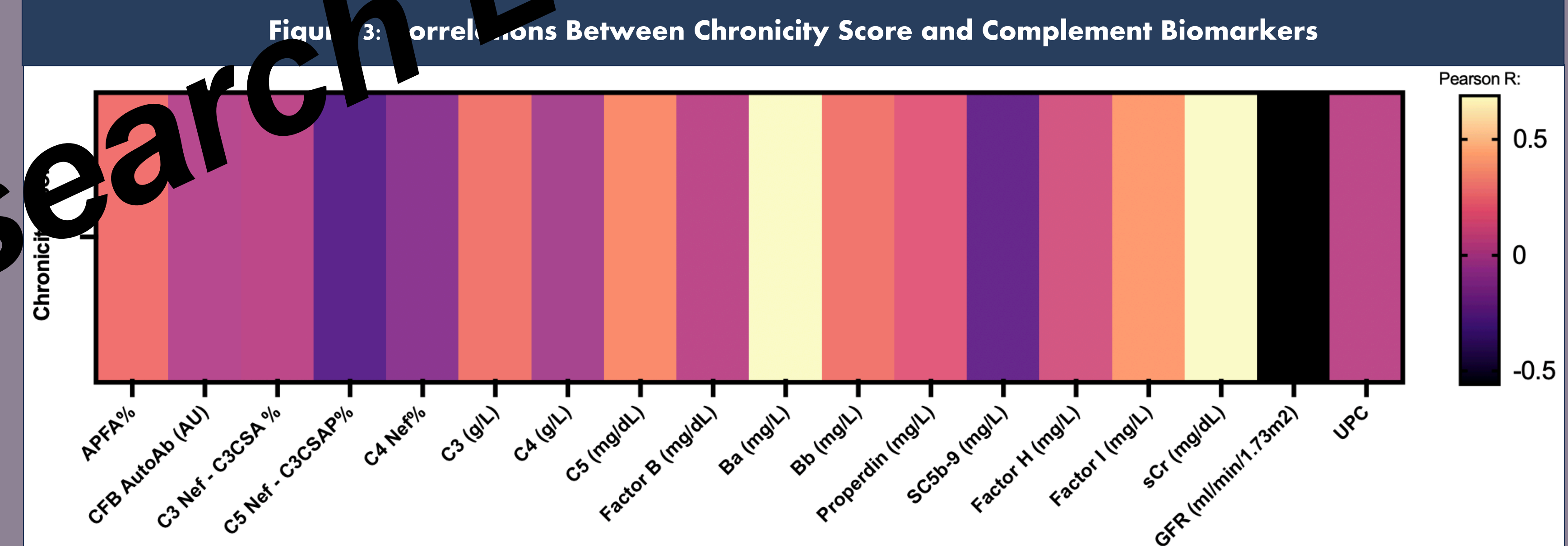
Figure 1: Higher chronicity scores were associated with an increase in Ba (mg/L) and APFA % at presentation. Clinically, higher chronicity scoring was associated with an increase in serum creatinine (mg/dL), and a decrease in GFR (mL/min/1.73m2) at presentation. Increased chronicity scoring was not significantly correlated with any other complement biomarker result.

Figure 2: Higher activity scores were not significantly correlated with both clinical markers and complement biomarkers.



## Results

### Chronicity:



Heat maps were used to visualize the strength of identified statistical relationships:

Figure 3: Of the significant relationships identified, the strongest correlation is between chronicity scoring and serum creatinine (mg/dL), followed by that of Ba (mg/L). Increased chronicity scoring was correlated with elevated sCr (R = 0.698) and elevated Ba (R = 0.663) at presentation. Conversely, higher chronicity scoring was correlated with decreased GFR (R = -0.578). While still statistically significant, the weakest correlation was observed between chronicity scoring and APFA %. Higher chronicity scoring was correlated with increased APFA % (R=0.314).

### Activity:

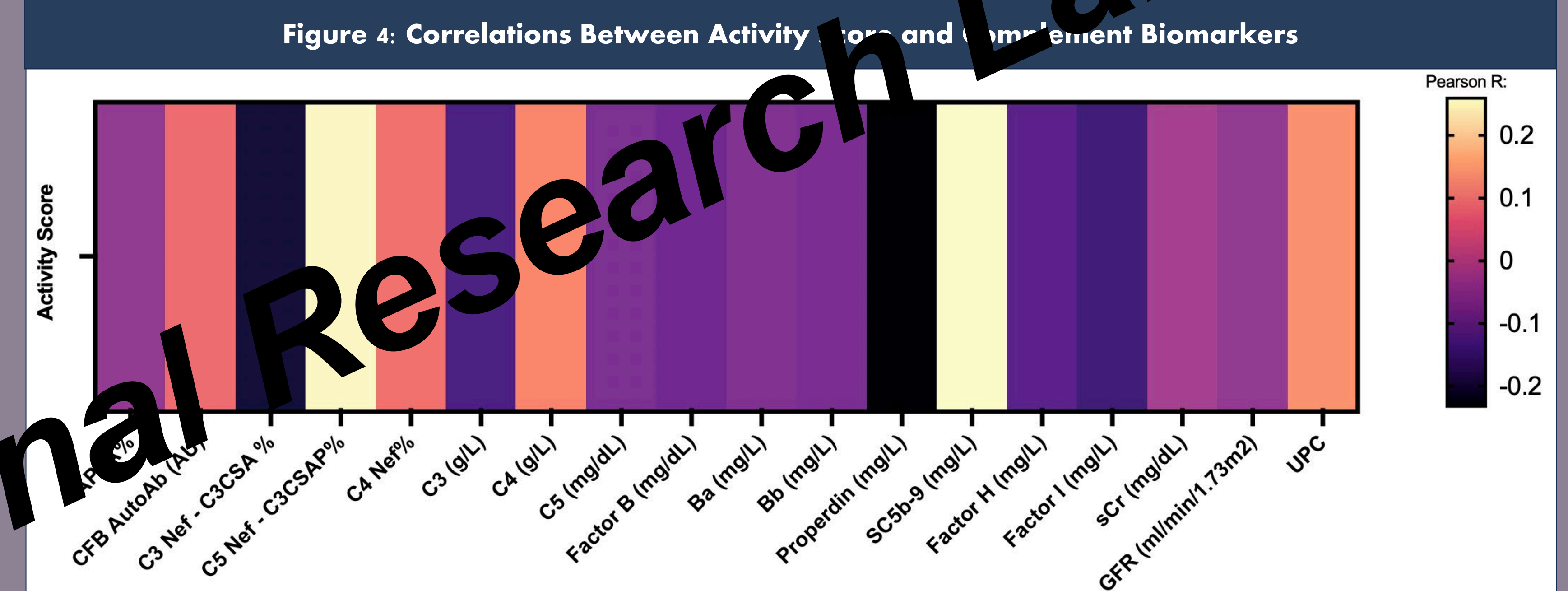


Figure 4: As no significant associations were observed between activity scoring and clinical and complement biomarkers, no strong correlations were observed.

## Conclusions

The association of increased chronicity scores with higher Ba and serum creatinine, as well as lower GFR, is consistent with the fact that Ba rises as renal function decreases. The lack of observed relationships between activity scoring and complement biomarkers suggests that the relationship between Ba and renal function exists independently of complement activity. No significant relationships between either form of histological scoring and the components of the terminal complement pathway were observed, suggesting that terminal pathway activity is not a significant driver of inflammation in this sample. Future directions of this project include investigation of whether changes in biomarker results over time confer changes in chronicity and activity scoring. Additionally, we plan to pursue analysis of other biomarkers as a predictor of disease progression.