



# FERRITIN, CRP, AND SOLUBLE CD25 DISTINGUISH TAFRO FROM HLH

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## BACKGROUND

Hemophagocytic lymphohistiocytosis (HLH) and TAFRO (thrombocytopenia, anasarca, fever, reticulon myelofibrosis, and organomegaly) are rare cytokine storm syndromes that mimic each other but have differing treatment algorithms.<sup>1</sup>

We have previously shown that serum inflammatory markers can distinguish Still's disease from HLH.<sup>2</sup>

## OBJECTIVE

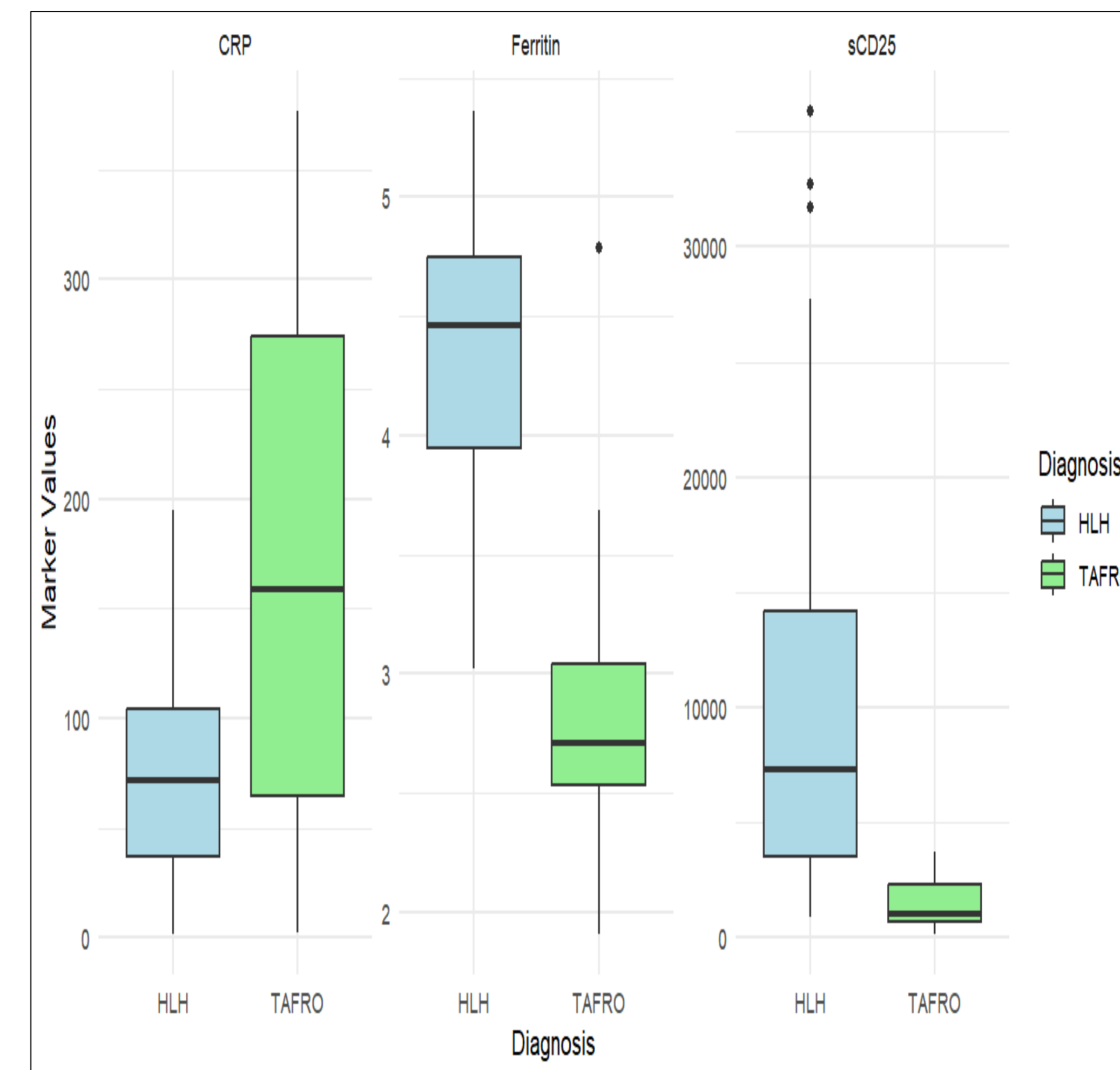
**We hypothesized that readily available bloodwork tests – ferritin, C-reactive protein (CRP), and soluble CD25 (sCD25) – can help distinguish HLH and TAFRO.**

The goal of the study was to determine whether serum inflammatory markers could reliably distinguish HLH and TAFRO.

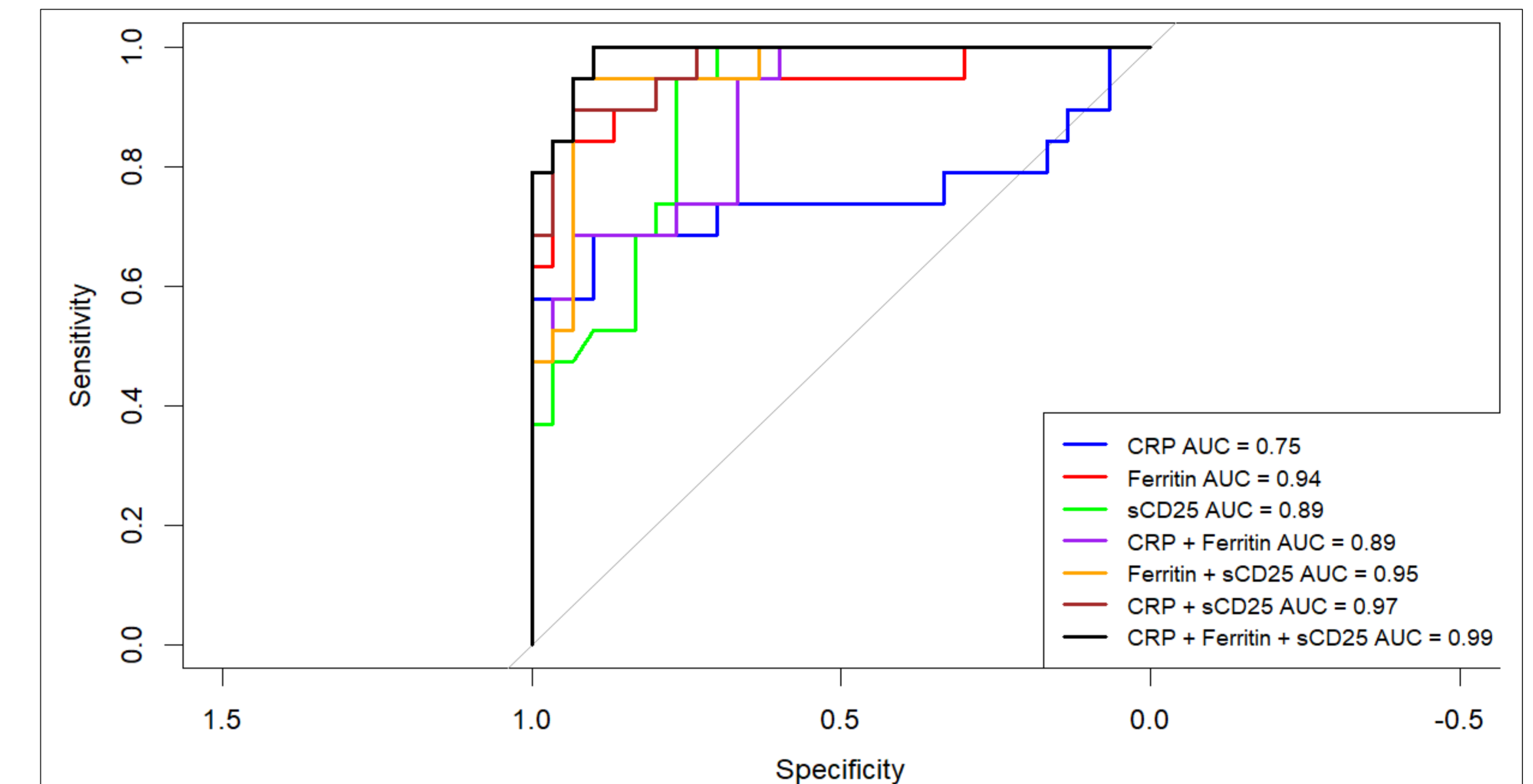
## RESULTS

**Table 1: Characteristics of sampled patients with HLH and TAFRO.**

Characteristic	HLH	TAFRO
Age (mean [range])	53 (19-89)	33 (2-74)
Sex (% female)	47	38
Laboratory values; Median (Interquartile Range)		
Creatinine (µmol/L)	No data	186 (131-473)
Hemoglobin (g/L)	84 (77-94)	68 (65-80)
Platelets (x 10 <sup>9</sup> /L)	54 (29-99)	28 (15-51)
WBC (x 10 <sup>9</sup> /L)	3.4 (1.3-8.0)	4.3 (2.8-6.4)
CRP (mg/L)	71 (34-104)	159 (61-277)
Ferritin (µg/L)	29,020 (8888-56,289)	514 (340-1116)
sCD25 (U/mL)	7280 (2487-12,341)	1033 (639-2364)
ALT (U/L)	96 (64-264)	62 (42-119)
AST (U/L)	227 (83-480)	57 (36-105)



**Figure 1: TAFRO (median [IQR]). Median (IQR) Box plots (log scale) of CRP, ferritin and sCD25 in HLH and TAFRO are 71 mg/L (34-104) and 159 mg/L (61-277), respectively; Median (IQR) ferritin for HLH and TAFRO are 29,020 µg/L (8888-56,289) and 514 µg/L (340-1116), respectively. Median (IQR) sCD25 for HLH and TAFRO are 7280 U/mL (2487-12,341) and 1033 U/mL (639-2364), respectively. All p<0.001.**



**Figure 2: Combined ROC Curves for Ferritin, CRP, and sCD25** Optimal cutoffs are: CRP = 128.6 mg/L (sensitivity 60.4%, specificity of 90.9%, area under the curve, AUC 0.75). Ferritin = 1854 µg/L (sensitivity 93.1%, specificity of 97.7%, AUC 0.94). sCD25 = 3354 U/mL (sensitivity 95.8%, specificity 76.7%, AUC 0.89). The combined cutoff of CRP > 129, ferritin < 1854, and sCD25 < 3354 has a sensitivity of 100% and specificity of 53%. Using a grid search analysis, the combined optimal cutoffs are CRP > 80, ferritin < 4900, and sCD25 < 3300 with a sensitivity of 100% and specificity of 68.4% for TAFRO over HLH.

## METHODS

### Retrospective cohort study (total N=113)

- HLH cases from Vancouver General Hospital (n=44)
- TAFRO cases from ACCELERATE database (n=69; 24 with sCD25 measured)
- Compared ferritin, CRP, and sCD25 levels (with 72 hours of diagnosis for HLH patients, within 10 days for TAFRO patients)

## CONCLUSIONS

HLH and TAFRO are cytokine storm syndromes that are difficult to diagnose due to lack of specific biomarkers and can result in death without rapid identification and disease-specific therapy.<sup>1</sup>

**Our research demonstrates that ferritin, CRP, and soluble CD25 levels reliably distinguish between HLH and TAFRO.**

This serves to improve speed and accuracy of diagnosis when clinicians encounter cytokine storm, and thus allow for earlier administration of life-saving treatments.

## TAKE HOME FINDING

**Table 2: Guide for differentiating between HLH, Still's disease, and TAFRO in the setting of undifferentiated cytokine storm.**

Disease	Ferritin (µg/L)	CRP (mg/L)	sCD25 (U/mL)
HLH	>> 10,000	< 130	>> 3350
TAFRO	< 1850	>> 130	<< 3350
Still's disease	> 10,000	> 130	< 3900

## REFERENCES

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2. Beckett M, Spaner C, Goubran M, Wade J, Avina-Zubieta JA, Setiadi A, Tucker L, Shojania K, Au S, Mattman A, Lee AYY, Fajgenbaum DC, Chen LYC. CRP and sCD25 help distinguish between adult-onset Still's disease and HLH. Eur J Haematol. 2024 Nov;113(5):576-583. doi: 10.1111/ejh.14267. Epub 2024 Jul 10. PMID: 38984483.

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