IFNγ-IL18 AXIS CYTOKINES DISCERN MYCOBACTERIAL AND KSHV INFLAMMATORY SYNDROMES IN PWH

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Joseph M Rocco[1], Ramya Ramaswami[2], Kathryn Lurain[2], Elizabeth Laidlaw[1] Andrea Lisco[1], Frances Galindo[1], Adam Rupert[3], Denise Whitby[2], Maura Manion[1], Robert Yarchoan[2], Irini Sereti[1]

[1]Laboratory of Immunoregulation, NIAID, Bethesda, USA , [2]HIV-AIDS Malignancy Branch, Center for Cancer Research, NCI, Bethesda, USA, [3]AIDS Monitoring Laboratory, Leidos Biomedical Research, Frederick, USA

BACKGROUND

- Identify unique biomarker profiles which can differentiate mycobacterial IRIS and KSHV-inflammatory diseases

→ Both mycobacteria and KSHV can cause clinically similar inflammatory syndromes in advanced HIV

→ The pathogenesis of both involves the IFNγ-IL18 axis

METHODS

Cohort (n=77) → On ART with KSHV or mycobacteria infection

- **Mycobacterial IRIS (Myco-IRIS):**
  →Tuberculosis (n=21), Non-tuberculosis mycobacteria (n=29)
- **KSHV-associated diseases (KAD):**
  →Multicentric Castleman's (n=16), Primary Effusion Lymphoma (n=10), KSHV-Inflammatory Cytokine Syndrome (n=6)

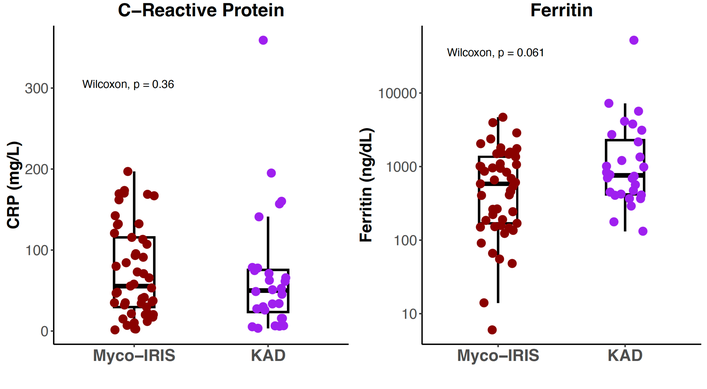
Testing → all inflammatory episodes after starting ART

- Clinical characteristics, labs from prospective NIH cohorts
- **ELISA/MSD:** IL6, IL10, IL18, IL18BP, IFNγ, CXCL9, sCD163

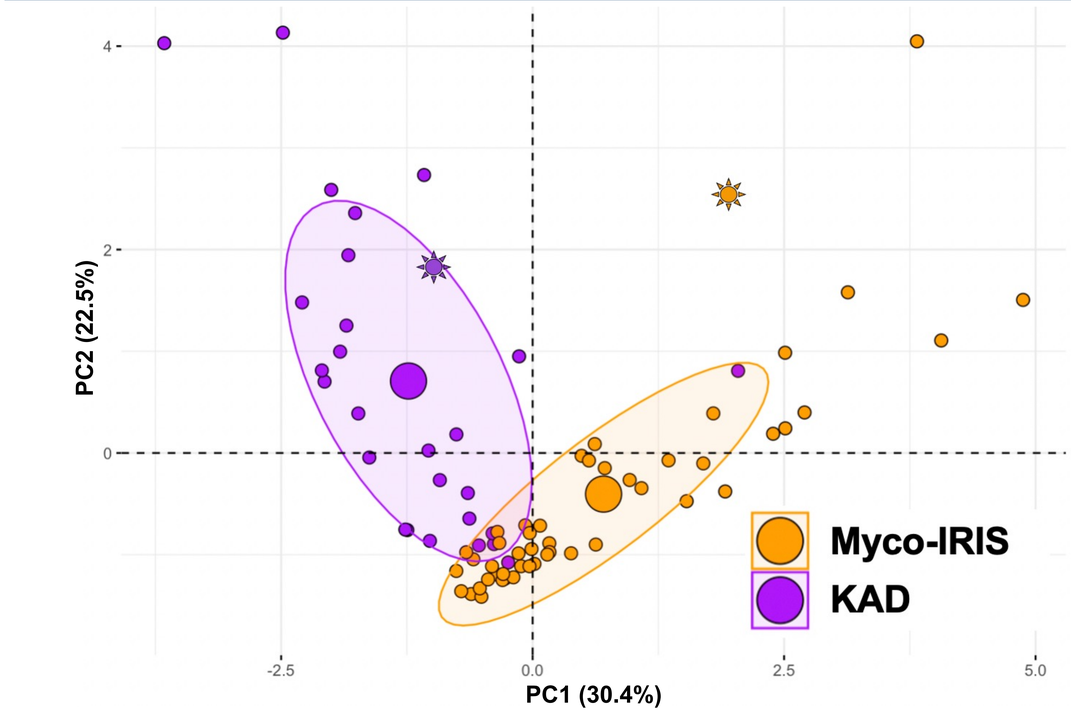
Characteristic	Myco-IRIS	KAD
N	**50**	**27**
Age – y	37 (33-43)	43 (36-55)
Cis Male – no. (%)	32 (64)	27 (100)
Race/ethnicity – no. (%)		
White Caucasian	7	11
African/American	29	9
Hispanic (non-White)	14	3
CD4 T-cells (cells/μl)	94 (58-159)	140 (69-286)
HIV (copies/mL)	335 (25-1610)	67 (25-1021)

RESULTS – CLINICAL LABS

- Clinical labs do not distinguish HIV-associated inflammatory syndromes due to mycobacteria versus KSHV



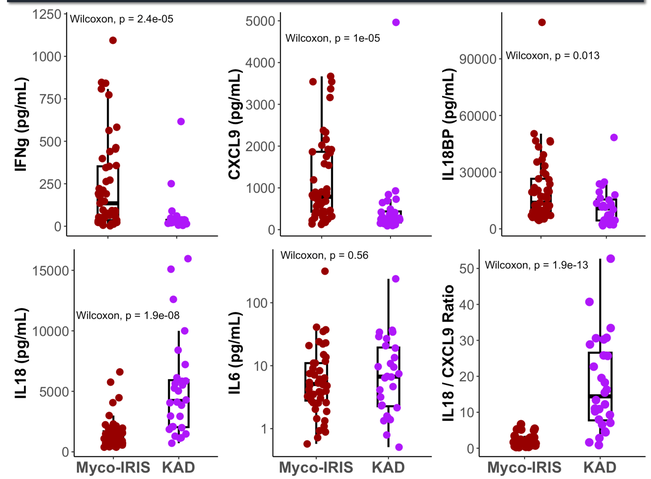
<u>CXCL9</u> and **<u>IL-18</u>** can differentiate inflammatory syndromes in people with advanced HIV driven by **mycobacterial-IRIS** or **KSHV-associated diseases**.



☀ Individuals with both mycobacterial and KSHV infections at the onset of the inflammatory syndrome

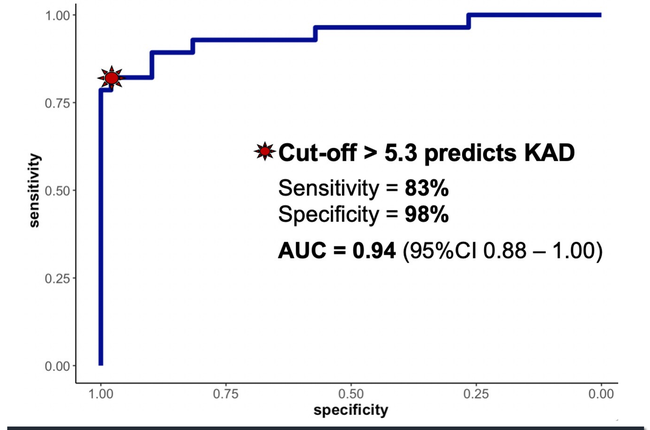
- Principal component analysis incorporating biomarkers and labs reveal distinct clustering of HIV-associated inflammatory syndromes
- Two individuals with concomitant disseminated mycobacterial infection and KSHV viremia map into separate inflammatory clusters indicating unique pathogeneses

RESULTS – BIOMARKERS



- IL18/CXCL9 ratio was most predictive of KAD over myco-IRIS at clinical presentation

IL-18/CXCL-9 Ratio



CONCLUSIONS

- Although clinically indistinguishable, myco-IRIS and KAD demonstrate unique immune profiles and differences in immunopathogenesis.
- Biomarkers could improve risk stratification and diagnosis even in resource-limited settings and could aid in optimizing therapeutic interventions

Author Contact: Joseph Rocco, email: roccojm@nih.gov

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