

Developing a Protein Signature of Early Latent Tuberculosis Infection

Charles M. Bark^{1,2}, Mary N. Nsereko², Noah Kiwanuka³, Christopher C. Whalen⁴, Catherine M. Stein², Henry Boom², Harriet Mayanja-Kizza^{2,3}, Sophie Nalukwago², Robert Kakaire⁴, JohnPaul K. Jingo³, and Eustache Paramithiotis⁵
¹MetroHealth Medical Center, ²Uganda-CWRU Research Collaboration, ³Makerere University, ⁴University of Georgia, ⁵CellCarta Biosciences

Introduction

- To curb the tuberculosis (TB) epidemic, new cases must be prevented.
- Preventive therapy for latent TB infection (LTBI) is not currently feasible
- New assays of LTBI are needed that can identify patients at risk for active TB

Methods and Materials

- Plasma was collected in a TB household contact study in Kampala, Uganda.
- Longitudinal sample sets (0,6,12 months) from 81 participants
- Proteomic and multiplex cytokine analysis was done
- Proteomic analysis targeted 163 host proteins that significantly changed during *Mtb* infection in our previous study of household contact converters.

Study Subjects

- Household TB Contacts in Kampala, Uganda
- 24 TST/IGRA converters, 29 resisters (contacts who remained TST/IGRA negative), and 28 baseline positives (LTBI)
- Age 15 and older
- Enrolled 2016 – 2019
- Followed x 1 year
- Quantiferon (QFT) baseline, 6 months, 12 months
- TST measured at baseline and 12 months

Discussion

- Conversion discordance was not anticipated and remains unexplained
- Household contacts who converted both the IGRA and TST were identified by a protein signature, which may serve as a potential biomarker for infection
- Overlaps exists between converters and LTBI, likely due to recent conversion among the latter group

Results

- Nearly 1/3 of converters had discordant IGRA and TST (Table 1)
- Concordant “Strong Converters” IGRA/TST – positive vs others is unclear
- Our previous protein signature based on our previous household contact study where conversion was measured by TST did not predict conversion in this study
- A new protein pattern of IGRA/TST converters is emerging (Figure 1)
- A subset of latent TB subjects also shared the protein signature suggestive of a recent conversion event (Figure 2)

Table 1. TST and IGRA characteristics of converters

	Age	Conversion Month	Quantiferon	TST change Mo 12
CONCORDANT	23	6	Pos C,D	0 to 19.5
	27	6	Pos C,D	0 to 18.3
	18	6	Pos C,D	0 to 21.2
	25	6	Pos C,D	0 to 15.2
	40	6	Pos C,D	0 to 15.3
	30	6	Pos C,D	0 to 17.5
	26	6	Pos C,D	0 to 12.5
	23	6	Pos C,D	0 to 15
	29	6	Pos C,D	0 to 23.2
	44	6	Pos C,D	0 to 14.4
	44	6	Pos C,D	0 to 17.7
	39	6	Pos C,D	0 to 10.4
DISCORDANT	43	6	Pos C,D	0 to 14.4
	17	12	Pos D	0 to 10.4
	15	6	Pos C,D	5.8 to 19
	29	6	Pos C,D	9.2 to 14.6
	15	6	Pos C,D	7.4 to 16.2
	20	6	Pos C,D	0 to 0
	66	12	All negative	0 to 15.9
	22	12	All negative	0 to 14.9
	58	12	All negative	0 to 12
	40	12	All negative	0 to 12.8
	15	6	Pos C, neg D	8.4 to 10.9
	44	6	Pos C, neg D	4 to 12.9

Figure 1: Biomarkers of month 6 IGRA/TST converters

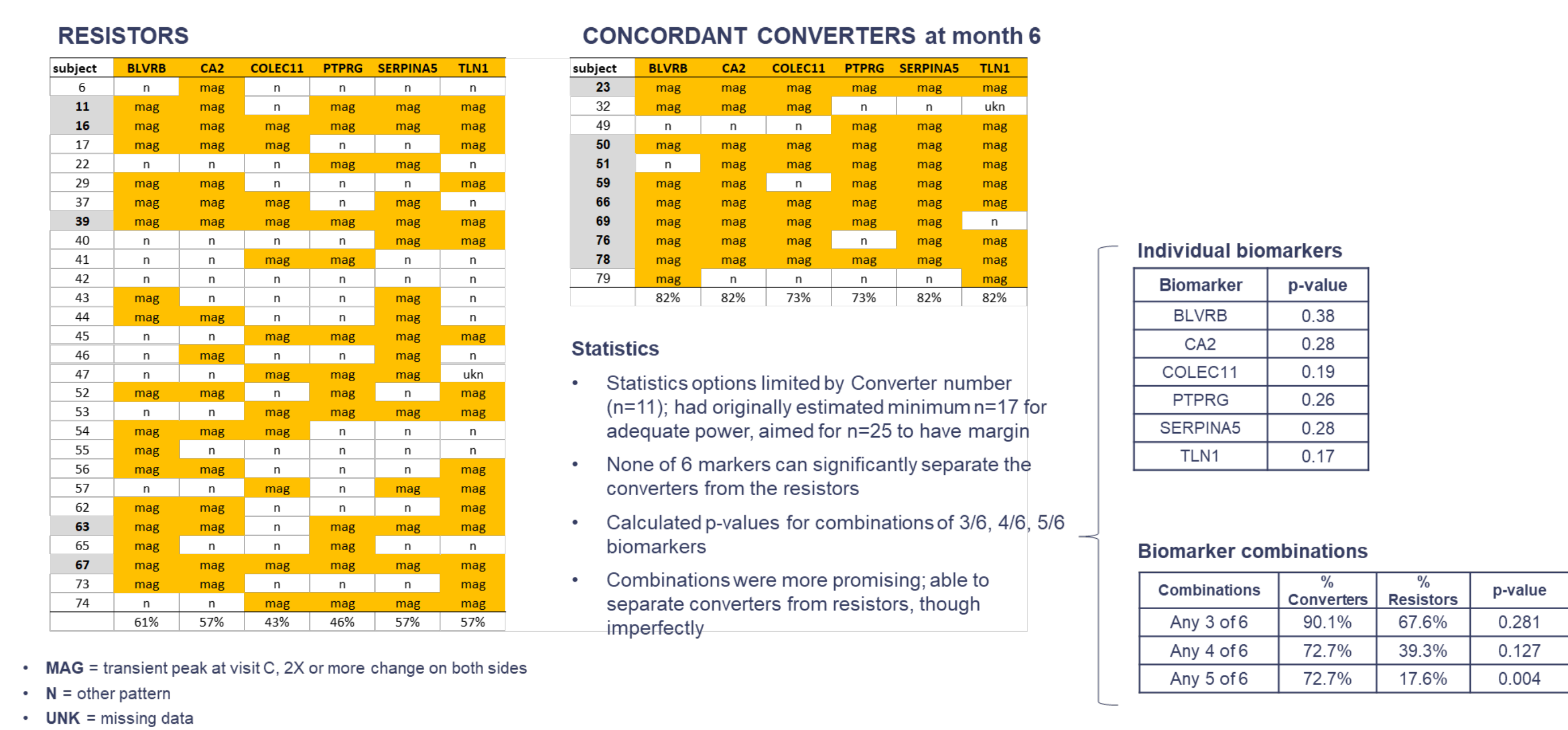
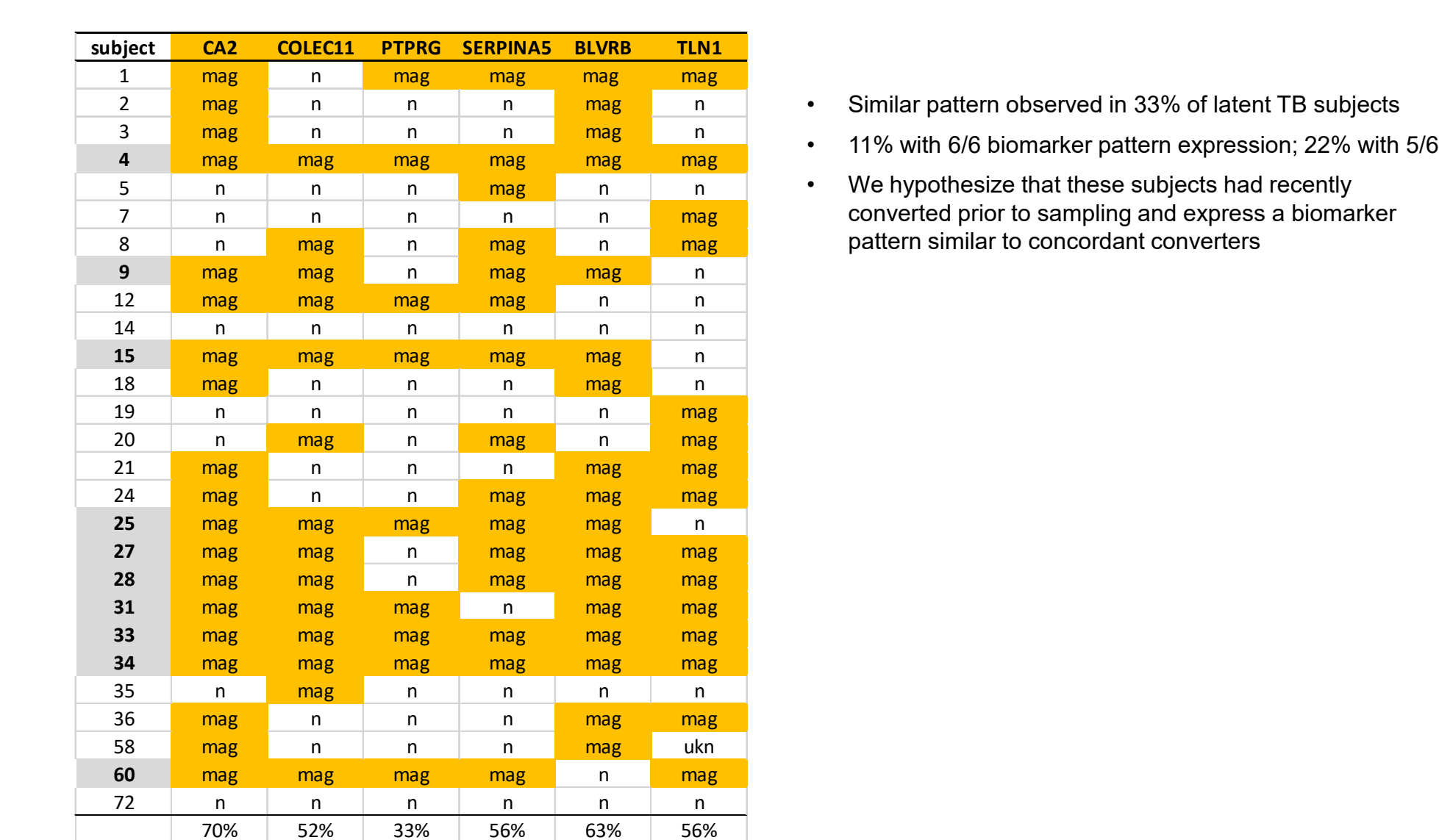


Figure 2: Expression of converter biomarkers in latent TB



Next Steps

- Our community cohort study is enrolling TST/IGRA negative people with quarterly QTF and GPS tracking to determine where conversion is occurring



Contact

Charlie Bark, MD, MS
 Division of Infectious Diseases
 MetroHealth Medical Center
 Case Western Reserve University
 cmb148@case.edu

References

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