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Pattern-based medicine

Novel TB diagnostics

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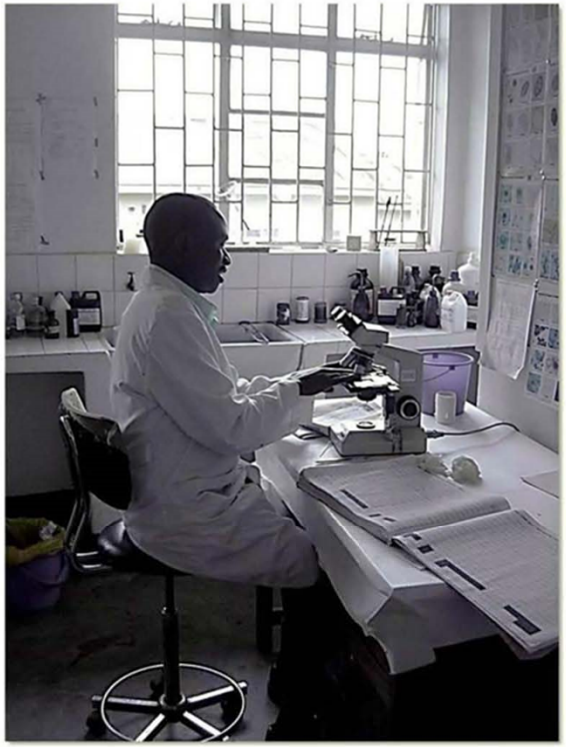
Background



TB signature development

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Sample numbers (Total = 405)

	Pilot study Uganda	London 2011	London 2012	London 2012
Active disease	20 AFB positive	40 pTB & EPTB	7	94 pTB & EPTB
	20 AFB/HIV positive			
Asymptomatic	20			
Asymptomatic IGRA Positive		40		89
Asymptomatic IGRA Negative		30	16	
Sick control			8 (Atypical Mycobaceria)	21

AUC summary for initial samples

	Healthy Ctrl/TB	Active /Latent	Sick Ctrl/TB	Sick 2 /TB	Sick 2 /Active	Sick2 /Latent
Markers 6 & 7	**73% (0.03)**	**88% (0.01)**	**71% (0.02)**	**69% (0.07)**	**87% (0.03)**	**61% (0.05)**
Combined Markers 1-8	**91% (0.01)**	**90% (0.00)**	**73% (0.05)**	**73% (0.03)**	**87% (0.04)**	**60% (0.01)**

TB = Active + latent disease
Sick 2 = Sick control – atypical Mycobacteria

Reported are area under the curves (AUC) and +- 1 standard deviation estimated from 3 repeat experiments.

TB signature development
Selection strategies

- Early discovery panel (multiplexed panel)
- Literature information
- Biological/immunological plausibility
- Microarray studies

TB Prediction
Independent test cohorts (Total = 420)

	Healthy	Latent	Active (smear pos)	Active (smear neg)	Sick
South Africa	26	68	100		
Vietnamese		47	92	47	44

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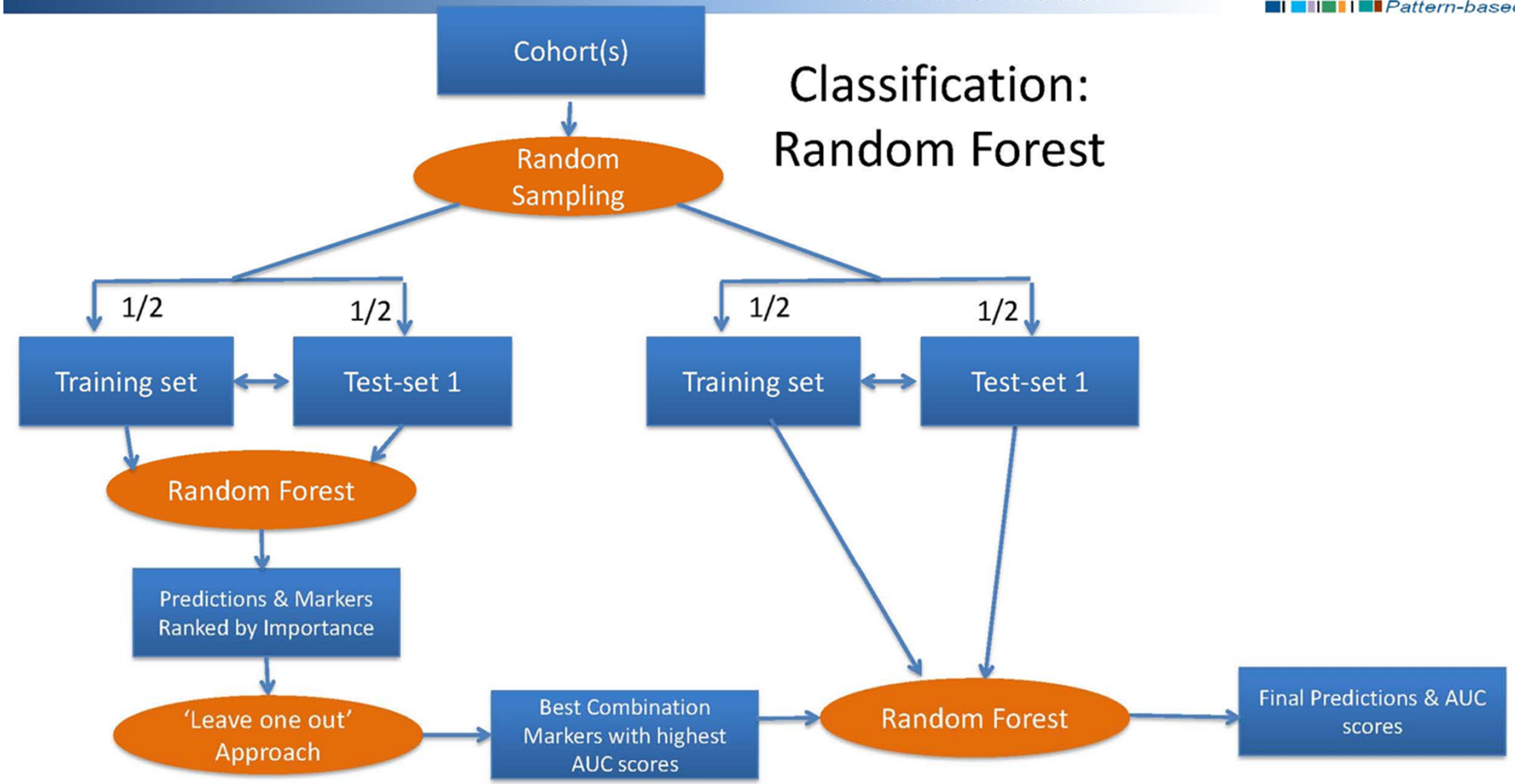

AUC Summary

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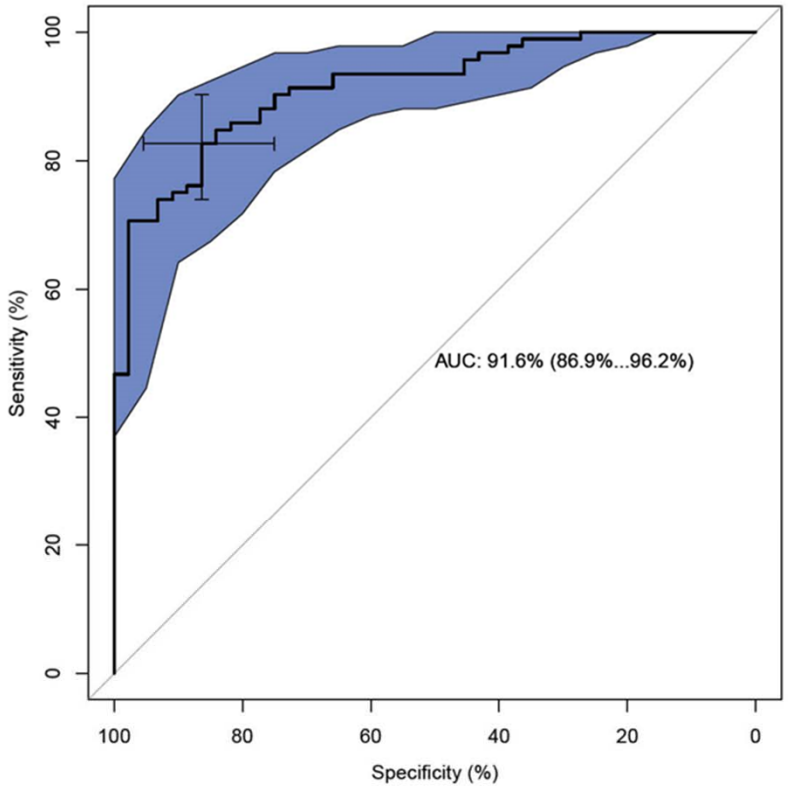
Prediction	Specifics	Country	AUC (all)	AUC (best)
Sick/Active TB	Smear pos	VN	89.2	91.6
	Smear neg	VN	79.4	83.6
	All	VN	86	89.5
Active/Latent	All	VN	91.8	94.3
	Smear pos	SA	99.8	100
	Smear pos	VN	97.2	98.5
	Smear neg	VN	77.8	87.7
Healthy/Active	Smear pos	SA	100	100.0
Sick/Latent		VN	57.9	71.0

Comparison of ProteinLogic Test vs WHO TPP for Triage Test

		TPP	ProteinLogic
Sensitivity	Sputum positive	>90-95%	95%
	Sputum negative	>90-95%	91.5%
	EPTB	-	-
Specificity	Sputum positive	>70-80%	72%
	Sputum negative	>70-80%	56.8%
	EPTB	-	-

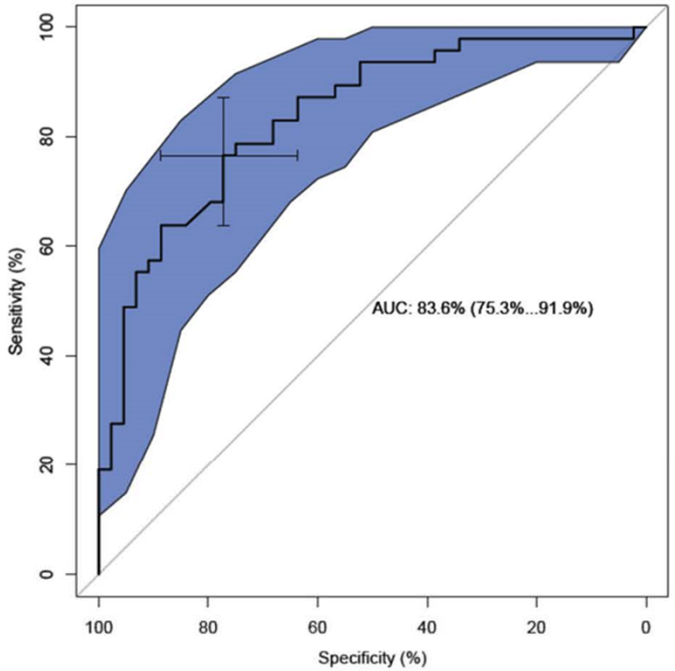
AFB sputum positive, culture positive vs sick control



	Result
SENS	95%
SPEC	72%
PPV	62.68 %
NPV	97.10 %

AFB & Culture + ve: N = 192
Sick N = 44

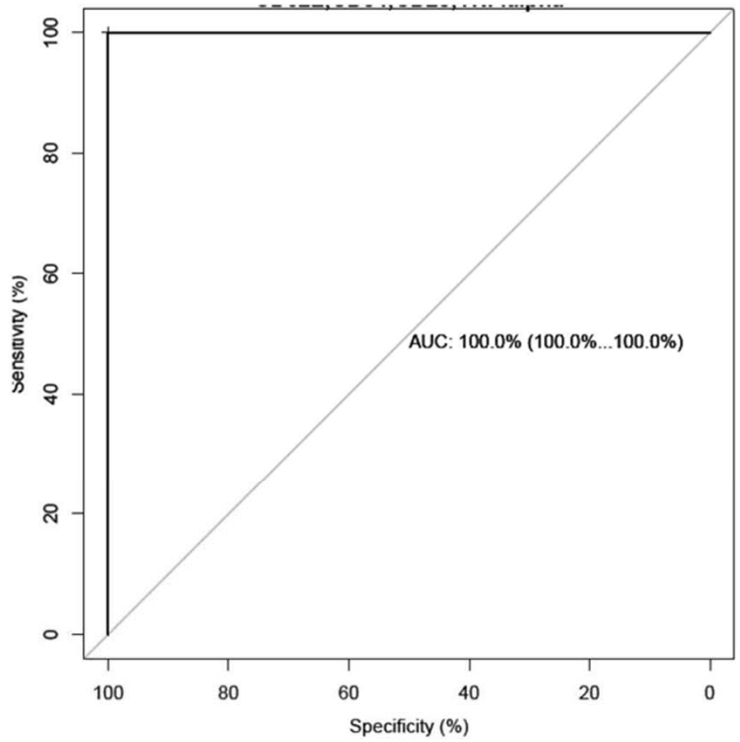
AFB sputum negative, culture positive vs sick control



	Result
SENS	91.5%
SPEC	56.8%
PPV	69.3%
NPV	86.2%

AFB –ve & culture +ve N = 47
Sick N = 44

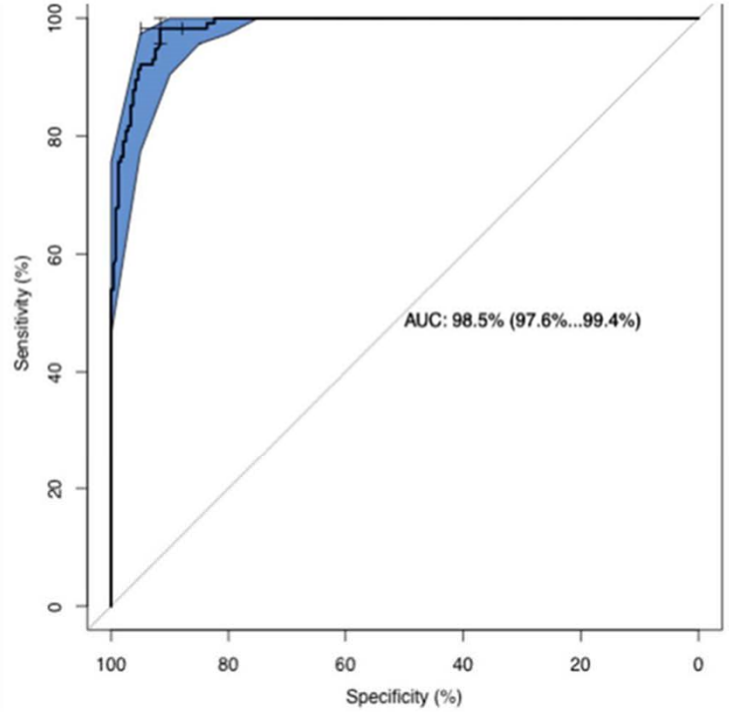
AFB sputum positive, culture positive vs healthy control



	Results
Sens	100%
Spec	100%
PPV	100%
NPV	100%

AFB & culture +ve:
N = 192
Healthy control: N= 26

Culture positive vs latent TB



	Results
Sens	100
Spec	97.2
NPV	100
PPV	95.2

Culture +ve: N = 239
Latent: N= 115

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Prediction	Specifics	Country	AUC (all) Method 1	AUC (best) Method 2	AUC Method 3
Active/Latent		South Africa	100	100	98.9
Active/Latent		Vietnam	89	94.3	94.9
Active/Latent	Smear positive	Vietnam	95	98.5	98.5
Active/Latent	Smear negative	Vietnam	80	87.7	89.2

Diagnostic landscape

- Rule out test used as first line to Xpert.
- IGRA plus.
- Progression from latent to active.
- Response to treatment.
- Novel pathways for vaccine development.
- Second generation definitive diagnostic.

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