The Molecular 'MDR Screen' is an Important Tool in the Diagnosis and Initiation of Appropriate Therapy in TB Patients in the State of Florida

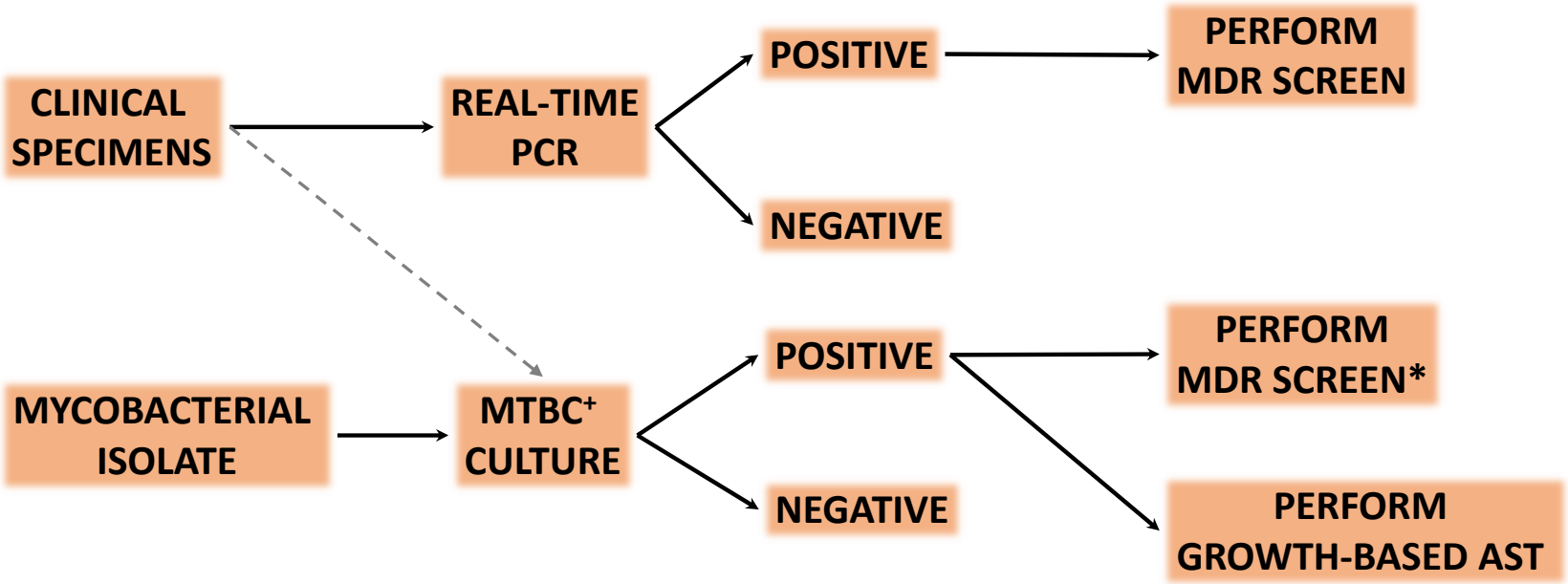
Calin B. Chiribau,[1] M-C. Rowlinson,[1] S.Crowe,[1] B. Jones,[1] A. Ashkin,[1] H. Perera,[1] D. Ashkin,[1] M. Lauzardo,[2] D. Urbine[2]

[1]Florida Department of Health, Tallahassee, FL, [2]University of Florida, Department of Medicine, Division of Infectious Diseases and Global Medicine, Gainesville, FL

Background

- Multi-drug resistant TB (MDR-TB) is defined as resistance to at least RIF and INH
- Molecular detection of MDR-TB is a rapid and accurate method for resistance screening
  - 97% of the cases of resistance to RIF are associated with mutations in *rpoB* gene RRDR
  - 80-90% of cases of resistance to INH are caused by mutations in either the *katG* gene or *mabA-inhA* gene promoter region
- Florida Bureau of Public Health Laboratories (FL-BPHL) utilizes the MTBDR*plus* assay (HAIN Lifescience) as its molecular "MDR Screen" since July 2009 (assay performed twice/ week)
  - Performed directly on clinical specimens
  - Assay turnaround time (TAT) ~ 8 hours
  - Inexpensive instrumentation
  - Results relatively easily visualized and interpreted
- This study analyzed the performance of the Hain MTBDR*plus* assay over two-year period (2014-2015) and the impact of test results on patient therapy

Integration of the MDR screen in the Laboratory Algorithm



* IF NOT ALREADY PERFORMED @ SPECIMEN LEVEL

Study design

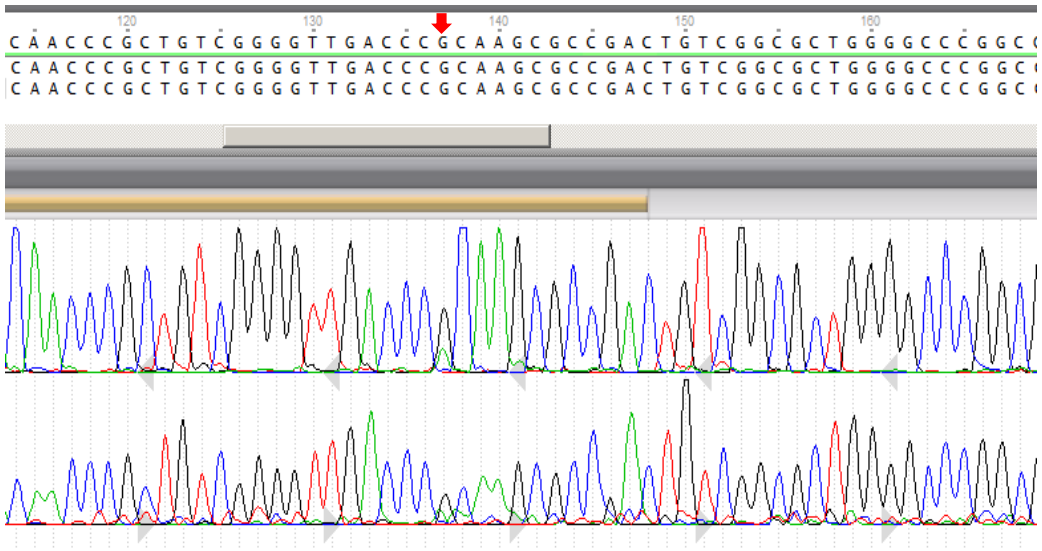
Analysis of AST data for n=603 clinical specimens over a 2-year period (2014-2015)

- Date of specimen **receipt**
- Date of **MDR screen** result by Hain Genotype® MTBDR*plus* assay, version 2 (Hain LifeScience)
- Date of **phenotypic AST** result by Sensititre MIC assay (TREK Diagnostic Systems, Thermo-Fisher)
- Date of initiation of appropriate **therapy:**
  - MDR patients: Addition of **fluoroquinolone(s)**
  - INH-resistant: **Modification** of treatment regimen

Laboratory Methods: MDR screen

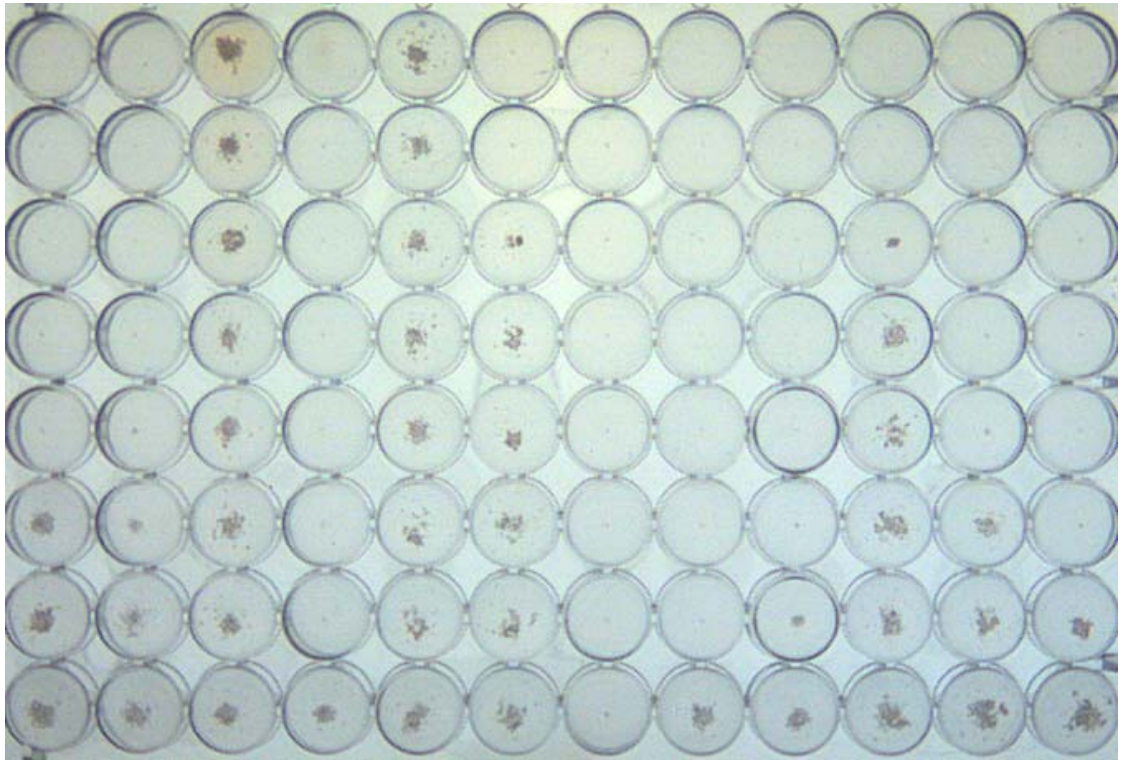
MDR patient detected by MDR screen (by Hain GenoType MTBDR*plus* Assay)
rpoB:Ser531Leu, *katG*:Ser315Thr

CC: conjugate control, AC: amplification control



rpoB His526Arg mutation
identified by Sanger DNA sequencing

Laboratory Methods: Growth-based AST



MIC (µg/ml): >16 >32 4 2

MDR patient detected by growth based assay
(by Sensititre)

Results: MDR screen turnaround time

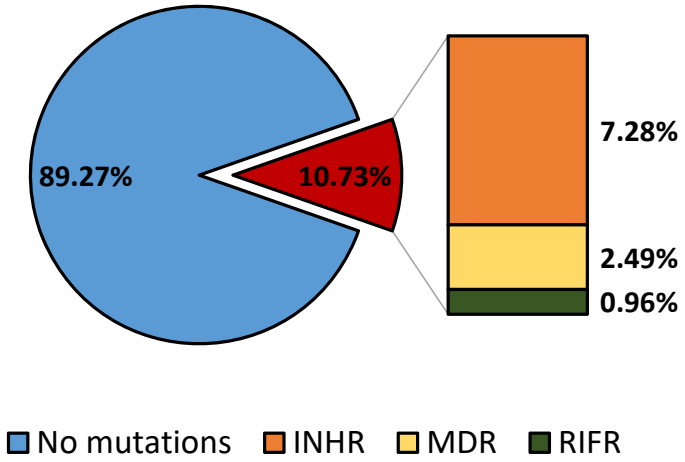
- **The average TAT (date of specimen receipt to result release) for the MDR Screen was 9.44 days**
- 82.9% of all specimens tested by MDR Screen were resulted within 10 days or less from the receipt of the specimen in our laboratory and more than 55% within 5 days

TAT for MDR Screen	< 5 days (avg. 3.57)	6-10 days (avg. 7.48)	11-15 days (avg. 13.73)	>16 days (avg. 35.95)	Total
Number of specimens (%)	334 (55.38)	166 (27.52)	20 (3.31)	83 (13.75)	603

Results: Mutations

- Out of n=603 tested, 81 could not be resulted (missing TUB^{+} bands, indeterminate)
- 522 specimens had valid results that could be analyzed. Relevant mutations were detected in n=56 specimens (10.73%)

MDR screen result	Specimens tested (%)
No mutations	466 (89.27)
Isoniazid resistant (*katG/inhA*)	38 (7.28)
Rifampin resistance (*rpoB*)	5 (0.96)
MDR (*rpoB* + *katG/inhA*)	13 (2.49)
Total	522



Results: Molecular AST vs Growth based AST

MDR Screen results were available, on average, 34.26 days earlier than growth-based AST results

- An assessment of **n=384** clinical specimens tested by both GenoType MTBDR*plus* Assay and Sensititre MIC revealed an average TAT for Sensititre MIC of **43.67 days** (from date of receipt to growth-based AST result) compared to **9.41** days for the molecular MDR Screen

Results: Impact on patient care. MDR patients

- n=9 Florida patients with RIF and INH resistance were detected by MDR Screen
- Modifications to the drug regimen were documented in all 9 cases, upon receipt of MDR screen results
- The average number of days from date of MDR Screen result to change to appropriate therapy was n=6.9 days (range 1-16 days)
- The average number of days from change in appropriate therapy to when the phenotypic AST was available was n=30.2 days (range 11-77 days)
- Of the 9 patients, 7 completed the treatment and were considered cured (average of 19.2 months or 581 days). One patient left the state/country having completed 8 months of treatment, and one is still under treatment (started on 5/28/2015)

Results: Impact on patient care. Isoniazid mono-resistance

Isoniazid mono-resistant cases (*katG/ inhA*), n=33

- n=33 Florida patients with INH resistance were detected by MDR Screen
- Modifications to the drug regimen due to MDR screen results were documented in 19 patients (n=9: increased dosage, n=10: discontinuation)

Conclusions

The MDR Screen is a reliable tool in early detection of resistance to first line drugs

- The average overall TAT for MDR Screen results is considerably less than for growth-based AST. 83% of the tested specimens could be resulted within 10 days and results were made available in most cases on average 34 days earlier than the growth-based AST results
- The MDR Screen detected mutations in 9.3 % of patients tested at FBPHL over a 2-year period, a significant number for which valuable information on susceptibility could be determined early on

The MDR Screen has a significant impact on drug regimen modifications

- Examination of drug regimen data of 33 Florida patients infected with INH-mono-resistant strains revealed that modification of regimen occurred in 19 patients upon receipt of MDR screen laboratory results
- Nine MDR-TB patients were identified by the MDR Screen and were switched to appropriate therapy 23 days (on average) sooner


PATRICK
MICHAELA
KATRINA
ALI
RONNIE
BETH
CHARISE
STEVE
CHRISTINE
JENNIFER
RICHARD
DERRICK
WE ARE...
FAST TRACKING TB
TESTING - 24150
SPECIMENS IN 2016
TO END TB
#Unite2EndTB