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of Health

Wadsworth
Center

Whole Genome Sequencing for TB Diagnostics

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Wadsworth Center



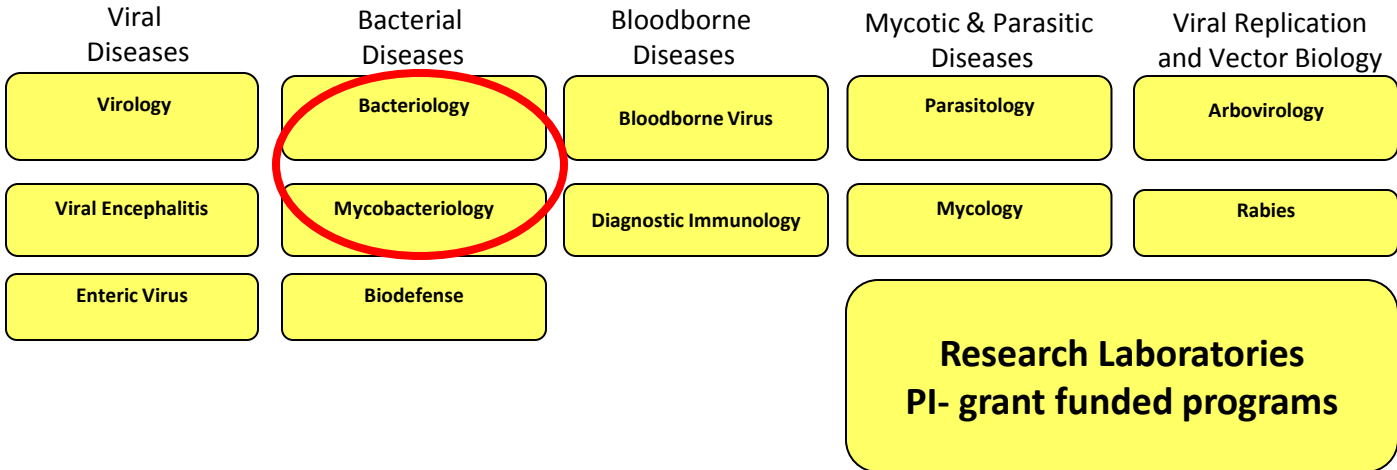
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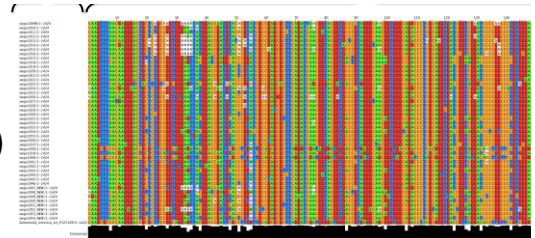
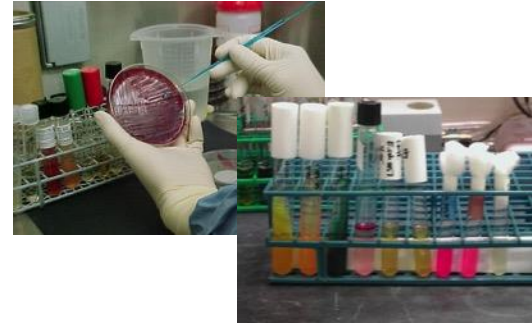
- 900,000 sq. ft. state-of-the-art-facilities- 5 locations
- ~700 staff, >150 doctoral level scientists
- \$25 million in external grant funding
- Laboratories in four scientific divisions:
 - Environmental Health, Infectious Disease, Genetics, Translational Medicine

Division of Infectious Diseases



Roles of the Wadsworth Center Bacteriology and Mycobacteriology Laboratories

- Reference services
- Outbreak and hospital investigations
- Specialized testing
- Support of disease surveillance and epidemiology investigations
- Preparedness and response
- Applied research (NIH, CDC, contracts)



TB Background



- **Caused by *Mycobacterium tuberculosis* and other MTBC species**
- **Roughly one third of the world's population is infected with TB**
- **2013: 9 million new infections, 1.5 million deaths**
- **Second only to HIV/AIDS as a worldwide killer**

<http://www.cdc.gov/tb/statistics/>



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A Typical TB Case Requires:



PLUS

- X-rays
- Lab tests
- Follow-up & testing of contacts



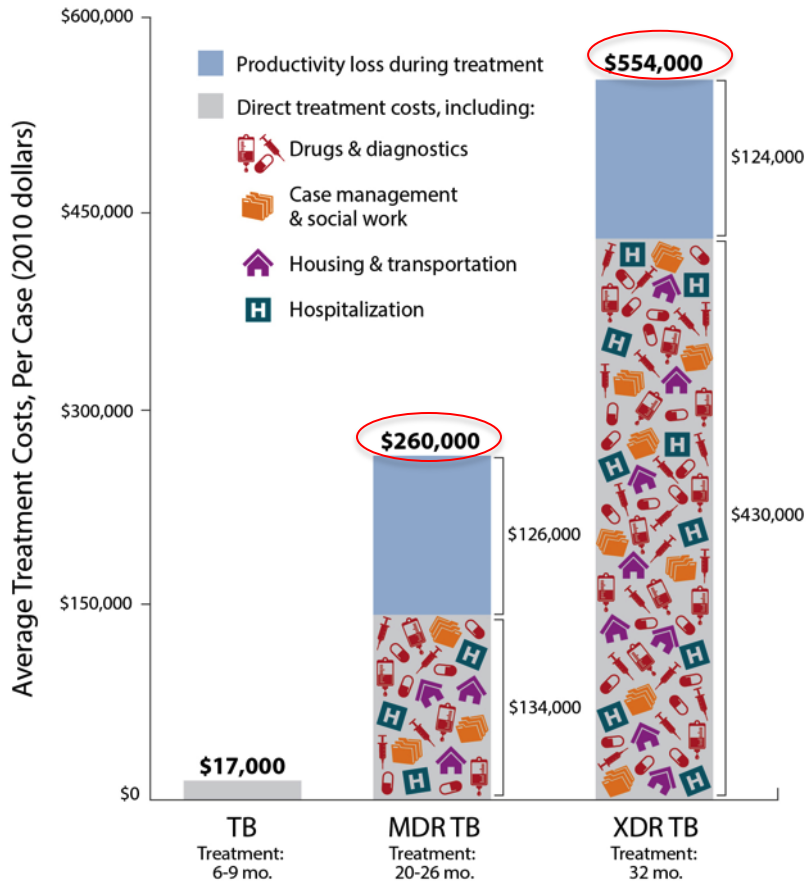
Total cost to U.S.
for TB cases in 2014.



Centers for Disease
Control and Prevention
National Center for HIV/AIDS,
Viral Hepatitis, STD, and
TB Prevention

The Outsized Financial Toll of MDR and XDR TB

Cost increases with greater resistance:



Preventing and Controlling MDR and XDR TB in the U.S. Requires:

**BETTER
TREATMENT
OPTIONS**

**RAPID
DIAGNOSIS**

**EXPERT
TREATMENT
OF EVERY
TB CASE**

**IMPROVING
GLOBAL TB
DIAGNOSIS AND
TREATMENT**

<http://www.cdc.gov/nchhstp/newsroom/2014/WorldTBDay-graphics.html>



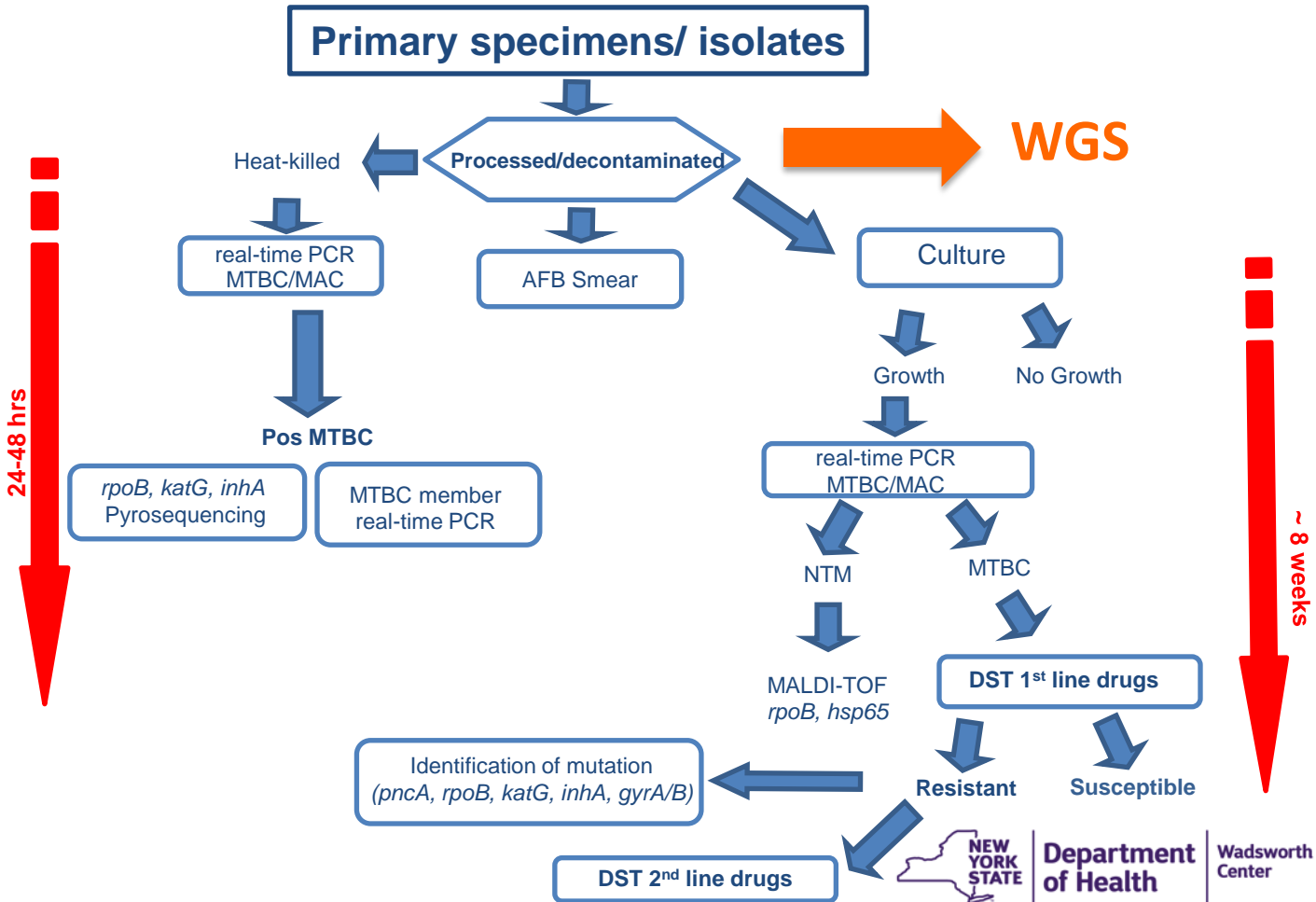
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Rapid Diagnosis of *Mycobacterium tuberculosis* with WGS

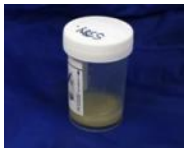
- **Faster turn-around time**
- **More comprehensive results**
 - **Detect mixed infections**
 - **Many predictors of drug resistance**
 - **Emerging resistance**
- **Cost effective**
 - **Replace existing assays (real-time PCR, pyrosequencing, spoligotyping)**
 - **Staff time savings**





Whole Genome Sequencing

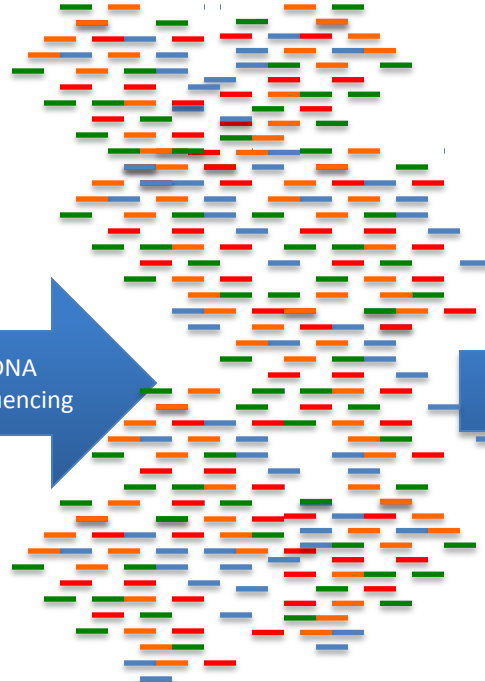
Next Generation Sequencing



Extract TB
DNA



DNA
sequencing

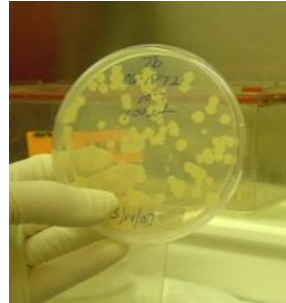


Bioinformatics

Sequencing on MiSeq, 2 x 250bp PE reads

Where to start?

- Isolates
 - Solid
 - MGITs
- Primary specimens
 - sputum
 - other



Optimizing TB isolate preparation for WGS

- Assess methods used in lab
- Research TB WGS methods
- Assess worse case scenario
 - 1- 2 ml MGIT
 - early MGIT positive (Day 0-3 flagged positive)
- Ease of use, cost
- DNA concentration
- Ultimately- WGS 40X depth and close to 100% coverage



Breaking TB Open is Critical for DNA Extraction

Important TB Characteristics

- ~24 hour doubling time
- TB clumps together
- Unique cell wall
 - Rich in lipids (>60%)
 - Mycolic acids



Initial Methods Tested

- Typical bacterial extraction
- Zymo Research Kit
 - Meant for tough to lyse fungi/ bacteria
- CTAB method
 - Ideal for plant cell nucleic acid extraction/ MTB

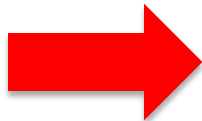


**DNA yield too low,
labor intensive, WGS
variable results**



InstaGene Matrix and Tissue Homogenizer

- **InstaGene matrix (Chelex resin)**
 - The Chelex matrix binds to PCR inhibitors rather than DNA, preventing DNA loss due to irreversible DNA binding.
- **Fastprep tissue homogenizer**
 - Good enough yield to provide reliable WGS data even with 0 day MGIT

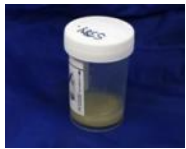


Success!

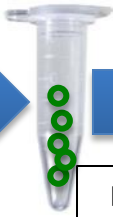
Whole Genome Sequencing

Next Generation Sequencing

40X Depth and 100% Coverage



Extract TB
DNA

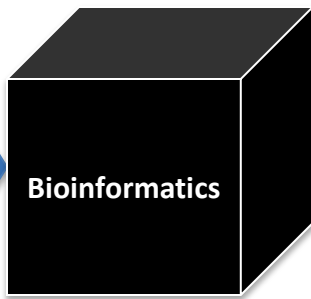


Library
Preparation

Nextera XT



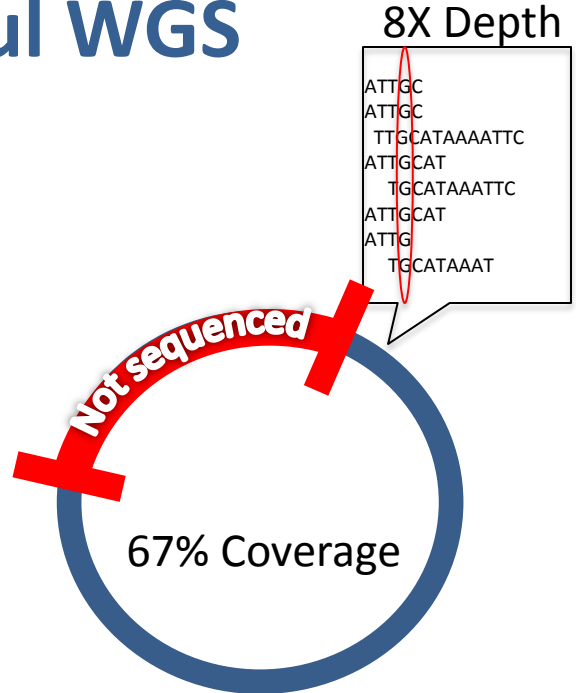
DNA
sequencing



Sequencing on MiSeq, 2 x 250bp PE reads

Successful WGS

- **Depth:** Essentially the number of times the base was read; measure of confidence in correct call
 - Can be given as a genome average
 - We are aiming for 40X
- **Coverage:** A percentage that describes how much of the genome was sequenced
 - Best 100%

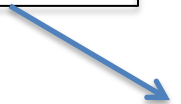
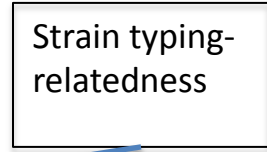
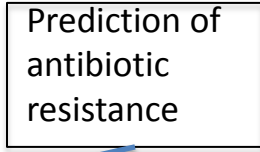
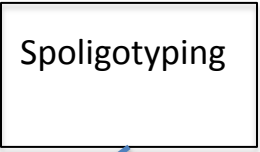
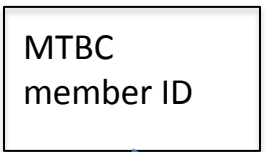
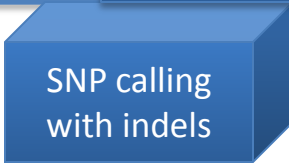
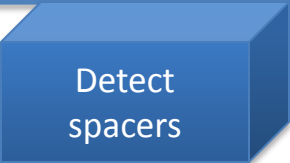
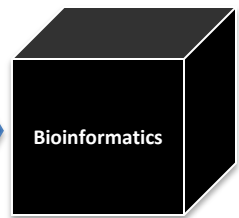


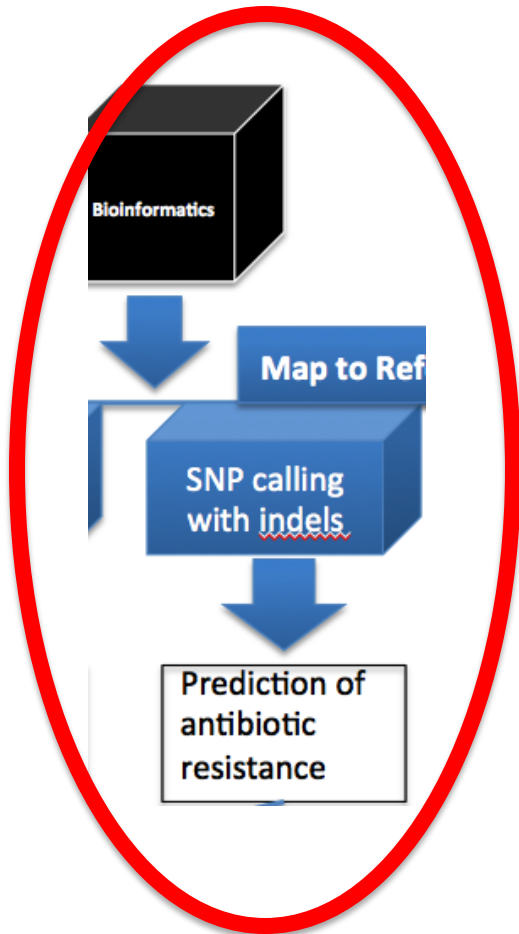
Library Preparation is Another Key Factor

- *Votintseva et al.* suggested using 15 cycle library preparation
 - 2015 paper about WGS of early positive MGIT

| | | | <u>12 cycle library prep</u> | | <u>15 cycle library prep</u> | |
|----------------------------|-----------|-------------|------------------------------|------|------------------------------|------------|
| Sample | Method | stock ng/ul | Avg depth coverage % | | Avg depth | coverage % |
| <i>M. bovis</i> BCG (0day) | InstaGene | 0.268 | FAIL | FAIL | 27.66 | 97.23 |
| | InstaGene | 0.344 | FAIL | FAIL | 19.4 | 97.07 |
| | InstaGene | 0.346 | FAIL | FAIL | 14.22 | 96.78 |

TB Bioinformatics Pipeline





- Evaluating 8 Drug Classes
 - 12 loci
 - Hundreds of potential SNPs
- Additional loci throughout the genome
 - frameshifts
 - insertions
 - deletions

Validation of TB WGS for isolates

- SOP, reports, interpretation, QC, assay controls, metrics
- Specificity, intra-assay and inter-assay reproducibility ✓
- Retrospective testing ✓
- Prospective testing
- Evaluate each drug ✓



Sequence Confirmation- Using another molecular method (used to predict resistance)

| Drug | Gene | # Mutations found | # Confirmed | # Not Confirmed |
|-------------------------|---|-------------------|-------------|---------------------|
| Rifampin | <u><i>rpoB</i></u> | 46 | 44 | 2 ¹ |
| Isoniazid | <u><i>katG</i></u> | 40 | 36 | 4 ¹ |
| Isoniazid & Ethionamide | <u><i>inhA/</i></u> <u><i>mabA</i></u> | 22 | 17 | 5 ¹ |
| Fluoroquinolones | <u><i>gyrA</i></u> | 13 | 12 | 1 ² |
| Streptomycin | <u><i>rrs</i></u> | 11 | 11 | 0 |
| | <u><i>rpsL</i></u> | 28 | 26 | 2 ^{2,3} |
| Pyrazinamide | <u><i>pncA</i></u> | 31 | 19 | 12 ^{1,2,3} |
| Ethambutol | <u><i>embB</i></u> | 28 | 26 | 2 ^{1,3} |
| Kanamycin | <u><i>rrs</i></u> | 8 | 8 | 0 |
| | <u><i>eis</i></u> | 1 | 0 | 1 ¹ |

¹No assay/ Mutation found outside range of confirmatory assay/ deletion caused assay failure

²pending

³No remaining DNA stock

Fluoroquinolone comparison

| | | DST Phenotype | |
|-----------------|------------------|---------------|----|
| | | R | S |
| WGS Genotype | Fluoroquinolones | | |
| | R | 13 | 0 |
| | S | 0 | 61 |

Resistance Predictive Value= 100%
Susceptible Predictive value= 100%

Isoniazid comparison

| | | DST Phenotype | |
|--------------|-------------|----------------|----------------|
| | | R | S |
| WGS Genotype | Isoniazid R | 55 | 1 ¹ |
| | Isoniazid S | 6 ² | 32 |

¹This SNP is known to be a good but not perfect predictor of INH resistance (14/15 resistant)

² Each of the 6 has a different mutation that could potentially account for the missed resistance

Resistance Predictive Value= 98%

Susceptible Predictive value= 84%



Prospective Testing



First Batch of Prospective specimens

Results as of 8/3/15:

| Sample | Current method results | | | WGS results | | | | | |
|-------------|------------------------|--------------|---------|-----------------|-----------|-----|--|--|---------------|
| | DST | Pyro results | spoligo | Genome coverage | Ave Depth | ID | High confidence mutations detected | Frameshift and/or large deletions detected | spoligo |
| IDR15-51087 | invalid; PZAS | No mutations | ND | 98.36 | 91.05 | Mtb | None | none | S00034 |
| IDR15-52024 | pending; PZAS | ND | ND | 98.46 | 75.32 | Mtb | gyrA Ala90Val; gyrA Asp94Gly (FLQ) | none | Unknown (new) |
| IDR15-52248 | pending | ND | ND | 98.82 | 79.08 | Mtb | embB Met305Val (EMB); gyrA Ser91Pro (FLQ); katG Ser315Thr (INH) | rpoB(+TTC) in-frame insertion (RIF) | S00034 |

No Results

WGS complete



First Batch of Prospective specimens

Results as of 8/18/15:

| Sample | Current method results | | | WGS results | | | | | |
|-------------|------------------------|--|---------|-----------------|-----------|-----|---|--|---------------|
| | DST | Pyro results | spoligo | Genome coverage | Ave Depth | ID | High confidence mutations detected | Frameshift and/or large deletions detected | spoligo |
| IDR15-51087 | Pan-Susceptible | No mutations | ND | 98.36 | 91.05 | Mtb | None | none | S00034 |
| IDR15-52024 | pending; PZA | gyrA: Asp94Gly | pending | 98.46 | 75.32 | Mtb | gyrA Ala90Val; gyrA Asp94Gly (FLQ) | none | Unknown (new) |
| IDR15-52248 | pending | rpoB: insertion of bases at codon 514; katG: Ser315Thr; gyrA: Ser91Pro | ND | 98.82 | 79.08 | Mtb | embB Met305Val (EMB); gyrA Ser91Pro (FLQ); katG Ser315Thr (INH) | rpoB+TTC in-frame insertion (RIF) | S00034 |

Some Results

WGS complete



First Batch of Prospective specimens

Results as of 10/8/15:

| Sample | Current method results | | | WGS results | | | | | |
|-------------|--|--|---------|-----------------|-----------|-----|--|--|---------------|
| | DST | Pyro results | spoligo | Genome coverage | Ave Depth | ID | High confidence mutations detected | Frameshift and/or large deletions detected | spoligo |
| IDR15-51087 | Pan-Susceptible | No mutations | ND | 98.36 | 91.05 | Mtb | None | none | S00034 |
| IDR15-52024 | FLQ | gyrA: Asp94Gly | S02467 | 98.46 | 75.32 | Mtb | gyrA: Ala90Val; gyrA: Asp94Gly (FLQ) | none | Unknown (new) |
| IDR15-52248 | 1 st line invalid; 2 nd line pending | rpoB: insertion of bases at codon 514; katG: Ser315Thr; gyrA: Ser91Pro | S00034 | 98.82 | 79.08 | Mtb | embB: Met305Val (EMB); gyrA: Ser91Pro (FLQ); katG: Ser315Thr (INH) | rpoB: +TTC in-frame insertion (RIF) | S00034 |

More Results

WGS complete



Heteroresistance



S/N G:270 A:151 T:145 C:418

KB.bcp

KB 1.4.1.8 Cap:6

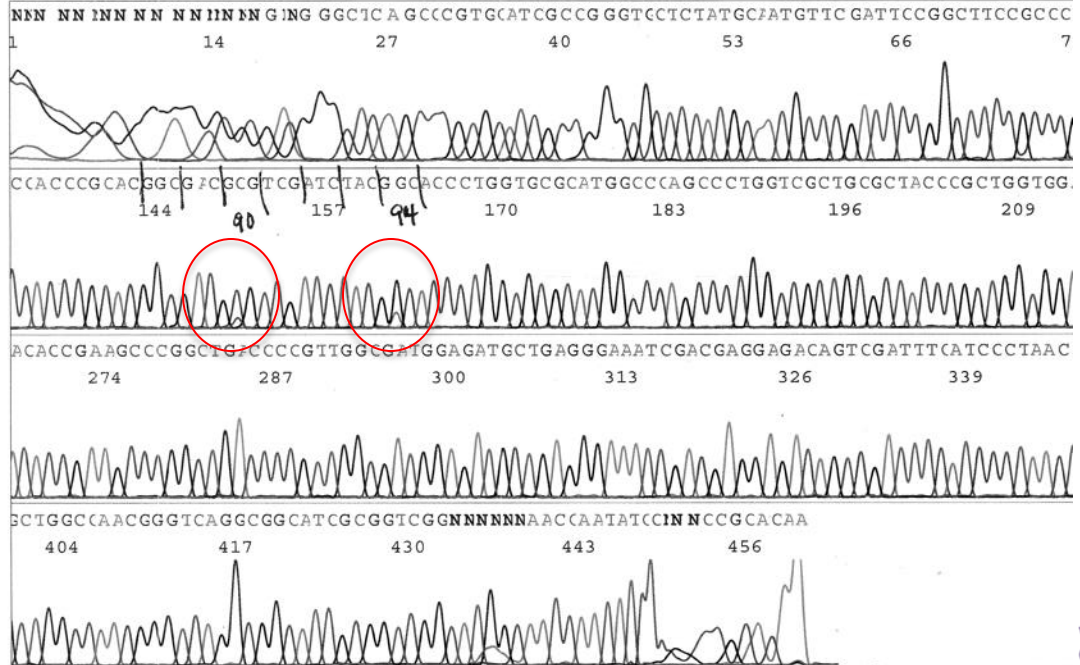
4068_C08_15-52024-gyrAF_006

15-52024-gyrAF

KB_3130_POP7_BDTv3.mob

Pts 1720 to 7333 Pk1 Loc:1697

Version 6.0 HiSQV Bases: 429 4068-59 C8



Turn-Around Time

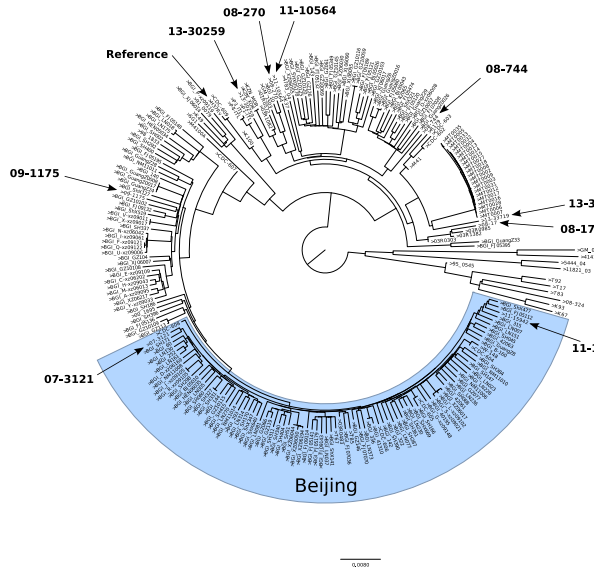
| Sample | Date Received | Date processed and sent to core | Date of DST results | Date of WGS report | DST TAT from receipt of specimen to DST results (days) | WGS TAT from receipt of specimen to report (days) |
|-------------|---------------|---------------------------------|---|--------------------|--|---|
| IDR15-51087 | 7/3/15 | 7/17/15 | 8/13/15 | 7/30/15 | 41 | 27 |
| IDR15-52024 | 7/10/15 | 7/17/15 | 8/24/15 (1 st line); 9/1/15 (2 nd line) | 7/30/15 | 53 | 20 |
| IDR15-52248 | 7/13/15 | 7/17/15 | 1 st line invalid; 2 nd line still pending | 7/30/15 | >60 | 17 |



Imagine this is
4-5 days!



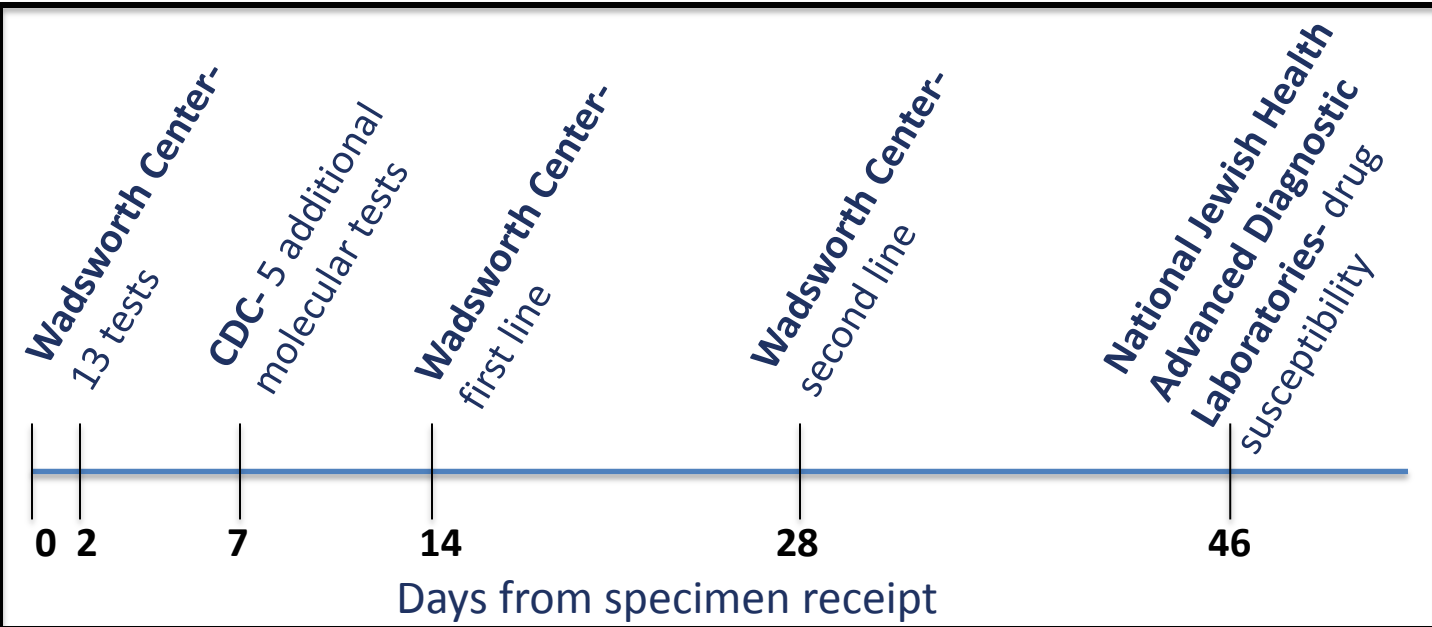
WGS prediction spoligotypes and genotyping with increased resolution



| Sample # | Extraction | Accid. | Phenotype (DST) | Resistance Associated Mutations (WGS) | Other mutations noted (WGS) | WGS Spoligotype | CLIMS spoligo. NYS | Do results correlate? |
|----------|------------|---------|---|---|--|-----------------|--------------------|-----------------------|
| 21 | CTAB | 14-7386 | SM (low level in 2 nd line), INH, RIF, RBT | <i>mcbA</i> aa 450 (RIF) <i>tpsl</i> aa 88 (SM) <i>katG</i> aa 315 (INH) | | S00034 | Scheduled 12/15/14 | Yes |
| 22 | CTAB | 14-7387 | INH (low level), RIF, RBT | <i>mcbA</i> aa 445 (RIF) <i>intergenic hyp-fabG1 aa</i> -15 (INH) | | S00197 | S00197 | Yes |
| 23 | CTAB | 14-7388 | SM, INH, PZA, EMB (2 nd line only), KM, AN, | <i>mcbA</i> aa 450 (RIF) <i>tpsl</i> aa 43 (SM) <i>katG</i> aa 315 (INH) <i>embB</i> aa 306 (EMB/INH) | <i>rrs</i> (AN/SM) <i>pncA</i> aa 119 (PZA) | S00034 | S00034 | Yes |
| 24 | CTAB | 14-7391 | SM, EMB, CAP, KM, AN | <i>rrs</i> (AN/SM) | <i>embC</i> aa 981 (EMB) <i>gid</i> aa 97 (SM) | S00241 | S00241 | Yes |
| 25 | CTAB | 14-7392 | SM, RIF, EMB, PZA, KM, RBT, FLQ | <i>gyrA</i> aa 94 (FLQ) <i>mcbA</i> aa 450 (RIF) <i>tpoC</i> aa 452 (RIF) <i>embB</i> aa 306 (EMB/INH) <i>embB</i> aa 497 (EMB/INH) | <i>gid</i> aa 92 (SM) <i>rrs</i> (AN/SM) <i>tpsl</i> aa 43 (SM) <i>pncA</i> TG-TGG (PZA) <i>eis</i> promoter (AN/KM) | S00034 | S00034 | Yes |
| 26 | CTAB | 14-7393 | INH, RIF, PZA, EMB 5.0 (2 nd line only), ETA, RBT, | <i>mcbA</i> aa 450 (RIF) <i>intergenic hyp-fabG1 aa</i> -15 (INH/ETA) <i>embB</i> aa 306 (EMB/INH) | | S00002 | S00002 | Yes |
| 27 | CTAB | 14-7395 | SM, INH, RIF, EMB, PZA, RBT | <i>mcbA</i> aa 450 (RIF) <i>tpsl</i> aa 43 (SM) <i>katG</i> aa 315 (INH) <i>pncA</i> aa 12 (PZA) <i>embB</i> aa 306 (EMB/INH) | | S00034 | S00034 | Yes |
| 28 | CTAB | 14-7396 | SM, INH, RIF, PZA, EMB (2 nd line only), RBT | <i>mcbA</i> aa 450 (RIF) <i>tpsl</i> aa 43 (SM) <i>katG</i> aa 315 (INH) <i>embB</i> aa 306 (EMB/INH) | <i>pncA</i> aa 151 (PZA) | S00034 | S00034 | Yes |



XDR Case (November 2014)



Can we develop one assay capable of generating the same results...and more?
Can we do it in <1 week?

XDR Case (November 2014)

Spoligotype: S00062 (777740777760771)

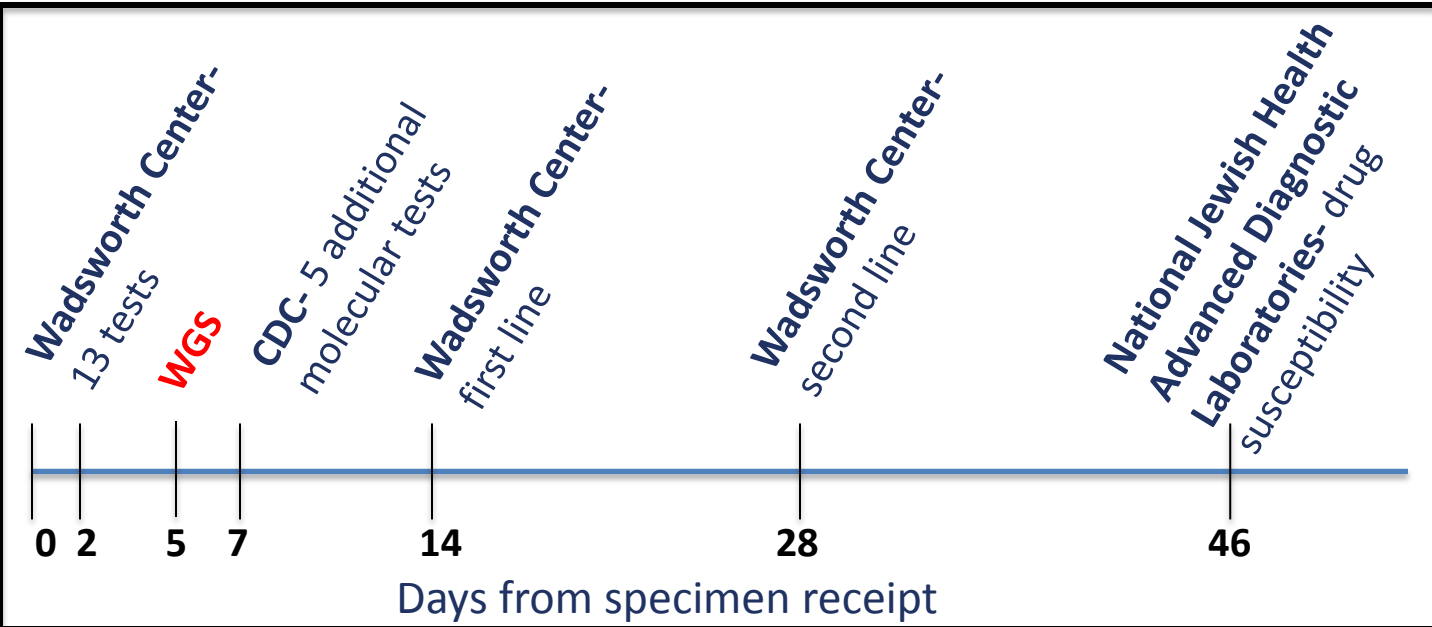
| Gene change | Genome position | Gene Known mutation? | Position | SNP | Res. associated | Codon AA |
|---------------------|-----------------|-----------------------|----------------|------------------|--------------------|----------------------------------|
| rrs | 1473246 | 1400 A -> G | | AMI/SM | | Putative |
| mutation* | | | | | | |
| gyrA | 7362 61 | G -> C | FLQ | 21 | Glu/Gln | No GAG -> CAG |
| gyrA | 7582 281 | A -> G | FLQ | 94 | Asp/Gly | HC mutation GAC -> GGC |
| gyrA | 7585 284 | G -> C | FLQ | 95 | Ser/Thr | No AGC -> ACC |
| gyrA | 9304 2003 | G -> A | FLQ | 668 | Gly/Asp | No GGC -> GAC |
| rpoB | 761155 | 1349 C -> T | | RIF | 450 Ser/Leu | HC mutation TCG |
| -> TTG | | | | | | |
| rpoC | 764948 | 1579 T -> G | RIF | 527 | Leu/Val | No TTG -> GTG |
| rpoC | 765150 | 1781 G -> A | RIF | 594 | Gly/Glu | No GGG -> GAG |
| tlyA | 1917972 | 33 A -> G | AMI | 11 | Leu/Leu | No Silent |
| CTA -> CTG | | | | | | |
| katG | 2154678 | 1434 G -> C | INH | 478 | Ala/Ala | No Silent |
| GCG -> GCC | | | | | | |
| katG | 2155168 | 944 G -> C | | INH | 315 Ser/Thr | HC mutation AGC |
| -> ACC | | | | | | |
| pncA | 2289049 | 193 T -> TA | PZA | Insertion | Frameshift | No |
| ahpC | 2726409 | 217 G -> C | INH | 73 | Asp/His | No GAC -> CAC |
| embC | 4242643 | 2781 C -> T | EMB | 927 | Arg/Arg | No Silent |
| CGC -> CGT | | | | | | |
| embC | 4242803 | 2941 G -> C | EMB | 981 | Val/Leu | No GTG -> CTG |
| embB | 4247730 | 1217 G -> C | EMB/INH | 406 | Gly/Ala | HC |
| mutation GGC -> GCC | | | | | | |
| embB | 4249408 | 2895 G -> A | EMB/INH | 965 | Pro/Pro | No |
| Silent | | CCG -> CCA | | | | |
| embB | 4249678 | 3165 C -> A | EMB/INH | 1055 | Arg/Arg | No |
| Silent | | CGC -> CGA | | | | |
| ethA | 4326718 | 756 CCGCG -> | CGCGCG | ETH | Insertion | Frameshift No |
| gid | 4407934 | 269 T -> G | SM | 90 | Leu/Arg | No CTC -> CGC |

Lineage Euro-American
M. tuberculosis X1 family

Drug Resistant phenotype:

- ✓ FLQ (OFL, LVX, MX)
- ✓ RIF
- ✓ INH
- ✓ SM
- ✓ EMB
- ✓ PZA
- ✓ RBT
- ✓ KAN
- ✓ AMI
- ✓ CAP (11%)

XDR Case (November 2014)



TB WGS Predicted Drug Resistant phenotype:

FLQ (OFL, LVX, MX)

RIF, INH, SM, EMB

PZA, RBT, KAN, AMI

CAP (11%)

Exciting Anecdotal Findings

- 1- MDR identification in ~ 2 weeks on not even known as TB case months before DST available.
- 2- Resolution/ early identification of mixed samples (NTM/TB)
- 3- Resolves inconclusive identifications MTB complex due to missing RD regions
- 4- Resolves issues where pyrosequencing or Sanger sequencing will FAIL due to deletion in target genes
- 5- Finds mutations outside of pyrosequencing region of target genes
- 6- Finds mutations in 2nd line drugs which would never have been found when 1st line drugs are susceptible
- 8- Clears up spoligotyping issues
- 9- Can identify heteroresistance
- 10- Predicts resistance when DST is invalid. WGS is even more valuable because the normal time to susceptibility results is pushed back. In some cases these specimens turn out to have contamination so that DST can never be completed and is canceled.



What does it really cost?

Existing Testing Methods

| | Cost per specimen (\$) | |
|---|------------------------|----------------------|
| | Reagents | Labor ^{a,b} |
| Real-time PCR-detect MTBC | 3.98 | 10.02 |
| Real-time PCR-detect MTBC members | 4.62 | 10.02 |
| Molecular DST (<i>rpoB</i> , <i>katG</i> , <i>inhA</i>) | 16.78 | 42.06 |
| Spoligotyping | 7.91 | 21.52 |
| Total costs | \$33.29 | \$83.62 |
| | \$116.91 | |

Whole Genome Sequencing*

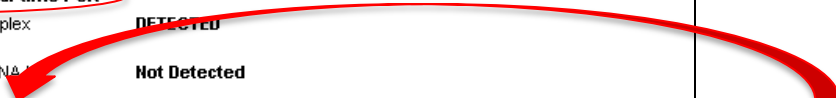
| | Cost per specimen (\$) | |
|----------------------------|------------------------|----------------------|
| | Reagents | Labor ^{a,b} |
| DNA Extraction | 3.49 | 11.02 |
| MiSeq® library preparation | 45.00 | 67.00 |
| MiSeq® Sequencing | 77.00 | 13.00 |
| Total costs | \$125.49 | \$91.02 |
| | \$216.51 | |



TB WGS Reports

| | |
|---|---|
| Concentrated Smear(Ziehl - Neelsen/1,000 X) (03/13/14): | Numerous (>9 acid-fast bacilli per field) |
| Direct Molecular Detection - Real-time PCR Mycobacterium tuberculosis complex DNA by real-time PCR: | DETECTED |
| Mycobacterium avium complex DNA by real-time PCR: | Not Detected |
| Molecular Identification - Real-time PCR Mycobacterium tuberculosis complex species DNA identified: | Mycobacterium tuberculosis |
| Culture (03/25/14): | acid-fast bacillus was isolated |
| Direct Molecular Drug Susceptibility Detection- Pyrosequencing Rifampin (rpoB): | Mutation present (Ser531Leu) suggests Rifampin resistance. Result must be confirmed by culture based susceptibility testing. |
| Isoniazid (katG): | Mutation absent. Culture must be performed for final susceptibility result. |
| Isoniazid (inhA): | Mutation absent. Culture must be performed for final susceptibility result. |
| Identification (03/26/14): | Mycobacterium tuberculosis was identified by culture and molecular analysis. |
| Susceptibility Testing for M. tuberculosis complex (MGIT) Streptomycin [1.0 ug/ml]: | Susceptible |
| Isoniazid [0.1 ug/ml]: | Susceptible |
| Rifampin [1.0 ug/ml]: | RESISTANT |
| Ethambutol [5.0 ug/ml]: | Susceptible |
| Pyrazinamide [100 ug/ml]: | Susceptible |

Whole genome sequencing



Molecular Drug Susceptibility Prediction- Whole Genome Sequencing

Rifampin

rpoB: Mutation present: Ser531Trp suggests resistance

Note: XX% of isolates in our in-house evaluation of XX clinical isolates with this mutation are resistant.

Isoniazid

katG: Mutation present: Ser315Thr suggests resistance

Note: XX% of isolates in our in-house evaluation of XX clinical isolates with this mutation are resistant.

inhA: Mutation present: C-15T suggests resistance

Note: XX% of isolates in our in-house evaluation of XX clinical isolates with this mutation are resistant.

Pyrazinamide

pncA: Mutation present: Trp68Arg suggests resistance

Ethambutol

embB: Mutation present: Met306Ile suggests resistance

Note: XX% of isolates in our in-house evaluation of XX clinical isolates with this mutation are resistant.

Streptomycin

rrs: Mutation present A>C at 513 suggests resistance

Note: XX% of isolates in our in-house evaluation of XX clinical isolates with this mutation are resistant.

Ofloxacin

gyrA No Mutation

gyrB No mutation

Kanamycin

eis: No mutation

rrs: No mutation

Ethionamid

inhA: Mutation: C-15T suggests resistance

Note: XX% of isolates in our in-house evaluation of XX clinical isolates with this mutation are resistant.

Disclaimer: A negative result (e.g. no mutation) does not rule out contributory mutations present elsewhere in the genome. **CULTURE MUST BE PERFORMED FOR FINAL SUSCEPTIBILITY RESULT.**

Whole Genome Sequencing of TB: A “One Stop Shop”

WGS

Single assay

Species identification

Genotyping (more accurate)

Drug resistance mutations

(more comprehensive)

COST

Estimated around \$100-\$200 per sample

TURNAROUND TIME

DNA preparation (1 days)

WGS result (4-5 days)

Reality for TB Cultures!


Next challenge TB specimens



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Future Directions WGS TB

- Finalize validation and implement WGS for TB culture testing
- Evaluate TAT, sample numbers
- Finalizing pipeline →  (server access?)
- Data interpretation/ notes
- LIMS importing
- NCBI
- Data Storage/ assessing data over time
- TB Primary specimens

Wadsworth Center
NEW YORK STATE DEPARTMENT OF HEALTH

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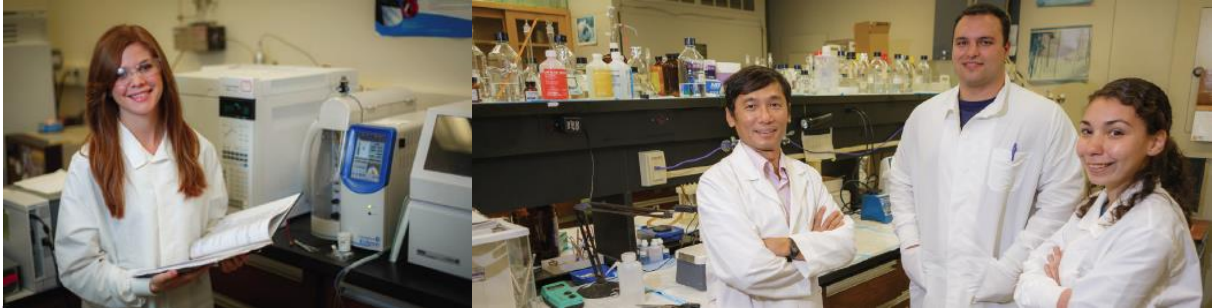


R03 NIH- Use of whole genome sequencing for
tuberculosis diagnostics



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Training in public health investigation, environmental assessment, Genetic and infectious disease testing, and novel technologies

Imagine a career:

- Protecting and improving the health of our communities
- Diagnosing diseases of public health importance
- Developing cutting edge testing methods



24 Month Full-time intensive program:

- 27 didactic credits
- 8 eight-week rotations through different scientific focus areas
- 1 Capstone research project

Tuition and Scholarships:

- No tuition fees
- Maximum of 4 scholarships of \$10,000 will be awarded each year based on academic merit.

*** Applications due: March 2016**



Questions?

