IMPLEMENTATION OF GHOST IN THE STATES FOR DETECTION OF HCV TRANSMISSION NETWORK

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Source: CDC, National Notifiable Diseases Surveillance System (NNDSS)†


During 2010–2015, HCV incidence increased by 294% with the highest rates among young persons who inject drugs (PWID)†

Reported number of acute hepatitis C cases - United States 2000 - 2015

Source: CDC, National Notifiable Diseases Surveillance System (NNDSS)
† https://www.cdc.gov/hepatitis/statistics/index.html
**FASTQ/FASTA**

Clinical samples Deep sequencing: E1/E2 (HVR1) amplicon

**GLOBAL HEALTH, OUTBREAK & SURVEILLANCE TECHNOLOGY (GHOST)**

Cyber-Molecular Detection of Hepatitis C Surveillance

- Clinical samples
- Deep sequencing: E1/E2 (HVR1) amplicon

**GHOST Portal**

- Uploaded NGS files are **automatically** analyzed and results are visualized in a form of transmission networks
- GHOST web-site contains bioinformatics tools for outbreak investigation and molecular surveillance

https://webappx.cdc.gov/GHOST/
GHOST-identified HCV Transmission Network
Indiana HIV outbreak

<table>
<thead>
<tr>
<th>Groups</th>
<th>Clusters</th>
<th>Cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Related cases as clusters</td>
<td>23</td>
<td>198</td>
<td>70.46</td>
</tr>
<tr>
<td>Unrelated</td>
<td>0</td>
<td>83</td>
<td>29.54</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>281</td>
<td>100</td>
</tr>
</tbody>
</table>

Node = 1 patient
Links = Sharing of variants among patients (>96.3% identity)

GHOST Implementation in the States

<table>
<thead>
<tr>
<th></th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
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<tbody>
<tr>
<td>US</td>
<td>case rate</td>
<td>0.3</td>
<td>0.4</td>
<td>0.6</td>
<td>0.7</td>
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<tr>
<td></td>
<td>cases</td>
<td>850</td>
<td>1,229</td>
<td>1,778</td>
<td>2,138</td>
</tr>
<tr>
<td>TN</td>
<td>case rate</td>
<td>0.7</td>
<td>1.3</td>
<td>2.0</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>cases</td>
<td>46</td>
<td>83</td>
<td>129</td>
<td>98</td>
</tr>
<tr>
<td></td>
<td>rank</td>
<td>4th</td>
<td>4th</td>
<td>4th</td>
<td>6th</td>
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</tbody>
</table>

GHOST Piloting in Tennessee (2016-17)

* 4,753 persons tested for HCV

GHOST Hands-on Training and Workshops

13 participants from 11 states
AK, CA, KY, MI, GA, NY, MD, NH, TN and NM

† Upcoming GHOST Workshop, Non-3rd, 2017

TN - GHOST Pilot activities (since June 2016)

QC - Proficiency Testing

<table>
<thead>
<tr>
<th>Work plan</th>
<th>Sample 1</th>
<th>Sample 2</th>
<th>Sample 3</th>
<th>Sample 4</th>
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<tbody>
<tr>
<td></td>
<td>Unrelated 1a case</td>
<td>1b Outbreak source</td>
<td>1a incident case</td>
<td>Negative case</td>
</tr>
<tr>
<td>Sample 5</td>
<td>1b Outbreak source</td>
<td>1b Incident case-1</td>
<td>1b Incident case-2</td>
<td>Unrelated 1b case</td>
</tr>
</tbody>
</table>

CDC run

GHOST Results

TN run

Sample 1: S6_1,001
Sample 2: S6_1,001
Sample 3: S6_1,001
Sample 4: S6_1,001
Sample 5: S6_1,001
Sample 6: S6_1,001
Sample 7: S6_1,001
Sample 8: S6_1,001
TN GHOST Pilot Testing: Cross Validation of specimens

- 4,753 persons tested for HCV
- 8.4% Ab positive; 73.2% RNA positive

(n=291 samples)

- Independent runs made by TN and uploaded on GHOST
- 10% of random samples tested at CDC

<table>
<thead>
<tr>
<th>CDC runs</th>
<th>TN runs</th>
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<tbody>
<tr>
<td>TN40_S10_Smp0_L001</td>
<td>224_S25_Smp0_L001</td>
</tr>
<tr>
<td>TN11_S11_Smp0_L001</td>
<td>226_S26_Smp0_L001</td>
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<td>TN13_S13_Smp0_L001</td>
<td>274_S28_Smp0_L001</td>
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<td>400_S25_Smp0_L001</td>
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<td>407_S27_Smp0_L001</td>
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<td>424_S30_Smp0_L001</td>
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<td>447_S31_Smp0_L001</td>
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<td>TN25_S32_Smp0_L001</td>
<td>454_S32_Smp0_L001</td>
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<td>TN38_S31_Smp0_L001</td>
<td>510_S31_Smp0_L001</td>
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</tbody>
</table>

Tennessee HCV Phylogenetic Analysis of 9 cases
(E1-HVR1 region, 264 bp in length, only Freq > 3 unique NGS sequences are shown)

Case 1
Case 2
Case 3
Case 4
Case 5
Case 6
Case 7
Case 8
Transmission cluster 1
Transmission cluster 2

Single Strain
Multiple Strains of same genotype
Multiple sub-genotype / genotype

TN GHOST Pilot Testing: Complexity of specimens
TN Pilot Completion
GHOST-identified transmission networks

TN GHOST Pilot:
291 GHOST tested cases

Transmission clusters:
8 (21 cases)

Mixed infection
(Same/different genotypes):
7 cases

Linkage by transmission
(>96.3% seq. identity)

Unrelated cases

Ongoing TN HCV surveillance

291 Pilot cases +
22 HIV Outbreak investigation cases

3 additional clusters
(total of 11 clusters)
Indicators of high risk population

Increasing transmission threshold from 3.7% to 3.8%
additional 4 clusters

GHOST network based approach for ‘Linkage to Care’ and to improve treatment efficiency

Treatment Strategy Using Network-Based Approach

From: M. Hellard et al. Hepatology 2014 Dec;60(6):1861-70
GHOST Trained sites (2016 & 2017)

22 US states, 2 global, 35 trainees

Phase 1 (2016-17)
- GHOST Pilot States
  - TN
  - NY
  - NH
  - MI
  - AK

Phase 2 (2017-18)
- GHOST Implementation
  - IA
  - IN
  - CO

NIDA - Rural Communities Affected by Opioid Injection Drug Epidemics

GHOST Center

Implications of GHOST

- Capacity building in states & local public health departments
- Reduces turn around time - sampling, processing, cluster detection, triage and executing interventions
- Streamlines targeted use of resources to continue field investigations
- Linkage analysis is done on a continuous scale aiming towards comprehensive HCV surveillance
- Enables network-based guided treatment strategy
Acknowledgements

CDC

State partners

APHL

CDC-DVH GHOST Team

Federal partners

Global partners

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov  Web: http://www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.