National pilot survey for Hepatitis C (HCV) whole genome sequencing for future quality assurance programs (QAPs) demonstrates readiness for routine diagnostic integration

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Background:

The elimination of HCV infection as a public health threat requires enhanced testing and surveillance strategies. Near real-time genomic surveillance of HCV allows for better transmission cluster identification to guide public health interventions. Whole genome sequencing (WGS) of HCV is not currently performed routinely in Australian diagnostic laboratories, with typing currently based on partial-genome or non-sequence-based methods.

The MRFF-funded H2Seq initiative developed a cost-effective and readily deployable tiling amplicon method for integration of HCV WGS into diagnostic workflows. We conducted a national feasibility survey to assess laboratory capacity to adopt this method and generate complete HCV genomes, and to inform design of future large-scale QAPs.

Methods:

Five Australian diagnostic laboratories received a four-sample panel including one negative control, representing HCV genotypes 1b, 1a, 3a at concentrations of 9.7 – 19.5 x 10^6 IU/mL. Participants were invited to use their existing in-house sequencing methods or the provided H2Seq tiling method to produce genomic data and genotype designations. This iterative survey was non-evaluative, with participants receiving anonymously benchmarked results and performance feedback.

Results:

All participants generated sufficient genomic coverage for downstream cluster analysis (defined as ≥70% E1E2 with at least 3 kb of any other genomic region) and correctly identified the genotypes of positive specimens when using the H2Seq method or in-house probe-based methods. Genomic coverage ranged from 90.08 – 99.07%, 89.33 – 100%, and 81.75 – 100% for samples 1 (G1b), 2 (G3a) and 3

(G1a), respectively. There were no reports of difficulties implementing the H2Seq laboratory methodologies.

Conclusions

The first national feasibility survey for HCV WGS demonstrated the capacity of Australian laboratories to implement H2Seq WGS methods effectively . This survey established a foundation for continuous larger-scale evaluative external QAP to expand HCV WGS on existing and future analytes (for example, dried blood spot samples) to implement national HCV elimination.

Disclosure of Interest Statement

The authors declare no conflicts of interest related to this work.