Custom Gene Fusion Assays for the Rapid Diagnosis of Pediatric Cancers in Low-Resourced Settings

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PURPOSE

Risk stratification and molecular targeting have been key to increasing cure rates for pediatric cancers in high-income countries. Precise diagnosis and successful treatment of pediatric cancer in low-resource settings are often hindered by insufficient pathology infrastructure, including lack of laboratory platforms for molecular analysis. Given the high frequency of gene fusions in pediatric cancers, identifying such fusions would greatly aid cost-effective pediatric cancer diagnosis, risk stratification, and precision medicine in low-resource settings.

METHODS

To allow for implementation of gene fusion detection at Global HOPE sites in Sub-Saharan Africa (SSA), methodologies were reviewed to consider minimal technical expertise required, the ability to utilize samples with sub-optimal RNA quality, and rapid turn-around-time. Literature review, clinical laboratory results, public databases, and large-scale genomic studies were used to obtain exact breakpoint sequence information for gene fusions associated with pediatric and adolescent cancers (Figure 1).

RESULTS

Two custom pediatric gene fusions panels were designed using the NanoString nCounter Elements technology (Figures 2 and 3). The hematologic malignancy panel was designed to detect 439 breakpoints for 223 non-IGH/TCR fusions reported in ALL, AML, lymphomas, and histiocytosis. The solid tumor panel was designed to detect 436 breakpoints for 204 fusions associated with pediatric sarcomas, brain tumors, and renal malignancies. Each panel is being tested using 96 samples with known fusion status to determine specificity, sensitivity, precision, and ease of workflow (Figure 4).

CONCLUSION

The design, testing, and implementation of a rapid assay to detect gene fusions with diagnostic, prognostic, and therapeutic impact would be transformational in the care of pediatric cancer patients in low-resource settings. The custom designed panels will allow for large-scale fusion detection in 2-3 days with only 15-30 minutes of hands-on technician time after RNA isolation. Additional steps are now needed to follow-up borderline samples from the validation set and solidify the cutoffs of positivity for each probe set. The platform will then be implemented at the Global HOPE site Uganda to enable faster and more specific diagnostics.

REFERENCES