Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

(NM_000090.4(COL3A1):c.944G>C, p.Gly315Ala; GRCh37). This variant has been previously reported in an individual with a presentation consistent with vEDS and is classified in a public variant archive as both pathogenic and likely pathogenic. Following outreach regarding his high-risk result, a genetic counseling appointment was declined.

This same individual then ordered a second CIGT test which also included testing of the COL3A1 gene via NGS at a separate CLIA-certified laboratory. Outreach to determine his expectation for the second CIGT test resulted in a genetic counseling appointment. The patient reported having ordered a second CIGT because the wait time to confirm his first CIGT result in a traditional genetics clinic was too great. No history of vEDS was known in his family. One first-degree relative died in their sleep at age 52. A second first-degree relative had a cardiac event at age 40 and died of a stroke at age 62.

The second CIGT returned the same likely-pathogenic variant in *COL3A1* using the same reference sequence. Following the confirmation of the variant by the second test, the patient followed up with a vEDS specialist and cascade testing of his family members was initiated. Three additional first-degree relatives have been identified to have the likely pathogenic variant and have initiated follow-up for this result.

Conclusion: Consumer-initiated genetic testing, performed by a CLIA-certified laboratory and with oversight by board-certified genetic counselors, provides alternative, and possibly more timely, access to clinical-grade genetic testing. CIGT marketed to the general adult population has the ability to identify disease-causing variants in individuals whose family histories may not be known or which lack features striking for hereditary disease. The downstream effect of CIGT, in the form of readily accessible cascade testing, is largely impactful. In addition, by identifying disease-causing variants in individuals who seek testing due to health curiosity, it aids in defining the phenotypic spectrum. Additional work should be done to determine outreach practices which increase uptake of CIGT genetic counseling services, further elevating the benefit of this testing modality.

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eP487

Universal newborn screening of congenital cytomegalovirus using dried blood spots and qPCR

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Introduction: Cytomegalovirus is prevalent and usually benign in healthy populations. Permanent health problems can arise when transmission occurs pre-natally, resulting in congenital cytomegalovirus (cCMV). Screening for cCMV is currently not universal but reactionary to symptoms. Because of this, molecular methods using saliva, urine, or blood freshly collected are inadequate as symptomatic patients may no longer be infected or become infected postnatally. Newborn Screening (NBS) currently uses dried blood spot (DBS) cards that are collected neonatally for other screening. This makes DBS a prime sample input for universal screening of cCMV, as well as retrospective testing using archived samples.

Historically, issues with DBS for NBS of cCMV were due to sensitivity, scalability, and input needs. To address these concerns, we have developed a relatively sensitive, high-throughput compatible, simple workflow, sample extraction to qPCR assay kit using only one or two 3.2 mm DBS punches.

Methods: Two manual DBS extraction methods were tested and compared, the simplified Eonis alkaline based extraction and Thermal Shock. Both methods used 2x 3.2 mm DBS punches and a 65 µL elution volume for compatible comparison. In addition, three automated DBS extraction methods were evaluated: standard Eonis alkaline extraction with 1x 3.2 mm DBS punch and 80 µL elution, and simplified Eonis alkaline extraction with either 1x 3.2 mm DBS punch and 50 µL elution or 2x 3.2 mm DBS punches and 65 µL elution. Each scheme's eluents were used as direct input into a 15 µL PCR reaction using the Eonis cCMV Kit reagents. The assay quantifies a CMV gene marker in FAM, and a human housekeeping gene, *RPP30*, in Cy5, as well as a background baseline reading in ROX. This design is compatible with all commercially available real-time PCR instruments without the need of additional instrument color compensation. For each test, the assay uses DBS controls that monitor the overall workflow from sample extraction to real-time PCR detection. Due to the lack of access to cCMV confirmed newborn DBS, contrived DBS samples were used for development.

Results: The simplified Eonis extraction takes around 30 minutes manually for 96-wells, with only two buffer exchanges and two incubation temperatures. The Thermal Shock method does not involve a DBS wash step and thus, when used in the assay as a 10 µL input for the qPCR reaction, no amplification of the targets occurred due to inhibition whereas the Eonis-based extraction showed an increase in detection with the increased sample input. Automation tests support use of the Eonis cCMV kit in a high-throughput environment. The limit of detection (LoD) of the qPCR assay is 3.3 international units (IU) per reaction. The LoD of the extraction to qPCR workflow is 10 IU/µL based on contrived DBS.

Conclusion: The Eonis cCMV kit can be used for different throughput labs due to its scalable extraction protocol and 96-well and 384-well compatibility for qPCR. Due to hospitals and testing sites already collecting and testing DBS, it is the easiest sample type to implement. Having a high-throughput compatible and sensitive DBS based assay is instrumental to adding cCMV to NBS as well as retrospective testing of high-risk patients. This makes the Eonis cCMV kit a steppingstone to universal screening of cCMV though access to relevant/known clinical samples is needed to further vet robustness.

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eP488

Patient-centric adaptations for pheNIX clinical trial evaluating HMI-102 gene therapy in adults with PKU in the era of COVID-19

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Introduction: In June 2019, Homology Medicines Inc. initiated pheNIX, a Phase 1/2 open-label, randomized, concurrently controlled, dose-escalation trial evaluating the safety and efficacy of HMI-102, a one-time gene therapy development candidate for the treatment of adults with PKU due to PAH deficiency. Less than one year later, the World Health Organization (WHO) formally declared COVID-19 a pandemic, which initiated the modification of public health

care in the United States on a state-by-state basis. Many major healthcare centers across the United States began the conversion to COVID-19 testing and treatment sites were no longer allowed in-person clinic or research visits for non-life-threatening disorders. As a result, many clinical trials, including pheNIX, required logistical modifications to avoid trial hiatus or protocol deviations.

Methods: States of emergency due to COVID-19 were declared in multiple cities, including those where pheNIX clinical trial sites were located, creating an immediate need for study-related adaptations while maintaining protocol procedures. As study participants were administered a single administration of HMI-102, the clinical team at Homology engaged with pheNIX trial sites to quickly identify any unmet needs related to data collection and patient monitoring with the goal of developing mitigation strategies. These strategies included transitioning to a home health visit model to minimize study interruption and/or protocol deviations, all while maintaining patient safety as a top priority.

Results: Protocol-compliant modifications were identified and implemented, such as home health monitoring visits and lab collections. These changes required contracting and budgeting with phlebotomy and home health providers, identifying licensed professionals residing within the study patient's home state, creating educational materials and training these professionals on the study protocol. Additionally, study participants and their families were notified and trained to allow for proper coordination of all new home health visits and assessments. These modifications were initiated and in place within 20 days of initial discussions for the first home phlebotomy visit and by day 36 the first home health visit. Six patients have completed the 52-week dose-escalation portion of the study, and the Phase 2 dose expansion is ongoing. The majority of lab samples processed were collected in the patient's home, and other data inputs including vital signs, patient weight, patient questionnaires and corticosteroid compliance logs were and continue to be obtained in the patients' home environments.

Conclusion: The goal of continuity for the pheNIX gene therapy trial during the ongoing COVID-19 pandemic was accomplished with a rapid response by the clinical team in identifying the potential effect on study participants, clinical trial sites and protocol compliance. Strategies were developed to mitigate the impact and, as a result, blood draws and home health visits were implemented within 20 and 36 days, respectively, of initial discussions, allowing for continued trial enrollment and post-dose monitoring for safety and efficacy, all while reducing the number of in-person study site visits.

This rapid shift to home health visits and lab assessments during the pandemic also led to a significant reduction in overall patient burden, primarily due to less travel time to the clinical study site for all routine visits. Homology is leveraging these important learnings with plans to continue administration of health visits and study assessments in patient's homes throughout the remainder of the pheNIX trial to foster a patient-centric approach and to optimize compliance. In addition, this well-received transition to home-based evaluations provides a patient-focused model that can be adopted in other clinical trials, particularly those that include patients with rare diseases who may be unable to commit to frequent visits to trial sites.

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eP489

Exploring engagement and uptake of a comprehensive family history-based cancer risk assessment tool

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Introduction: It is challenging to identify individuals at risk of a hereditary cancer syndrome as it requires assessment of both personal and family health history, the latter of which may not be routinely collected and/or updated by healthcare providers. A possible solution is to use a patient-facing computer platform that electronically collects family health history (FHH) information for hereditary cancer syndromes and other health conditions. This could improve genomic healthcare by identifying at-risk individuals in a health system. As our capacity to develop electronic tools to engage patients and identify those in need of genetic services increases, it is important to assess whether patients will choose to participate.

Engagement in health behaviors can be studied using the framework of the Precaution Adoption Process Model (PAPM). The PAPM describes the process of decision-making in which individuals can be placed in stages of readiness to adopt a new behavior. This model can be used to stage those who are engaged in the process of making health decisions, unengaged in that they are not interested in being part of the decision-making process, or unaware of the decision that needs to be made. Engagement in healthcare may also be conceptualized as the consequence of cognitive, internal engagement with a health topic, sufficient to motivate action. We report on the early phases of the NCI funded Family History and Cancer Risk Study (FOREST) which was initiated to improve identification of high-risk patients and access to hereditary cancer services for the general adult patient population at Vanderbilt University Medical Center (VUMC). We aimed to assess participation in the stages from recruitment to completion of the computerized FHH tool and describe participant characteristics that could influence their level of engagement in the process of learning more about their risks for cancer.

Methods: VUMC patients who previously agreed to be contacted about research opportunities were sent an invitation through their health portal to participate in FOREST. The message directed them to a pre-screen survey through REDCap, a HIPAA secure online survey tool, to determine eligibility and willingness to participate. Eligible patients then completed eConsent and a baseline survey prior to completing the FHH questionnaire. FHH was collected using MeTree, a platform developed by Duke University. Once this survey was complete, participants were then provided the link to the FHH platform. Upon completion, the platform created a personalized patient report with hereditary cancer risks and included evidence-based clinical decision support for the healthcare provider (HCP). IRB approval was granted for this project.

Guided by the framework of the PAPM, we asked participants about their stage of readiness to learn more about their risk for cancer on the pre-screen survey. We included an assessment of internal engagement on the baseline survey by asking participants how often they think about their risk to develop cancer. Also included on the baseline survey were questions that assessed several variables hypothesized to predict engagement level.

To analyze the data, we determined the number of individuals who completed each stage of the study procedure from recruitment to the completion of the FHH questionnaire. We then calculated the frequency and mean for variables of interest on the pre-screen and baseline surveys.

Results: Between October 2021 and November 2021, a total of 1650 patients received an electronic invitation to join the study. Approximately 16% (256) expressed interest in participating. Among these individuals, 3.9% (10) completed the pre-screen survey but were ineligible due to having a serious condition that requires hospice or long-term care or having already been seen at the Vanderbilt Hereditary Cancer Clinic in the past, 5.5% (14) completed the pre-screen survey but did not sign the consent form, and 36.3% (93) completed the pre-screen survey and the consent form to participate in the study. Of the consented participants, 98.9% (92) completed the baseline survey and 28.0% (26) completed the FHH questionnaire.

Among consented participants, 2.2% (2) indicated that they don't know how to learn about their risk for cancer and 97.8% (91) indicated they are interested in learning more about their risk for cancer. When asked how often they think about their risk of developing cancer 9.8% (9) indicated never, 33.7% (31) indicated once a year, 45.7% (42) indicated once a month, 7.6% (7) indicated once a week, and 3.3% (3) indicated every day. Participants were asked to report their level of health and 0% (0) reported poor, 10.9% (10) reported fair, 41.3% (38) reported good, 38.0% (35) reported very good, and 9.8% (9) reported excellent. On a Likert