Design and Implementation of a Comprehensive Genomic Profiling Protocol for Rare and Refractory Pediatric Cancer and Hematologic Disease

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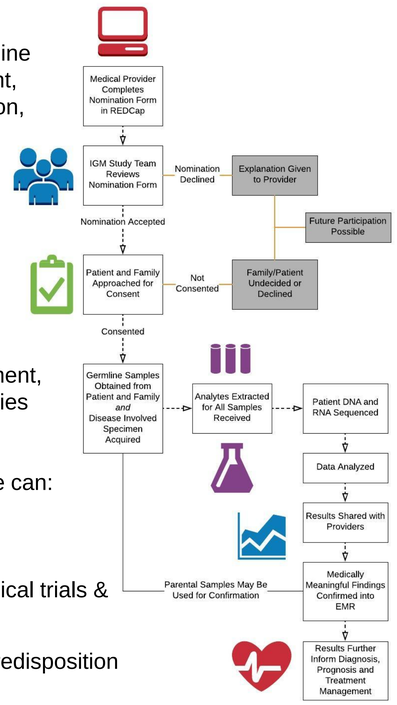
Introduction

The Institute for Genomic Medicine developed a translational protocol to evaluate the genomic landscape of cancer and hematologic disease in a focused, patient-specific manner.

Central to the protocol is a multifunctional REDCap database designed to streamline workflows including enrollment, consenting, specimen selection, assay methodology, and documentation of results/ patient metadata. Patient enrollment begins following completion of a provider survey by a nominating clinician. Once reviewed by the study team, an eligible patient/family is approached for consent. Following enrollment, genomic profiling methodologies are employed.



Studies of precision medicine can:

- Refine diagnosis
- Inform prognosis
- Determine eligibility for clinical trials & targeted therapeutics
- Detect germline disease predisposition

IGM REDCap™ Project

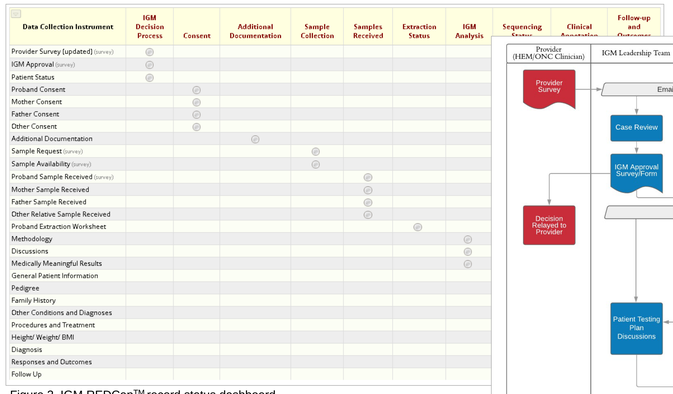


Figure 2. IGM REDCap™ record status dashboard

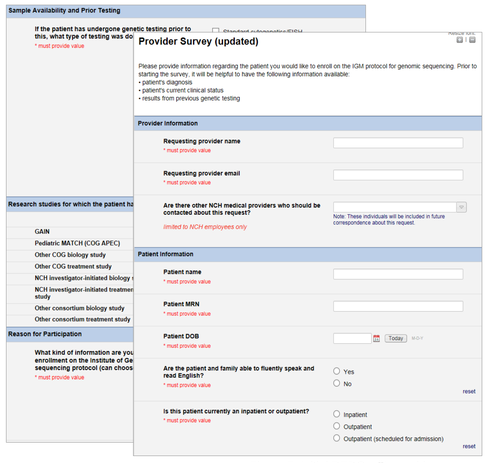


Figure 5. Initial REDCap™ provider survey

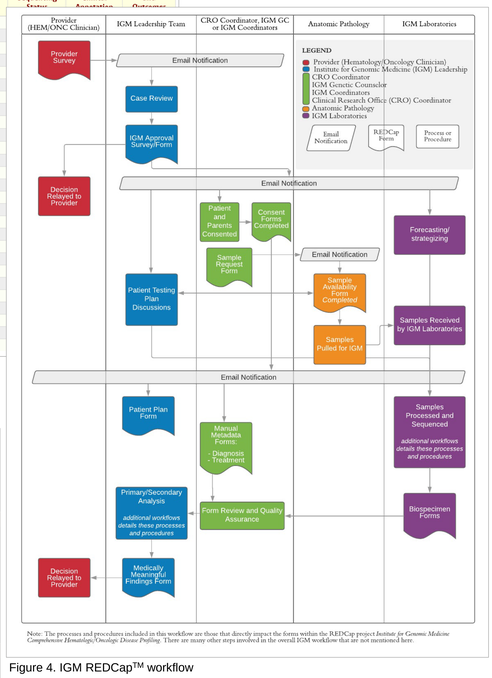
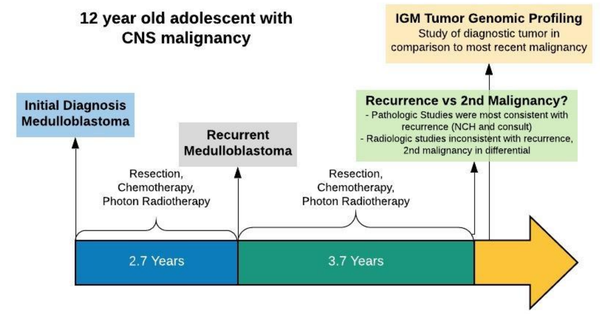


Figure 4. IGM REDCap™ workflow

REDCap is being used to manage protocol workflows and data both internal to IGM and by other key project collaborators within NCH (e.g. heme/onc and pathology). It is currently the central hub for data collection and enables communication about patient status within the workflow.

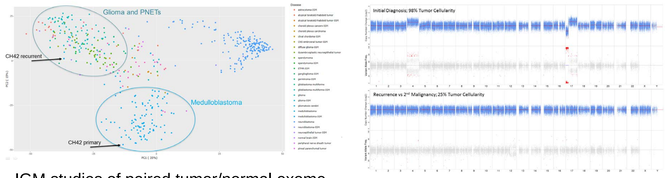
Patient Case Study

PRESENTATION



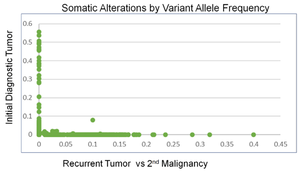
ASSAY AND RESULTS

Enhanced Paired Tumor/Normal Sequencing; RNASeq



IGM studies of paired tumor/normal exome, and expression analyses derived from RNASeq support a 2nd malignancy rather than a recurrence of medulloblastoma.

Mutational and expression profile are most consistent with glioma/glioblastoma on the basis of RAS-MAPK pathway variation (*PTPN11, PIK3CA*) and principal component analysis.

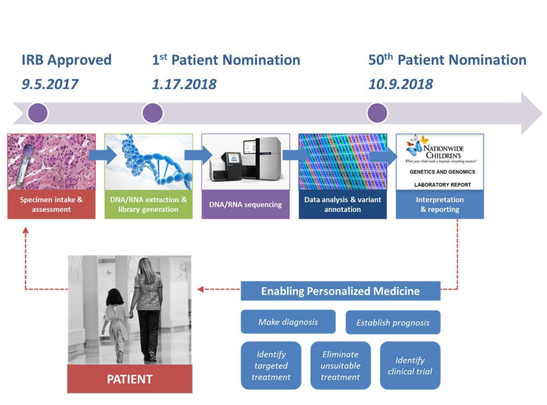


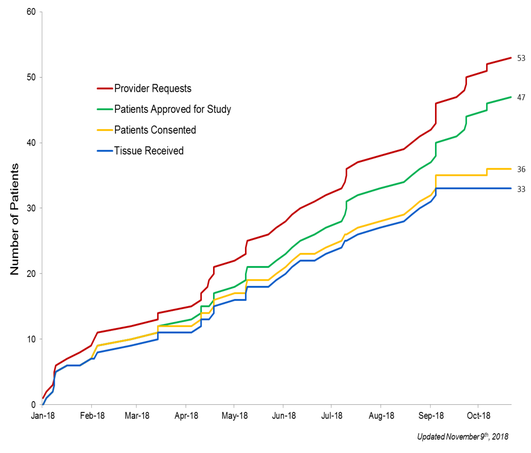
ACTIONS AND OUTCOMES

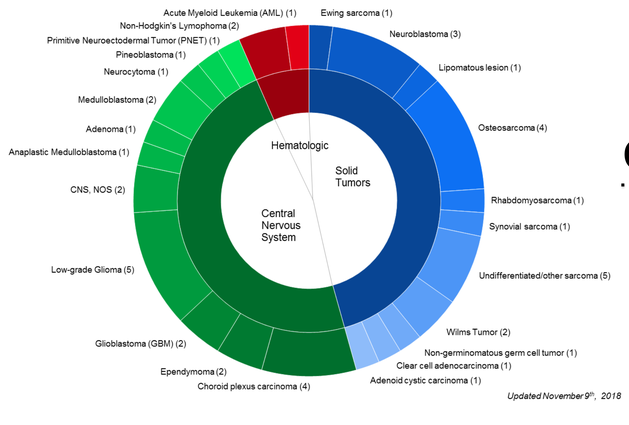
2nd malignancy is a rare event in medulloblastoma, however this phenomenon is described in a pediatric population receiving adjuvant chemotherapy and radiotherapy, most often as malignant glioma (Neuro-Oncology 15(1):97–103, 2013).

In this patient, IGM tumor profiling refined diagnosis, ultimately allowing for tailored treatment and improved management.

Current Status







Overall Study Results

In total, 53 patients have been nominated for enrollment onto the protocol with 47 (87%) deemed appropriate for inclusion. To date, 36 patients have consented, and of those IGM has sequenced 33 patient cases. Resulting analyses have allowed for refinement of diagnosis, improved understanding of prognosis, implementation of targeted therapies, as well as counseling and follow-up in these children and families.