Enhancing Tumor Profiling Strategies with Germline Cancer Pharmacogenetics

Need

The effectiveness and toxicity of several medications commonly prescribed to cancer patients vary with the patient's genetic makeup. Testing for well-known germline genetic variations can enable more effective treatments and better outcomes. Targeted panels of these variations can be tested with either PCR or sequencing technology. Translational Software's cloud-based reporting platform allows laboratories to process the results of these tests and provide reporting for clinicians that provides actionable guidance toward improving medication decisions.

Offering

Translational Software is developing tools for analysis and reporting of germline pharmacogenetic biomarkers for cancer treatments and related comorbidities. These tools will enrich tumor-profiling analytical reports with knowledge related to pharmacogenes known to affect the pharmacokinetics or pharmacodynamics of anticancer therapies as well as medications commonly used for comorbid conditions experienced by cancer patients. The combination of these two sources of information will enable oncologists and other care providers to select and optimize the course of therapy guided by knowledge of both the somatic (tumor) and the patient's (germline) unique genetic signatures.

Audience

Prospective identification of germline biomarkers is relevant to any oncologist using conventional cytotoxic chemotherapies as well as targeted therapies. The clinically significant drug-gene associations presented on the report will help manage dose-limiting toxicities of anticancer medications but will also help the oncologist and other members of the cancer care team in selecting the right treatment course with commonly used drugs such as antiemetics, anticoagulants, antidepressants and analgesics.

Benefits

- Provides a single resource for multiple medication hazards
- Notifies the physician when a medication type or dosage is inconsistent with a patient's genetic profile
- Allows the laboratory to maximize benefits derived from its NGS platform

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Relevant Drug-Gene Associations

The following table shows how relevant germline pharmacogenetic associations can inform therapeutic decision making during cancer care.

Drug	Pharmacogene	Conditions	Association
Cyclophosphamide	CYP2B6	Cancer	Nephrotoxicity risk
Paclitaxel	CYP2C8	Cancer	Peripheral neuropathy risk
Phenytoin	CYP2C9	Seizures	Neurotoxicity risk
Warfarin	CYP2C9/VKORC1	Coagulation	Hemorrhage and thrombosis risks
Tricyclics, SSRIs	CYP2C19	Depression	Loss of efficacy, toxicity risk
Opioids	CYP2D6	Pain	Loss of Efficacy
Ondansetron	CYP2D6	Nausea/Vomiting	Loss of Efficacy
Tamoxifen	CYP2D6	Cancer	Disease recurrence
SSRIs	CYP2D6	Depression	Loss of efficacy, toxicity risk
Gefitinib	CYP2D6	Cancer	Skin and liver toxicity risks
Vincristine	CYP3A4/CYP3A5	Cancer	Neurotoxicity risk
Fluorouracil, Capecitabine	DPYD	Cancer	Neutropenia, diarrhea, Stomatitis risks
Rasburicase	G6PD	Hyperuricemia	Hemolysis risk
Methotrexate	MTHFR	Cancer	Mucositis, thrombocytopenia, and hepatotoxicity risks
Methotrexate	SLCO1B1	Cancer	
Mercaptopurine, Azathioprine, Thioguanine	TPMT	Cancer	Myelosuppression risks
Cisplatin	TPMT	Cancer	Ototoxicity risk
Irinotecan	UGT1A1	Cancer	Neutropenia, hyperbilirubinemia risks

CYP2B6: Cytochrome P450 2B6; CYP2C8: Cytochrome P450 2C8; CYP2C9: Cytochrome P450 2C9; CYP2D6: Cytochrome P450 2D6; CYP3A4: Cytochrome P450 3A4; CYP3A5: Cytochrome P450 3A5; DPYD: Dihydropyrimidine dehydrogenase; G6PD: Glucose-6-Phosphate dehydrogenase; MTHFR: methylenetetrahydrofolate reductase; SLCO1B1: Solute Carrier Organic Anion Transporter 1B1; TPMT: Thiopurine S-methyltransferase; UGT1A1: UDP glucuronosyltransferase 1A1. VKORC1: Vitamin K epoxide reductase complex subunit 1.