The Cellworks Ventura™ Report Decoded

Cellworks

PERSONALIZED THERAPY. TRANSPARENT DESIGN

Ventura™ Assessment sections

1. Personalized Therapy Recommendation(s)

This section provides the combination(s), from FDA-approved drugs that are predicted to provide best clinical response for an individual patient. As a first step to the process of identifying these combinations, drugs in the Cellworks Digital Drug Library are simulated individually on the patient's profile. The drugs that are most efficacious as monotherapy are then combinatorially simulated. The three combinations that are most efficacious are listed in this table.

2. Patient Disease Characteristics: Key Biomarker(s)

Using biosimulation modeling, Cellworks determines key biomarkers in the patient's genomic profile. They are points of convergence of the pathways impacted by the mutations in the patient's profile. These key biomarkers are tumor promoter/suppressor genes that the drug needs to impact in order for the patient to respond to treatment.

3. Biomarker Impact

This table shows the impact that the therapies of interest have on the 'Key Biomarkers' identified for the patient profile. The check symbol ('✓') implies that the therapy is predicted to be successful in impacting the biomarker. Not all therapies impact key biomarkers equally. Please see the therapy rationale in Section 6 for a more thorough explanation.

4. Predicted Drug Sensitivity or Resistance (Histogram)

Drug Efficacy Score: This score includes Simulation Score and Biological Evidence Score for single and combination drugs. Simulation Score is the effect of the drug on the identified disease-specific biomarker(s) and phenotype(s). Biological Evidence Score is based on an algorithm that accounts for genes responsible for drug response and prioritization of indication-specific drug class.

4.1 Single Drug Efficacy Prediction

This histogram shows single drug efficacy for the patient's profile. The numbers on the Y-axis reflect the percentage of effectiveness of the drug on the patient's disease. Drugs are arranged in descending order - from the most efficacious drug, that the patient profile is predicted to be sensitive to, to the least efficacious drug, that the patient profile is predicted to be resistant to.

4.2 Drug Combination Efficacy Prediction

This histogram shows drug combinations to which the patient is predicted to respond, in order of efficacy. The single drugs found to show positive impact on the patient profile, are combinatorially simulated on the patient profile to provide this output. A maximum of 20 drug combinations will be included in this section. The numbers on the Y-axis reflect the percentage of effectiveness of the drug combinations on the patient's disease.

5. Summary of Patient Genomic Profile

This section provides an aggregated overview of the patient genomics used for therapy assessment. It shows the type of input received from the next generation sequencing data (NGS) with the number of genetic mutations, copy

number variations (CNVs) and any epigenetic data that is reported.

5.1 Detailed Information of Genomic Aberration(s) Modeled

This section lists all the mutations, CNVs and epigenetic data which are modeled via the Cellworks biosimulation for the patient. This information forms the patient-specific input on which a Cellworks assessment is based.

6. Therapy Rationales

A therapy rationale illustrates the role of key mutations in causing sensitivity or resistance to drugs. A drug will have a therapy rationale for every mutation that contributes significantly to its sensitivity or resistance.

The first illustration in the rationale defines the mechanism of action of the drug.

The second illustration articulates the signalling or metabolic pathway by which the mutation of interest contributes to drug sensitivity or resistance including the point of intersection (if any) with the drug's mechanism of action.

The description is accompanied by relevant PMIDs that were used to determine the interaction.

7. Genomic Aberration to Key Biomarker Pathway(s)

This section illustrates molecular biochemical pathways from a genomic aberration in the patient profile to critical biomarkers identified by Cellworks' biosimulation. The description is accompanied by relevant PMIDs that were used to determine the interaction.

Regarding Toxicity

The current assessment assumes that the drugs are faithfully delivered to the site of action. Cellworks considers all molecular interactions once delivered to the site of action (Pharmacodynamics of the drug compound). Cellworks does not account for absorption, distribution, metabolism & excretion (ADME) properties of the drug that determine how the drug is delivered to the site of action. Any toxicity in the delivery process, or pharmacokinetics, is not considered.