CSIR Technology Platform for Cancer Precision Medicine

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Abstract

The main issue with current Ovarian Cancer (OvCa), Chronic lymphocytic leukemia (CLL) and Multiple Myeloma (MM) treatment is the eventual resistance to standard chemotherapy which ultimately leads to patient relapse. Overcoming platinum resistance is an unmet medical need in OvCa, CLL, MM patients which we plan to address with our technology pipeline. We propose a game changing, disruptive technology pipeline with which we will identify drugs and drug combinations for relapsed CLL, MM and OvCa patients who exhausted all other treatment options. Our technology pipeline includes strategies where we combine new microfluidic-based technology with our established high-throughput drug screening platform. Using our pipeline, we aim to identify drug combinations that can overcome platinum resistance and ultimately provide tailored-specific therapy options for CLL, MM and OvCa patients . **Approach: The aim of the proposal is to establish robust drug screening platform which can identify drugs and drug combinations that are effective in precision medicine for individual CLL, MM and OvCa patients**. We propose a strategy where we use combination of our newly established platform for drug screening with patient samples, flow cytometry-based signaling analysis, and microfluidics based single cell drug screening methodology towards precision medicine for ovarian cancer patients.

Results

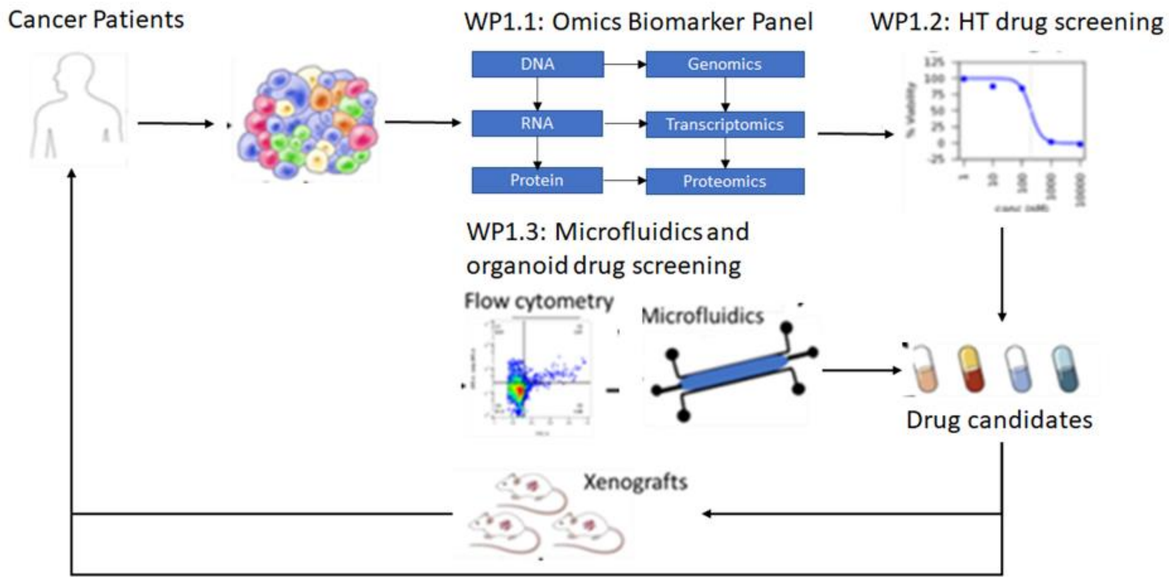

Figure 1: A streamlined integrative drug screening strategy designed for therapy resistant ovarian cancer patients. Here, cancer cell will be either directly analyzed using high-throughput drug screening or single cell drug screening analysis will be performed using flow cytometry and microfluidics to provide datasets on drug sensitivity for individual patients.
WP1 will directly test the effect of drugs panel in combinations on in- vitro proliferating cancer cells from patients.
WP2 will use microfluidics based single cell drug screening in order to identify cellular heterogeneity effects and save patient material.
Using limited material, WP3 will characterize signaling pathways using flow cytometry to identify biomarker readouts in each patient. Downstream of WP1-WP3 results will be validated in flow cytometry and appropriate bioassays. This strategy is designed to directly identify tailored drug regimens that target individual patient´s cancer cells and give benefit to the same donors by supporting clinical decision-making.

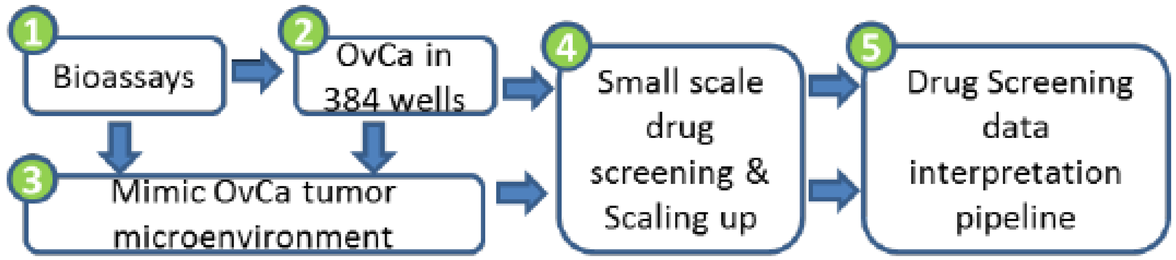

Figure 2: WP1 pipeline 1) establish in-vitro cell-based bioassay, 2) establishing 384 format in-vitro culture setting for OvCa samples; 3) Mimic tumor microenvironment, 4) perform 30 drugs and full library screening; 6) generate data interpretation pipeline.

Conclusion

Methods: We are currently establishing two research components in the CSIR Synthetic Biology and Precision Medicine Centre Bio-foundry program which includes industrial synthetic biology and functional precision medicine program. We implement Biofoundry biodesign and biological engineering Design-Build-Test-Learn (DBTL) cycle into our industrial synthetic biology and functional precision medicine program. In our Industrial synthetic biology program, we are working on a) ValitaCHO: Development of superior CHO cell line system for hyper-burst protein expression system using directed evolution and synthetic biology approaches; b) Lactochassis: Designer microbes for industrial synthetic biology platform applications; In our Cancer Precision Medicine program: we are working on drug repurposing based drug sensitivity screening platform for B-cell malignancies and ovarian cancer treatment for South African patient cohort.

Results: We are currently at the Design phase of the Design-Build-Test-Learn (DBTL) cycle in our industrial synthetic biology and functional precision medicine program. We have so far have progressed in generation of the preliminary data on ValitaCHO cell-line chemstress fingerprinting profiling. We are currently designing the directed evolution approach for generation superior CHO cell line. In the Lactochassis project, we are currently designing the computational biology based genome mapping for Lactochassis. In our precision medicine platform, we are currently progressing in design and build phase of platform where we have currently procured 770 cancer drugs for drug repurposing platform which can be applied for blood and ovarian cancer cohort.

Conclusion: Using Bio-design DBTL cycle, we aim to implement our industrial synthetic biology and cancer precision medicine platform at CSIR Synthetic Biology and Precision Medicine Centre. These platforms will enable establishment of one of the first Biofoundry and Precision Medicine labs in Africa.

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