



<https://cholangiocarcinoma.org/2020-annual-conference>

**Title:**

**ORGANOID BASED FUNCTIONAL TEST TO PREDICT PERSONALIZED TREATMENT IN CHOLANGIOCARCINOMA**

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**Objective:**

Cholangiocarcinoma (CCA), is a rare tumor and the mutation profile is heterogenous. For this reason, genetic sequencing has not resulted in substantial changes in treatment choices and it is difficult to find targeted therapies which work across the diverse patient population. We reasoned, that CCA patients would benefit from a highly personalized diagnostic test where the patient-derived tumor organoids are tested in a high-throughput functional assay with a library of targeted drugs.

**Methods:**

Sixteen consecutive patients with CCA who were undergoing a planned standard of care biopsy or resection were enrolled in an IRB-approved ongoing study resulting in 18 tumor samples from 2017 to 2019. Samples were shipped on ice overnight to the CLIA certified laboratory of SEngine Precision Medicine for growth of tumor-derived organoid culture and analysis of drug sensitivities. Organoids were evaluated using a multi-dose response to each drug in a library of up to 120 FDA-approved and investigational drugs. 14/16 samples were successfully screened. These results were compared to all previous patients. This established both functional sensitivity and the uniqueness of each patient's response. Clinical and genomic information was collected from each patient for retrospective and prospective analysis, as well as correlation with genomic data.

## **Results:**

We successfully evaluated 14 CCA cases and prepared functional test report. The mean age was 54.5 years (range 36 to 73). 4/18 samples failed screening due to limited amount of tumor cells in the specimen. We tested an average of 63 drugs per screen, with a turnaround time of 17 days (range 9 to 35). An average of 7 drugs per patient were considered top scoring drugs with an exceptional/good response. Results from the functional test correlated with known genomic anchors in 8/14 of the drug/mutation pairs. Comparing the functional drug sensitivity results to retrospective clinical data, we saw 100% correlation with previous therapies. Currently we have prospective data available from 1/14 patient who had stable disease for 2 months after receiving off-label use of Everolimus. However, after a large decrease of ascites, the patient had to stop the drug due to side effects.

## **Conclusions:**

This study shows the feasibility of functional testing of organoids derived from CCA patients in a CLIA certified diagnostic test. We achieved a high success rate and clinically relevant turnaround times. The results correlated well with drug sensitivities expected based on mutations. We also observed multiple mutation/drug pairs which did not show sensitivity in our functional screen highlighting the importance of functional data in a genetically heterogenous tumor type such as CCA. Retrospective analysis demonstrated a 100% correlation with previous therapies. All patient showed multiple additional drug sensitivities beyond the ones expected based on genomics offering additional treatment options. We showed successful translation of the screening results into the treatment success of one patient who was able to receive off-label use of Everolimus resulting in stable disease. This is an ongoing study and we expect additional prospective cases analysis in the future.