A Case Study Utilizing Caris GPSai
# To Ensure Correct Diagnosis Of Primary Tumor Site

Background:

- **Caris MI Profile™ Tissue testing performed at Caris Life Sciences®** includes Whole Exome Sequencing (WES), Whole Transcriptome Sequencing (WTS) and a panel of Immunohistochemical stains (IHCs). In addition, Caris GPSai™ scores are generated for cases that are successful sequenced for WES and WTS.

- **GPSai is an Artificial Intelligence (AI) algorithm** that compares the WES and WTS data generated to our library of 294,000+ molecular database of comprehensive tumor profile to generate a score predicting the primary tumor site.

- **Clinical utility of GPSai includes:**
  - Identify the tissue of origin for cancer of unknown primary (CUP) patients.
  - Identify patients that are incorrectly diagnosed.

Presented Case

- **Clinical presentation:**
  - 50 Year old female.
  - Presented with bilateral adnexal masses (largest measuring 22cm in greatest dimension).
  - Underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy with pelvic debulking of tumor.

- **The pathological diagnosis:**
  - Ovarian endometrioid adenocarcinoma FIGO grade 1.
  - This was based on morphological examination, no IHCs done.

- **Specimen received and testing performed at Caris.**
  - A representative specimen of the right adnexal lesion was sent to Caris to help decide the best options for therapy.
  - MI Profile Tissue for ovarian tumor was run, which includes WES and WTS and a panel of IHCs including ER, PR and MMR (MLH1, MSH2, MSH6 and PMS2).
  - Based on the sequencing results for WES and WTS, GPSai score was generated. This highly favored colorectal cancer (CRC).
  - Subsequently, a panel of diagnostic IHCs were performed that showed the tumor to be positive for CK20, CDX2 and SATB-2 and negative for CK7, PAX-8 and ER. This immunohistochemical profile also strongly favored CRC.

- **The findings were discussed in detail with ordering oncologist.**

- **Patient underwent colonoscopy that showed large nearly obstructive colonic lesion.**

- This case was reviewed at the respective hospital tumor board and there was consensus that this patient is best managed as metastatic colonic adenocarcinoma.

Key Findings: Specimens
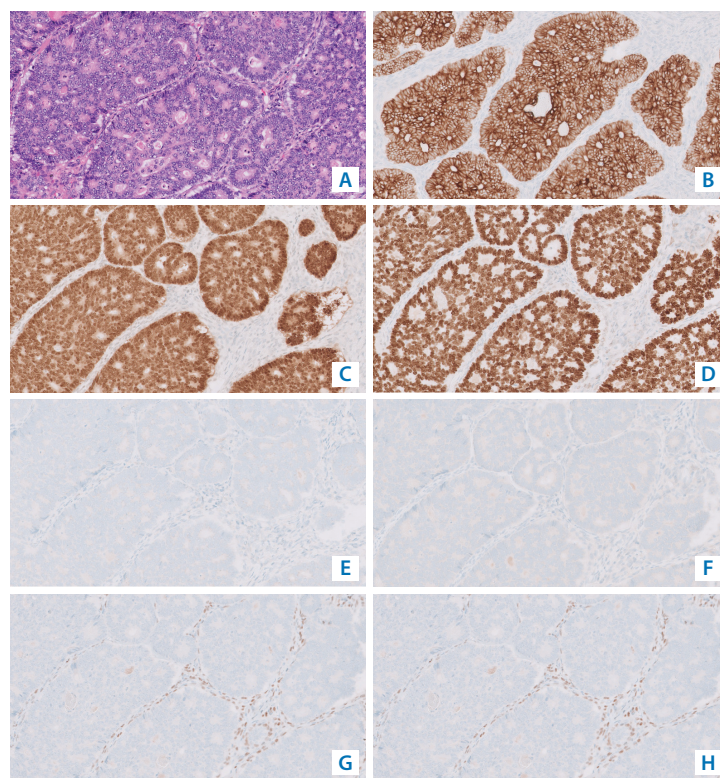
(A) Moderately differentiated adenocarcinoma (H&E 20X). Positive staining of CK20 (B), CDX2 (C) and SATB2 (D). Negative staining of CK7 (E), PAX8(F), ER (G) and PR (H).

Conclusions:

- **Caris GPSai™ was pivotal in identifying the primary cancer site.**

- **The primary cancer was initially thought to be ovarian endometrioid adenocarcinoma.**

- **GPSai strongly favored colonic adenocarcinoma which was confirmed by IHC and the identification of a large colonic lesion.**

- **The patient's diagnosis and course of treatment was altered based on the detailed discussion of the results with the ordering physician.**

Caris Report: Caris GPSai Result

The GPSai (Genomic Prevalence Score - Artificial Intelligence) is a cancer-type similarity assessment which compares the characteristics of a patient's tumor against other tumors in the Caris database. GPSai analyzes a tumor's molecular signature and provides the prevalence of that signature in the Caris genomic and transcriptomic database across 21 distinct cancer categories.

Cancer Category	Prevalence
Colon Adenocarcinoma	97%
Cholangiocarcinoma	<1%
Lung Adenocarcinoma	<1%
Ovarian, Fallopian Tube Adenocarcinoma	<1%
Urothelial Carcinoma	<1%
Uterine Endometrial Adenocarcinoma	<1%

Note: The above shows the relevant information from the GPSai report. It is not a full representation of all possible fields displayed.

Not currently available in New York.

Methods: GPSai is a machine learning platform that was trained on genomic data from 34,352 cases and transcriptomic data from over 11,000 cases. In a validation set of over 12,000 additional cases, GPSai accurately predicted the cancer category in the labeled data set with an accuracy of over 93%. The accuracy increased to 97% when the second highest ranking predicted cancer type was included. The profile has been validated to differentiate among 21 distinct cancer types. GPSai prevalence tables were produced at or above the required confidence level for 93% of samples in the validation set. Samples that do not generate a score at or above this confidence level will not receive a GPSai result.

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