

Liquid biopsy and Array Comparative Genomic Hybridization (aCGH)

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Introduction: Cancer of unknown primary origin (CUP) represents a metastatic cancer with unidentified primary origin. An efficient cancer treatment algorithm is based on detection and characterization of the tumor's origin. CUP is characterized by chromosomal instability; therefore the detection of chromosomal aberrations might contribute in tumor characterization. aCGH combines DNA microarray with CGH providing better detection rates than conventional cytogenetic methods. The present study aimed to evaluate aCGH as a technique for detection the origin of tumor, based on liquid biopsy and particular in circulating tumor cells.

Materials & Methods: Blood samples were collected from five patients suffering from prostate (2), lung (2) and breast (1) cancer and five healthy individuals. CTCs isolated using enrichment protocols while CD45 (-ve) cells isolated from healthy individuals. In addition to patients' samples, six commercial cancer cell lines provided by ECACC were used, representing prostate and lung cancer (DU145, 22Rv1, LNCaP, COLO699N, COR-L 105 and MOR). Genomic DNA extracted and aCGH experiments followed with Sureprint G3 platform (Agilent). The genes located in chromosomal aberrations were literately analyzed and potential cancer type suggested by another researcher. The researcher performed the analysis based only on aCGH raw data, ignoring the identity and medical history of all samples. Samples firstly analyzed based on normal vs cancer prediction and secondly whether the predicted type of cancer was correct.

Results: The sensitivity was around 90% while the specificity was 80%. Among eleven cancer samples only one predicted as normal, as well as one normal sample predicted as cancer. As far as the cancer type prediction the positive predictive value was 90.1%. Only one sample categorized wrongly in total cancer samples.

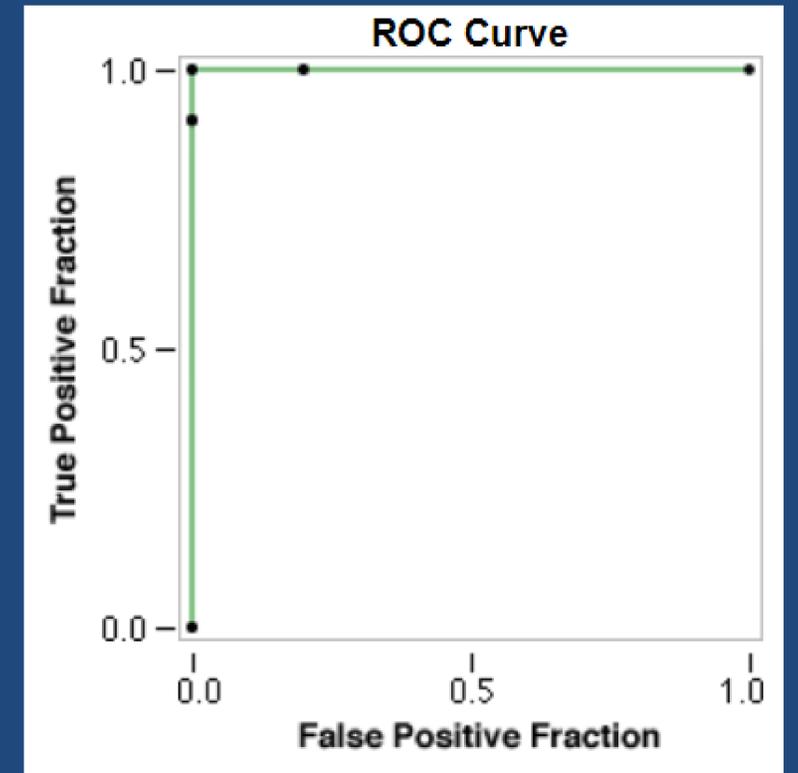


Figure 1: ROC curve analysis. The present figure represents the true positive rate (sensitivity) together with the false positive rate (1-specificity)

Conclusion: aCGH is a powerful technique with potential of discrimination of cancer and healthy samples, but most important with ability to distinguish the type of cancer. The identification of primary origin of cancer is very important in CUP, since it is correlated with more efficient treatment algorithm. The above encouraging data from the combination of aCGH and liquid biopsy need to be validated in more samples and types of cancer so to be used at clinical level.

	TESTED			Total
		POSITIVE (CANCER)	NEGATIVE (HEALTHY)	
REAL	POSITIVE (CANCER)	10	1	11
	NEGATIVE (HEALTHY)	1	4	5
Total		11	5	

Table1: Summarized results of patients.
 "Tested" : outcome from aCGH experiments,
 "Real" : data from patients' medical forms

Selected References:

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Disclosure of Potential Conflicts of Interest

None of the authors of the above study has declared any conflict of interest
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