Metabolic Fingerprinting of Cancer Cells

Summary

To demonstrate the application of the Biolog Phenotype MicroArray™ system in analyzing metabolic differences among human cancer cells, seven diverse cell lines were profiled using 367 substrate nutrients using Biolog MicroPlates PM-M1 through PM-M4. PM-M1 contains primarily carbohydrate and carboxylate substrates, whereas PM-M2, M3 and M4 contain individual L-amino acids and most dipeptide combinations. With the exception of abiotic color formation in a few wells containing reducing sugars (palatinose, D-turanose, D-tagatose, and L-sorbose), multiple lines of evidence (described in the reference below) suggest that the color formed from each substrate reflects the energy-producing activity of each cell's catabolic pathways. This analytical method is simple to perform and reproducible.

Results

All cell lines tested produced a strong reductive response in wells containing glucose (green boxes, all panels) and little or no response in negative control wells lacking any carbon source (red boxes, all panels). Two leukemic cell lines (A,B) show additional metabolism limited to D-mannose, D-maltose, and maltotriose (blue boxes). Prostate cancer cells (C) show additional metabolism of fructose, some nucleosides, and tricarboxylic acid (TCA) cycle intermediates (blue boxes) and lung cancer cells (D) show additional metabolism of dextrin, glycogen, and galactose (blue boxes). Both prostate and lung cancer cells show metabolism of glutamine and many glutamine-containing dipeptides (C, D: purple wells on PM-M2 to M4). Colon (E) and liver (F,G) cells demonstrate a more diverse catabolic response, with more wells showing a strong reductive response. For example, colon cells additionally metabolize lactic acid, butyric acid, and propionic acid (E, blue boxes), and liver cells metabolize alanine, arginine, and dipeptides (F,G: Ala=blue boxes, Arg=gold boxes).

Importantly, two genetically related liver cell lines have similar metabolic profiles. The HepG2/C3A cell line (G) was derived as a spontaneous clonal variant of HepG2 (F), selected for its ability to grow on pyruvate as the principal energy source. As is clearly seen, the related cell lines (F,G) show strong similarity in their metabolic profiles, and the clonal variant (G) shows stronger metabolism of pyruvate (G: magenta box) relative to its parent. The colon cell line Colo205 (E) has a similar metabolic profile to HepG2, with a salient difference being the observed increased metabolism of butyric acid and propionic acid, which are plentiful in the colonic environment due to their production by resident anaerobic bacteria.
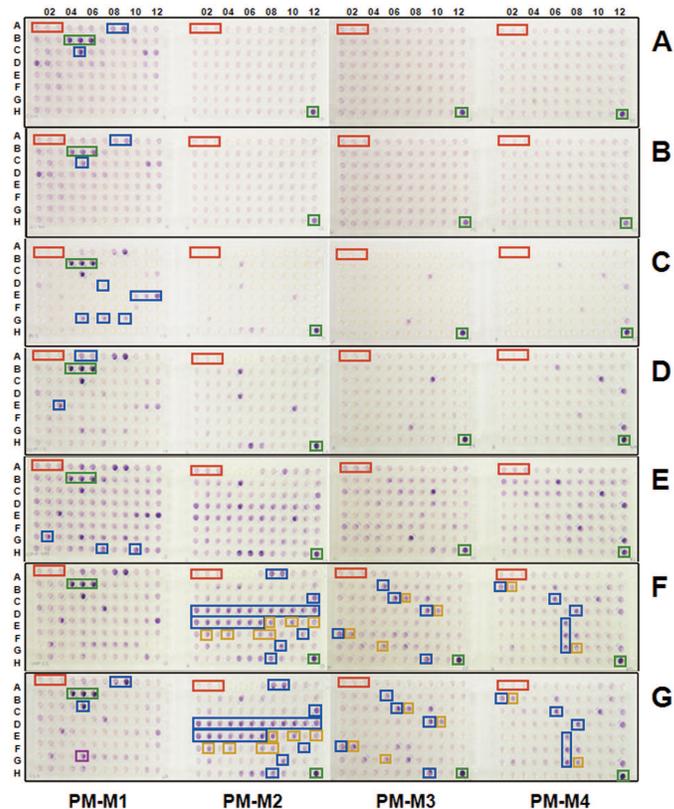

Figure 1: *Assay of seven human cancer cell lines in 367 metabolic assays. Suspensions of the following cancer cells were inoculated into Phenotype MicroArrays PM-M1 through PM-M4 which contained 367 biochemical substrates that could potentially be metabolized and provide energy for cells. (A) CCRF-CEM leukemia, (B) HL-60 leukemia, (C) PC-3 prostate cancer, (D) A549 non-small cell lung cancer, (E) Colo205 colon cancer, (F) HepG2 hepatocellular cancer, (G) HepG2/C3A, a clonal variant of HepG2. (Complete protocol is described in Ref 1, below).*

Conclusions

These data demonstrate that Biolog PM-M substrate utilization profiles provide a metabolic differentiation as well as characterization of organ-specific metabolic traits that differ among various types of cancers. The metabolic profiles are consistent with the known physiological properties of different cells. Cells lining the intestine are exposed to a more diverse and variable nutritional environment than blood, prostate, or lung cells. Liver cells are also fed directly from the intestine by the portal circulation. Therefore, it is reasonable to expect that colon and liver cells would have more diverse capabilities for substrate metabolism than cells from other tissues.

High throughput multiplexed phenotypic fingerprinting of cell lines provides a valuable tool for differentiating metabolic properties of cells (a) comparing cells from different organs, (b) comparing cells representing models of disease versus normal, and (c) comparing cells representing various cancer genotypes.

From: Bochner BR, Siri M, Huang RH, Noble S, Lei X-H, Clemons, P.A., Wagner, B.K., (2011) Assay of the Multiple Energy-Producing Pathways of Mammalian Cells. PLoS ONE 6(3):e18147. doi:10.1371/journal.pone.0018147

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