The importance of ancestry and diversity in cell line collection and analysis for people of African ancestry

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People of European ancestry tend to receive greater benefit from anticancer treatments than people of African ancestry. The recent attention on these different outcomes in patients globally with cancer is uncovering potential sources for these biases as significantly poor representation persists for Blacks when using cell line models. Similar observations are seen at the clinical level. To close the gaps and to ensure equal benefit for both Blacks and Whites with cancers, increased representation of cell lines needs to be achieved. A focused push from funding agencies, journal editors and policymakers can aid in this outcome.

Many drug leads for cancer treatment have emerged from the application of preclinical studies that have utilized cancer cell lines as 2D and 3D models and as xenografts in specialized mouse models. The application of cell lines in cancer research spans more than 70 years, a period that has generated many discoveries in cancer treatment towards improved patient survivorship *(1)*. Yet, the methodologies employed to generate cell lines remain lacking given the less than 10% success rates. This continues to stifle the advancement of cell lines; a requisite for the optimal application of these preclinical tools. While cell lines continue to pave the way for drug discoveries, the genetic drift encountered from the incessant propagation in vitro is an area warranting attention to advance drug leads with a personalized approach.

Cell lines representative of myriad tumours across various ethnicities are crucial to this end. Research by Barretina et al. *(2)*, and Garnet et al. *(3)*, have together shown gene-drug specificity across more than 1,000 cell lines exposed to almost 150 anticancer drugs. Similar findings were obtained by the NCI-60 study (4) whereby various cell line panels representative of different cancer subtypes yielded more effective drug leads than the usage of single cell lines for different cancers. Cell line panels typically provide representation of different tumour subtypes for specific cancers, and these are believed to be more effective in drug prediction than single cell lines *(1)*. Of the two main global suppliers for cell lines, American Type Culture Collection (ATCC) and The European Collection of Authenticated Cell Cultures (ECACC), cell line panels are only offered by ATCC, and of the 24 panels (Figure 1), representation for Blacks is only observed among three. While ECACC does not offer specific cell line panels, their offering of categories of different types of cancers (Table 1) shows majority representation for Caucasians as of September 2021.

The questions surrounding cancer disparities has forced an inquest into in vitro research models. Both socioeconomic factors and biological drivers play a role in the higher incidence and mortality rates for Black men and women with cancer. African American men have 25% higher incidence and 43% higher mortality rates than White American men with cancer *(5)*. Although, African American women have lower cancer incidence rates than White American women, they have a 20% higher mortality rate *(6)*. In general, the top two cancers of concern for African American men are prostate and lung while for African American women, they are breast and lung. Similar trends are observed in the Caribbean and Africa *(7)*. Of these cancers of concern (breast, lung and prostate), Black representation among the ATCC cell line panel is only observed for breast cancer and among the various cancer cell lines (colorectal, esophageal and neurobiology) offered by ECACC, there are no known representation for Blacks.

The most emphasized cancer disparity is observed for prostate cancer, especially in light of the global decline in mortality rates irrespective of the pervasive incidence and mortality rates for Black men in the Caribbean and Africa *(7)* and the two and a half times higher mortality rates for African American men compared to European American men *(8)*. One could argue that Blacks tend to make up most of the lower income status population but even when assessed grade for grade and stage for stage, survivorship for Whites is better than Blacks *(7)*. Despite the observed disparity, no prostate cancer cell line panel exists for Blacks among the ATCC cell line panel *(9)*. Moreover, more than 97% of the prostate cancer cell lines available at ATCC are Caucasian in origin. If cell lines

Figure 1: The ethnic representation of panels of cancer cell lines according to tissue specificity on ATCC's website. Taken from Badal et al., *(9)*

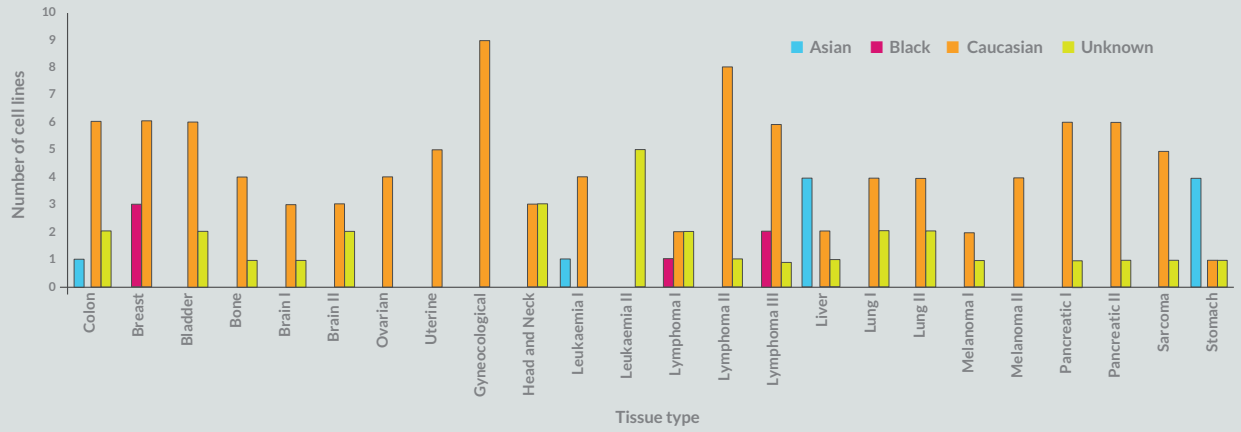

Table 1: The distribution of ethnicities of human cell lines offered by ECACC categorized by cancer type. Of the thirty-eight cell lines listed, representation for Blacks is 0%. ECACC also has other categories of human cell lines not shown in the table, serum free (4), induced pluripotent stem cells (1700), GPCR, Hybridoma collection (400), Chromosomal abnormality, HLA-Type Collection (430) and Human Random Collection, (700 all Caucasian)

Cancer	Ethnicity
Colorectal	
GP5d	Caucasian
MDST8	Unknown
HCA-46	Unknown
HCA-24	Unknown
HCA-2	Unknown
HCA-7	Unknown
HCA-7 Colony 29	Unknown
HT29 gluc C1	Caucasian
HT115	Unknown
HT55	Unknown
HT29/219	Caucasian
CACO-2	Caucasian
LS180	Caucasian
SW 620	Caucasian
LoVo	Unknown
LS174T	Caucasian
COLO 320DM	Caucasian
COLO 205	Caucasian
SW 1116	Caucasian
Neurobiology	
BE(2)-C	Caucasian
BE(2)-M17	Caucasian
SK-N-BE(2)	Caucasian
SK-N-DZ	Unknown
SH-SY5Y	Unknown
Oesophageal	
ESO26	Caucasian
ESO51	Caucasian
KYAE-1	Caucasian
KYSE-270	Asian
KYSE-30	Asian
KYSE-410	Asian
KYSE-70	Asian
OACM5.1 C	Caucasian
OACP4 C	Caucasian
OE19	Caucasian
OE21	Caucasian
OE33	Caucasian
SK-GT-2	Hispanic
SK-GT-4	Caucasian

are used in drug discovery, this begins to explain the enhanced responsiveness to chemotherapy drugs experienced among Whites compared to Blacks *(10,11)*. Of note, is that majority of prostate cancer deaths occur among men with advanced disease.

The other cancer with a focused attention on its disparity is breast. Unlike prostate, the incidence rate for breast cancer among African American women is lower than White American women, yet the mortality rates are higher among Black women. Of concern is that no treatments existed for the most aggressive breast cancer, triple-negative breast cancer (TNBC) until recently, the most common type of breast cancer in Black women with 30% higher incidence rates *(12)* and 42% higher mortality rates *(13)*. A similar pattern is observed for the availability of breast cancer cell lines, although representation for Blacks is observed among the six-breast cancer cell line panels on ATCC, more TNBC panels are needed for Black women with TNBC. TNBC cell line panel for Blacks is approximately 20% and there is a 14% representation for breast cancer cell lines overall. A larger gap was observed for breast cancer cell lines offered by ECACC as 94% were of European ethnicity and the remaining for Blacks. Similarly, poor representation of Blacks is observed at clinical trial accounting for less than 10% in general even for trials geared at TNBC *(14)*.

The other cancer of concern for both Black men and women is lung cancer and like prostate cancer, there is an overall reduction in incidence and mortality rates, but Blacks have roughly twice higher incidence rates than Whites and higher mortality rates *(15)*. While socioeconomic factors play a large role in this, with Blacks being less likely to receive optimal treatments including surgeries compared to Whites *(16,17)*, research has linked biological drivers that contribute to the disparities(18). There is evidence that Blacks experience inferior treatment response to chemotherapy drugs and more severe toxicity to platinum-

based chemotherapy drugs *(19)* which contributes to poorer patient survivability. Irrespective of the burden lung cancer presents and the noteworthy disparity that exists, there is no representation for Blacks among the cell line panels on ATCC for lung cancer. Furthermore, of the 64 lung cancer cell lines available, representation for Blacks is roughly 14% and for Whites, roughly 80%.

Research with a focus on primary cancers of concern for Blacks is lacking and cell lines when applied appropriately will guide the development of drug leads with a targeted approach. Organizations like, African Caribbean Cancer Consortium, (AC3 https://ac3online.org), Prostate Cancer Transatlantic Consortium (CaPTC) and Human Hereditary and Health in Africa (H3A https://h3africa.org/) are engaged in research efforts to understand cancers specific among the Black population in Africa, the Caribbean and America. It is believed that these research initiatives at the genome, transcriptome and proteome levels taking lifestyle factors into account will contribute to advancing more effective anticancer therapies for Black men and women with cancer. However, needs to be increased representation in cell line panels and among cell lines in general from major suppliers such as ATCC and ECACC, to better understand cancers of concern for Blacks. Towards this end, our lab (AntiCancer Research Jamaica, www.acrj.org.jm) has developed a methodology used to develop the first cell line, ACRJ-PC28 (a prostate cancer cell line) from the Caribbean, a region with high Black representation. We believe this methodology will expand the representation of all cancers of concern for Blacks. Concomitantly, there needs to be a concerted effort among funding agencies, journal editors and policymakers to steer the direction of research towards a more inclusive approach. ■

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