

Enhancing African American Participation in Biospecimens: A Case in Point for Pancreatic Cancer

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ABSTRACT

Diseases of the pancreas (i.e. chronic pancreatitis, diabetes, and pancreatic cancer) disproportionately affect the African American community. Challenges associated with engaging the African American community in biospecimen research are longstanding. We surveyed a number of pancreas-related biobanks, and data repositories for African American representation. While some of the biobanks and databases surveyed contain biospecimens and data from African American donors at levels that reflect minority representation among the general population, others do not. A number of factors have historically contributed to reduced participation of the African Americans community in biospecimen donation including medical mistrust, lack of transparency, fear, and a poor knowledge and understanding about the use of biospecimens for research. Suggestions for increasing African American participation in organ and biospecimen donation include educational interventions, particularly in community groups, and providing printed and online recruitment materials to patients, patient advocates, and care partners. Increasing awareness of the many benefits of biospecimen donation among African Americans will positively affect health disparities research into pancreatic cancer and other diseases.

KEYWORDS: Pancreatic Cancer, Health Disparities, Biospecimen

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INTRODUCTION

Many facets of biomedical research require the collection, dissemination, and cellular, molecular, and genetic analysis of human biological specimens. For genetic and associated biological studies of racial disparity, it is essential to collect and analyze biological specimens from donors at levels that reflect minority representation among the general population. Ensuring adequate representation is imperative as a matter of social justice, economics, and science (Regnante et al., 2020). Such biospecimens include normal and diseased tissues, blood, and other bodily fluids. While the most recent census data set the African American population at 13.2% (Colby and Ortman, 2015), biological specimen collection and associated data generated from those specimens may not reflect the representation of African Americans in the USA. In an analysis of studies involving genomic sequencing, African Americans are underrepresented for most cancers in The Cancer Genome Atlas (TCGA) Program and male African Americans are especially underrepresented compared to their female counterparts (Kim and Sarkar, 2019). These data underscore the need for appropriate samples. Genome-wide association studies (GWAS) of cancer have identified a large number of cancer risk loci, however, less than 1% were first discovered in African Americans compared to 80% in European ancestry populations mainly because the small percentage of African ancestry samples included in the discovery phase of these studies (84% European; 4% African) (Park et al., 2018).

In this report, we surveyed a number of pancreas-related biobanks, and data repositories for African American representation. We discuss how well those frequencies reflect minority representation among the general and specifically African American populations. We explore the challenges

associated with procuring African American biospecimens and how a lack of donation impacts research outcomes designed to reduce the burden of diseases of the pancreas for this population. We conclude this paper with suggestions designed to increase African American participation in organ and biospecimen donation.

Representation of African American biospecimens for diseases of the pancreas

Diseases of the pancreas (i.e. chronic pancreatitis, diabetes, and pancreatic cancer) disproportionately affect the African American community. The incidences (per 100,000) of chronic pancreatitis, and pancreatic cancer in African Americans are 11.3 and 11.7, respectively, compared to 5.1 and 7.5, respectively for Non-Hispanic Whites (2019; Yang et al., 2008). The percentage of diagnosed diabetes in the USA for African Americans and Non-Hispanic Whites are 13.3 and 9.4, respectively (2020). Health disparity research on diseases of the pancreas are impacted by the minority representation of tissues, tumors and other biospecimens related to pancreatic diseases. The Cancer Genome Atlas (TCGA) database contains only 3.6% of African American pancreatic cancers compared to 90% for Non-Hispanic Whites (Table 1). The largest repository of cancer cell lines in the world, the American Type Culture Collection (ATCC), offers no pancreatic cancer cell lines derived from African Americans (Table 1). Data from the three centers (Mid-Western, Eastern, and Mid-Atlantic) of the NCI-supported Cooperative Human Tissue Network (CHTN) report only 8.3% African American representation compared to 88.9% for Non-Hispanic Whites (Table 1). We are aware of ongoing GWAS of pancreatic cancer that has considerable higher African American representation. These include samples from the Multiethnic Cohort Study and the Southern Community Cohort Study (Park et al., 2018; Signorello et al., 2010; Signorello et al., 2005)

whereby most pancreatic cancer cases are African American (230 cases/5,235 controls), followed by Japanese American (181 cases/3,285 controls),

Non-Hispanic White (132 cases/570 controls), Latino (105 cases/ 2,935 controls), and Native Hawaiian (43 cases/1,753 controls).

Table 1. Racial representation of biobanks from diseases of the pancreas.

Biobank	Tissue type(s)	Inclusive years	% African American	% White	% Other	Total in biobank	Reference
The Cancer Genome Atlas	Pancreas Cancer, Normal Pancreas	2006-2018	3.3	88	8.7	150	(Cancer Genome Atlas Research Network. Electronic address and Cancer Genome Atlas Research, 2017)
American Type Culture Collection	Pancreas Cancer cell lines	N/A	0	66	33	12	https://www.atcc.org/
Prodo Labs	Pancreas	2011-2016	11.5	54.9	33.6	226	(Scharp et al., 2019)
NPOD ¹	Pancreas	2007-2020	18.3	68.1	13.6	492	
GWAS ²	Pancreas Cancer	1993-2014	33.3	19.1	47.6	691	(Park et al., 2018; Signorello et al., 2010; Signorello et al., 2005)
CHTN ³	Pancreas Cancer	2015-2020	8.3	88.9	2.8	36	
Allegheny Hospital	Pancreas	2013-2017	19.1	61.8	19.1	283	
University of Miami	Pancreas	2013-2017	19.5	54.9	25.6	195	

¹Network for Pancreatic Organ Donors with Diabetes

²Genome Wide Association Studies

³Cooperative Human Tissue Network

Health disparities research on pancreas transdifferentiation

We are presently engaged in a prospective study on how race affects the ability of normal human pancreas to transdifferentiate from an acinar to ductal phenotype; considered to be an early precursor to the development of pancreatic cancer (Storz, 2017). In our study, normal pancreatic acinar cells are procured from pancreatic islet

transplantation centers (Table 1); pancreata are from individuals who have consented to organ donation. Our study has been ongoing for 3 years, and to date we have collected 17, 7 and 14 pancreas specimens from Non-Hispanic White, African American, and Hispanic donors, respectively. While the overall percentage of specimens from African Americans in our study (18.4%), as well as the overall procurement from

these transplantation centers (Allegheny Hospital 19.1% and University of Miami 19.5%, Table 1), parallels the percentage of African Americans in the USA population (Colby and Ortman, 2015), the slow pace of procuring African American biospecimens has impacted our work's progress and conclusions from the study. In a 2011 study, Bratton, et al., reviewed the impact of race on organ donation over the years 1999-2008. They report that African American organ donation increased over these years to levels that reflect minority representation in the USA (Bratton et al., 2011).

Historical/Cultural Issues

A significant body of literature explores medical distrust of the research community by African Americans (Hughes et al., 2017). Warren, et al., reported the barriers to participation among African Americans in clinical trials. Thirty-five interviews were conducted among national African American leaders from historically Black health professions schools, Black health professional associations, faith leadership centers, and civic organizations (Warren RC, 2019).

Trustworthiness and trust were the top factors that determined research participation from the African American community; especially for the less understood clinical trials (Kennedy et al., 2007). Building trustworthiness in the research community forms the foundation for trust between African Americans and researchers. However, trust is unlikely when the research community is not trustworthy or when the researchers demonstrate no evidence of their trustworthiness (Smirnoff et al., 2018). In each instance, trustworthiness is a pre-condition for sustained trust. The historical evidence of bioethics and public health ethics violations, specifically related to African Americans (Crawley, 2001) is a challenge to sustaining trust.

African Americans have had regretful experiences related to seeking information about biospecimens. For example, in 2018, descendent family members of the men who were in the U.S. Public Health Service Syphilis Study at Tuskegee (Syphilis Study) formally requested the whereabouts of any Syphilis Study biospecimen from the Centers for Disease and Prevention and the National Institutes of Health (R.C. Warren, personal communication). The request came after a paper, published by the Milbank Quarterly, indicated that the biospecimen from the Syphilis Study existed (Spector-Bagdady and Lombardo, 2018). Through the Freedom of Information Act, the information should have been obtainable. While both agencies responded, the information was not provided. The NIH "All of Us Project", to collect genetic and biospecimen material from the African American population will not be successful unless the trustworthiness between the Black population and the research community is established and sustained.

Underrepresentation of African Americans in Biospecimens

Previous studies regarding African American underrepresentation in biospecimens suggest that there are several influential factors including mistrust of the medical community, a lack of transparency regarding how biospecimens will be used, and a lack of knowledge regarding the importance of participation. Using a standardized phone survey with Detroit area African Americans 55 years or older, Hagiwara, et al., (Hagiwara et al., 2014) reported that African Americans were rarely asked to participate in biobanking programs. Study participants reportedly were not as concerned with research exploitation or mistrust of medical researchers. When they were concerned, these concerns or mistrust did not translate into an actual unwillingness to participate in biobanking programs. Hagiwara, et al., found that

transparency in medical research and biobanking programs was a more important predictor of African Americans' willingness to donate biospecimens for medical research (Hagiwara et al., 2014).

In a mixed methods study of African Americans in Southeast and Southwest Washington, DC, Dash, et al., (Dash et al., 2014) also reported that "mistrust of the medical community" was not the most commonly reported barrier. A lack of transparency in and knowledge of how biospecimens would be used were cited most often. These findings highlight the importance of education on biospecimens to increase minority participation in biospecimen research (Dash et al., 2014).

Patel, et al., (Patel et al., 2018) assessed the impact of an educational intervention using video and brochures on biospecimen knowledge and attitudes using pre- and post-tests. Both average knowledge and attitude scores for biospecimen donation increased ($p < 0.0001$) for video and brochure conditions post-intervention. Those who received the educational video showed a significantly greater increase in knowledge pre-to-post compared to those who did not receive the educational brochure. There were significant interactions between both interventions for attitudes toward biospecimen donation. The results demonstrated the feasibility and efficacy of a university African American community partnership in developing educational tools for biospecimen donation (Patel et al., 2018; Rollins et al., 2018).

Rollins, et al., assessed the effectiveness of a community-engaged educational approach designed to increase clinical research participation among racial minorities (Rollins et al., 2018). Pre- and post-tests assessed changes in participants' (n

=60) knowledge, perceptions, and willingness to participate in clinical studies and biorepositories following a session about clinical research and biorepository participation. Statistically significant changes in knowledge about joining a clinical study and registry or biorepository were observed. There was no statistically significant change in willingness to participate in clinical research or biorepositories. Despite beliefs that participation would improve health, early detection, and care access, barriers included fear, lack of knowledge, historical mistrust of research, and time constraints.

Barrett, et al., reported that fear, mistrust and inflexible research protocols were barriers to African American recruitment (Barrett et al., 2017). Participants suggested that greater recruitment could be achieved by enhancing cross-cultural skillsets via training opportunities for recruiters, increasing greater community engagement among researchers, and improving engagement between clinic staff and research teams.

Knowledge, attitudes, and beliefs about biobanking and experiences with the donation of biospecimens among diverse participants were explored by Dang, et al., (Dang et al., 2014). Overall, there was a poor knowledge and understanding about the use of biospecimens for research. Racial and ethnic groups differed in the number of factors that were obstacles for participation. For African Americans in this study, the issue was continuing medical mistrust. Overall participants expressed interest and willingness to participate in biobanking for altruistic purposes, particularly to benefit future generations. However, interest was predicated on an expectation that requests be accompanied by an explication of study sponsorship and ownership, distribution, and use of biospecimens in a format that aligned with participants' backgrounds and experiences. While

the findings regarding medical mistrust may appear contradictory, it can be argued that a lack of transparency is related to trustworthiness.

Increasing Procurement

Concerted and deliberate actions must be undertaken to ensure the representativeness of African Americans in pancreatic cancer research. Continuing to ignore or failure to respond to this issue renders it no less of a concern. Potential strategies to include educational campaigns, testimonials, statistical messages, and community involvement (Reinhard AM, 2020). Evidence points to partial success of educational interventions. Culturally appropriate messaging in small community groups led to improved attitudes and beliefs among African Americans. The intervention was not effective in changing their beliefs about the negative consequences of organ and tissue donation and transplantation or increasing actual registration behaviors (Jacob Arriola et al., 2019). Nonetheless, creating an awareness of this issue, engaging the communities of interest in the conversation, explaining the dearth of tissue donation and its' impact on developing treatment for African Americans might be an important step. We concur with the recommendations of Regnante, et al., (Regnante et al., 2020): (1) launch community-based campaigns designed to raise awareness of cancer clinical trials research and support recruitment efforts, and (2) provide linguistically accessible printed and online recruitment materials to patients, patient advocates and care partners that are written in plain language and in the languages of desired participant population. They also propose providing transportation, meal vouchers, and childcare support to ease barriers and support patient participation.

We believe that considering both the message as well as the messenger are likely to be important to

enhance trustworthiness and to increasing biospecimen collection among African Americans. To address the issues of trust and trustworthiness, we recommend building collaborative partnerships that engage the communities in which bio-specimens are sought. First, it is important to engage trusted constituent gatekeeper groups, such as African American health professionals, and faith and civic leaders to ensure that the factors influencing African American underrepresentation in biospecimens are fully elucidated. Subsequent interactions should be convened by these groups with interested majority researchers to forge an understanding of the historical precedents whereby researchers seek strategic guidance from the constituent gatekeeper groups. Secondly, we recommend the development of a model curriculum that aims to heighten and increase participation among the trusted constituent gatekeeper groups. Following the implementation of a collaboratively developed curriculum, we propose measuring the pre-post testing of the related interventions.

CONCLUSIONS AND PROSPECTUS

Minority representation in biobanks or databases at levels that reflect their incidence in the general population is essential to biomedical research. Historically, African Americans have been less willing to participate in biospecimen and organ donation programs (Dash et al., 2014; Hagiwara et al., 2014; Patel et al., 2018). Reasons for the lack of participation include distrust in medical research, fear, lack of transparency, and misunderstanding of the use and perhaps benefits of biospecimen donation (Barrett et al., 2017; Dang et al., 2014; Rollins et al., 2018; Warren RC, 2019). The intent of this article was to survey a number of biobanks and repositories that supplied tissues and associated data used by pancreas and pancreatic cancer researchers. We conclude that several

biobanks contained African American tissues at levels that were significantly less than the African American population (Table 1) while others correspond to the most current census data that estimates the African American population in the USA at 13.2% (Colby and Ortman, 2015). Although the percentage of African American biospecimen participation may reflect the census data in many of these biobanks, the low number of pancreatic biospecimens available to researchers negatively affects the pace of disparity research, in particular prospective studies. For these reasons, grass root efforts to educate the African American community on the many benefits of biospecimen donation and its impact on biomedical research will have a positive influence on research into diseases of the pancreas.

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Conflicts of interest/Competing interests (include appropriate disclosures)

The authors declare no conflict of interest.

Authors' contributions

This manuscript was conceived by L.B.H.; R.C.W, T.D.S., and V.W.S., contributed to the manuscript

concept, T.D.S., V.W.S., and C.P. contributed to data synthesis. L.B.H. led the writing. All authors contributed to writing and editing the manuscript.

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