
National Institutes of Health

Francis Collins, MD, PhD.

Wholley, MPhil, interim president and executive director of the Foundation for the National Institutes of Health.

Collins started his career as a gene sleuth. Although most famous for co-discovering the gene responsible for cystic fibrosis, he made important contributions to cancer genetics through studies detailing how particular heritable mutations could confer susceptibility to breast and prostate cancers.

Throughout the 1990s, Collins, as director of what became the NHGRI, oversaw the mapping of the human genome—a scientific project that opened the doors to other massive sequencing efforts, such as The Cancer Genome Atlas, notes Lisa Butterfield, PhD, head of R&D at the Parker Institute for Cancer Immunotherapy in San Francisco, CA. "To have the genetic tools and big data tools that he supported is now huge for cancer immunotherapy," she says.

In addition to steering the NIH's pandemic response, Collins has spent the past 6 months advocating for a new multibillion-dollar entity, the Advanced Research Projects Agency for Health (ARPA-H), to support more high-risk, high-reward biomedical ventures. A new NIH director may see the idea through to fruition. But as with his other major initiatives, Collins will deserve credit for yet again reshaping the biomedical research enterprise. *–Elie Dolgin* ■

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Broadening Diversity in PDAC Trials

Findings from Virginia Commonwealth University's (VCU) Massey Cancer Center in Richmond support the need for broadly overhauling patient eligibility in clinical trials to ensure study populations that better reflect real-world practice.

"Although all patients should have equitable access to the newest therapies, cancer trials often lack diverse representation, which may contribute to disparities in survivorship," said Andrea Riner, MD, of the University of Florida in Gainesville. When it comes to pancreatic cancer studies, participant diversity is "alarmingly low," with white patients continuing to make up more than 80% of those enrolled. More troubling, "Black and Hispanic patients are enrolled at rates roughly 40% of what we'd expect based on their disease incidence," she noted.

Riner and fellow researchers wondered if trial eligibility criteria, albeit intended to minimize risk for participants, "might actually create biased results by representing only the healthiest patients, or those from certain racial and ethnic groups." They designed a retrospective study simulating the screening process for 676 patients with pancreatic ductal adenocarcinoma (PDAC) treated at VCU Massey between 2010 and 2019. Most identified as white (52%) or Black (42%). To model inclusion and exclusion, they extracted pertinent information from patients' medical records, comparing it with common phase I/II trial eligibility criteria.

At the 2021 American Association for Cancer Research Conference on the Science of Cancer Health Disparities, held virtually October 6–8, Riner reported the study results: Black patients were disproportionately ineligible—42.4% versus 33.2% of white patients—for PDAC trials, based on standard exclusions. These included high serum creatinine, indicating poor kidney function; low albumin, a nutrition marker; human immunodeficiency virus (HIV); and hepatitis B or C. In short, Black patients "were significantly more likely to be malnourished and to have comorbid infectious diseases," Riner said. Only one criterion, prior cancer treatment, excluded fewer Blacks than whites; even so, "this correlated with more white patients having received neoadjuvant therapy for their current pancreatic cancer before coming to VCU," she explained, "which still suggests differential access to and utilization of care."

This imbalance was eliminated when the researchers revised the criteria in their simulated trial, removing common exclusions, including HIV, hepatitis B and C, and diabetes. Because kidney function might be better assessed by creatinine clearance, Riner said patients were deemed eligible if this value was 30 or higher, instead of 40, the standard.

"It's an appropriate adjustment. We know the range of normal creatinine clearance is different in Black versus white patients," said Milind Javle, MD, of The University of Texas MD Anderson Cancer Center in Houston, who was not involved in the study. "As long as patients' comorbidities are under control, too, that's no reason to exclude them, especially given the close follow-up participants receive in trials."

Javle considers Riner's report "timely and generalizable" beyond VCU Massey. "At present, trial results often define treatment paradigms for broad patient populations, even those who are underrepresented," he said. "Instead of extrapolating findings from a limited group, we should ensure that the data reflect the real-world setting."

The FDA has issued guidance documents aimed at broadening some common eligibility criteria: Pediatric patients can participate in adult trials; patients with brain metastases, HIV or hepatitis B or C, and organ dysfunction or prior/concurrent malignancies can also be enrolled (see https://www.fda.gov/regulatory-information/search-fda-guidance-documents). Additional recommendations will soon be addressed by the agency.

"We need revamped eligibility that's based more on reason than tradition," observed Javle, who is working with the FDA on this initiative. "But ultimately, we also need a mandate, at the regulatory level, to compel widespread adoption of more inclusive criteria and ensure greater participant diversity in trials." *–Alissa Poh* ■

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Bicyclic Peptide Makes Targeting EphA2 Possible

A tumor-penetrating bicyclic peptide that delivers a toxic payload may have finally unlocked the therapeutic potential of targeting EphA2, a regulator of cancer progression overexpressed in several tumor types.

According to phase I trial data presented at the virtual International