

Editorial

Take it to the Bank



In this issue of the Journal of Cystic Fibrosis, Beekman and colleagues report on discussions surrounding the establishment of European CF specimen biobanks for research use, which is complimented by a short communication by Garratt and the AREST CF research team [1,2]. These articles highlight the challenges and considerations of developing a multi-country CF biobank (the former), but also highlight the experience of managing a large biobank and the research advancements that a robust and well-conceived bank can enable (the latter).

Research funding is often predicated on providing clear data sharing plans and greater access to research data and specimens [3,4]. With this push, biobanking should move from single investigator collections that are hoarded in personal freezers to more centralized collections available to the larger research community [5]. There are a number of key variables that need to be considered when developing and managing a specimen biobank, including the types of specimens obtained, standard operating procedures (SOPs) surrounding all steps (for the specimen) from the patient to the bank and ultimately the researcher (e.g.: sample acquisition, processing, handling, storage, transport, labeling, tracking, logging), ownership of specimens, processes for access to samples, systems to ensure quality of samples and accompanying information, location and management of the biorepository (e.g.: academic center, non-profit or for-profit storage facility), regulatory auditing, monitoring and ultimately the protection of patient health information. These considerations are certainly compounded in the context of a CF biobank with multiple contributing countries (and each with their accompanying regulations). However, establishing this type of multi-cultural and multi-ethnic biobank should be highly encouraged, particularly if the CF research community seeks to develop therapies and treatment approaches that allow all CF patients to live long, productive and fulfilled lives. The multi-cultural nature of a European CF biobank has great potential to shed light on cultural, environmental and societal impacts on patient outcomes, particularly since ~50% of disease heterogeneity is due to genetic influences and 50% is not [6]. Furthermore, as new therapies continue to enter care, banking of biospecimens is critical to maintain a ‘therapeutically relevant’ biobank that includes specimens from CF subjects with a variety of phenotypes and receiving a variety of therapies [7].

The US CF community has embraced the development of a robust centralized biobank sponsored by the US CFF [8]. Banked specimens have also been obtained for studies conducted outside of the US (e.g.: Australia, Ireland). Biospecimens for banking and future research from CFF-supported clinical trials are typically captured during study conduct (observational and interventional trials, including both active and placebo treatment arms). Consent for banking is performed at the time of study enrollment, and specimens that are specifically collected for the purpose of banking typically follow similar processes used for the study-specific outcome measures/specimens [9]. Thus, the collection process at study sites is research grade, ensuring that high quality specimens are sent for central storage. Samples have largely been stored in a fee-for-service facility (Fisher Bioservices) [10]. Access to samples for future studies follows a tiered system administered by the CFF in collaboration with CF experts in the research community, including sample request, assessment of sample availability, scientific (including statistical) analysis, regulatory considerations and finally approval (or disapproval) of the request. Specimen types vary (e.g.: serum, plasma, urine, stool, sputum, BALF, cells, etc) depending on the nature of the parent study, but are typically linked to clinical outcome measures captured in the CFF Patient Registry. The link to detailed clinical information makes this a particularly powerful research resource, and recent efforts have sought to drive research to capitalize on this for new CF biomarker development [11]. This process has been primarily utilized for CFFT-sponsored research. Independent investigators and industry sponsors are welcome to make requests from the biobank, but access to specimens obtained and banked during industry-sponsored trials are typically the property of the sponsor, and banked outside of the CFFT biorepository.

Most recently, four CFF-supported programs have been developed with a primary purpose of banking biospecimens for future research, and linking them to established and novel clinical outcome measures. These include i) the GOAL study (specimens from CF patients with gating mutations and the R117H mutation initiating ivacaftor treatment [12], ii) PROSPECT A (specimens from healthy controls and CF patients with partial and nonfunctional CFTR mutations), iii)

PROSPECT B (F508del homozygous patients initiating ivacaftor/lumacaftor therapy) and most recently iv) RARE (specimens from patients possessing premature termination codons – currently in development). The specimen types banked vary somewhat across these studies, but include blood specimens appropriate for cell, protein, RNA and DNA analysis, development of induced pluripotent stem cells (iPSCs), epithelial cell types (e.g.: brushed nasal cells, rectal biopsies), sputum and stool. These studies demonstrate the complexity of capturing multiple sample types for multiple research uses, and highlight the need of the research community to define add-on banking processes when developing protocols.

Biobanking has the potential to add significant value to current and future research in CF, filling gaps in disease understanding, and allowing discovery and validation of new disease insights. Coordinating specimen banking with clinical trial conduct helps to ensure that biobanks are robust and clinically relevant, and we hope will ultimately extend to novel therapies in development through industry partnerships. There are potential ethical challenges to consider, including how to manage the discovery of new information of potential relevance to specimen donors and accompanying ethical implications, addressing local Institutional Review Board (Human Research Ethics committees) input for centralized biobanks, and practical considerations such as ensuring sustainability through patient-based organizations (e.g.: Cystic Fibrosis Foundation Therapeutics Inc). Nevertheless, these challenges are surmountable, and should not dissuade the CF research community from ‘taking biospecimens to the bank’ to benefit the greater CF community.

References

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