Dr. Sonia Skarlatos and the National Heart, Lung, and Blood Institute Translational Research and Resource Programs

Cheryl L. McDonald

It is not enough that wisdom be merely set before us; it must be made use of.
—Cicero

Abstract

Sonia I. Skarlatos, PhD (September 28, 1953–August 6, 2013), was the deputy director of the Division of Cardiovascular Sciences at the National Heart, Lung, and Blood Institute (NHLBI). This article reviews her work in establishing, leading, or facilitating extramural translational research programs supported by the NHLBI, specifically focusing on her work as a consistent advocate for the advancement of gene and cell therapies.

Introduction

IN 2010, FRANCIS S. COLLINS, MD, PhD, the director of the National Institutes of Health (NIH), noted that the molecular medicine approach to health and disease is now “poised to catalyze a revolution in medicine,” and he identified “translational medicine” as one of the five areas “ripe for major advances that could reap substantial downstream benefits” (Collins, 2010). The National Heart, Lung, and Blood Institute (NHLBI) has a decades-long history of supporting multifaceted, multidisciplinary biomedical research and resource programs, effectively laying the foundation for translational medicine research (Lauer and Skarlatos, 2010). This is particularly true with respect to the field of gene therapy, where Sonia I. Skarlatos, PhD, was a staunch and relatively early champion.

The 1990s were busy and exciting years for gene therapy researchers. In September 1990, the first U.S. Food and Drug Administration (FDA)–approved human gene therapy trial in the United States, a trial for the treatment of adenosine deaminase-deficient severe combined immunodeficiency (ADA-SCID), was initiated. This was a joint effort between intramural researchers at NHLBI and the National Cancer Institute (NCI). In August 1995, the National Gene Vector Laboratories (NGVL) program was launched for gene therapy researchers in the extramural community. The NGVL was initiated by the National Center for Research Resources (NCRR), along with the NCI, NHLBI, and the National Institute of Diabetes and Digestive and Kidney Diseases

(NIDDK) as cosponsors. The goal of the NGVL was to provide shared resources to facilitate optimal vector production of clinical-grade vectors for human gene therapy research. Consisting of a central laboratory and four supporting centers, the NGVL manufactured vectors, confirmed their structure, and provided pharmacology/toxicology testing services for NIH-funded grantees with gene therapy products. Just after the launch of the NGVL, the field was buoyed by the successful results of the ADA-SCID trial published on October 20, 1995 (Blaese *et al.*, 1995). Also in 1995, Dr. Skarlatos became the leader of the Molecular Genetics and Medicine Group in what was then known as the extramural NHLBI Division of Heart and Vascular Diseases.

Recognizing the need to facilitate clinical gene therapy studies, Dr. Skarlatos, along with colleagues Dr. Susan Banks-Schlegel of the NHLBI Division of Lung Diseases and Dr. Greg Evans of the NHLBI Division of Blood Diseases and Resources, developed the Programs of Excellence in Gene Therapy (PEGT) in 1999. The goal of the PEGT program was to encourage multidisciplinary collaborations among investigators skilled in the application of gene therapy for cardiovascular, pulmonary, and hematologic diseases. This initiative sought to create an environment in which basic science advances could be rapidly translated into clinical applications by providing shared access to specialized services, such as preclinical toxicology testing; generating vectors for preclinical and clinical use; producing large-scale amounts of biological reagents; providing statistical support; and establishing a high-quality training program for both

MD and PhD scientists. In September 1999, just 10 weeks before the release of the Request for Applications (RFA) for this forward-looking program, the gene therapy field suffered a setback with the tragedy in the ornithine transcarbamylase deficiency trial. Despite the concerns of some people after these events, Sonia was steadfast in her support for the potential of gene therapy, and the PEGT program awards were issued in September 2000. Her prescience, patience, and perseverance were then, and would continue to be, invaluable in ensuring continued support for gene therapy researchers, as well as in creating additional novel programs for cell and biologics researchers. This article examines NHLBI-supported extramural translational research and resource programs that were established and led, or facilitated, by Dr. Skarlatos.

Gene Therapy from Past to Present

Dr. Skarlatos first came to NHLBI as a Staff Fellow in the intramural Section of Experimental Atherosclerosis in 1985 and then transferred to the extramural Vascular Biology Program in 1992. In the early years of her extramural career, she was pivotal in the development of several programs, including the Homocysteinemia and Atherosclerosis Program and the NHLBI Programs of Excellence in Molecular Biology, which fostered the use of molecular biology techniques and trained investigators in state-of-the-art molecular biology techniques. As noted above, the NGVL program began in 1995, and with that, Dr. Skarlatos became increasingly involved in the gene therapy field.

The PEGT program ran from 2000 to 2005, and despite successes in the program and advances in the field, particularly basic science advances, it became apparent that the translation of potential gene therapies from the bench to bedside was relatively slow and that both an assessment of the impediments to progress and new programs were needed. On June 1, 2005, under Sonia's leadership, the NHLBI convened a Working Group of experts to evaluate the state of gene therapy research and identify critically needed resources. The results of this Working Group meeting have been previously reported (Woo *et al.*, 2006), and many probably know that these recommendations served as the springboard for the NHLBI Gene Therapy Resource Program (GTRP), which was formally established in 2007 (Skarlatos, 2007).

While the results of the Working Group were still under review in 2005, Sonia, Dr. Banks-Schlegel, and Dr. Pankaj Qasba of the NHLBI blood division were formulating a new program announcement with review (PAR) for gene therapy vector development. This PAR, "New Approaches to Non-Viral Systems for Gene Transfer Applications for Heart, Lung, and Blood Diseases," was released in March 2006. It was designed to stimulate research on developing new and efficient nonviral delivery approaches for gene therapy in clinical trials and used the combined Exploratory/Development Grants and Exploratory/Developmental Grants Phase II (R21/R33) mechanism to offer a seamless transition between the exploratory and development phases of a project. This PAR provided an opportunity to foster work that would not be covered under the GTRP but clearly was important to the gene therapy field.

Beginning in 2001, Sonia served as the Program Officer for another newly established resource program, the Center for

Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases (CFMGT). Under the direction of Dr. Alice Tarantal at the California National Primate Research Center at UC Davis, the CFMGT was designed to provide researchers a unique resource for studies with nonhuman primates in all age groups, addressing essential questions in gene delivery and allowing for opportunities to test new vector constructs and approaches that advance the field. The goals of the program were to (1) evaluate the safety and efficiency of gene transfer strategies as they emerge, (2) use established and new monkey models to explore fetal and infant approaches for heart, lung, and blood diseases, and (3) provide NHLBI-funded investigators (and those with support from other NIH institutes) with essential expertise, services, and resources to enhance the gene therapy field. From the outset, this program was successful and Sonia was pivotal in helping ensure its continued success with two subsequent program renewals in 2006 and 2012.

From its initiation in 1995 through the end of 2006, the NGVL program produced 36 clinical vectors for use in human studies, and clinical investigators using those NGVL-produced vectors conducted gene therapy studies in 310 individuals across 18 academic centers (Department of Health and Human Services, 2007). As other NIH programs for vector production became available, the NCRR transitioned the NGVL to the National Gene Vector Biorepository (NGVB) and Coordinating Center in 2008, in order to provide continuity of services to the community. The NGVB program is located within the Department of Medical and Molecular Genetics and Indiana University School of Medicine, which under Dr. Ken Cornetta's leadership had also served as the Coordinating Center for the NGVL. In 2011, when the NCRR was to be phased out and the National Center for Advancing Translational Sciences (NCATS) was to be established, Dr. Skarlatos proactively sought and received the enthusiastic support of then-acting NHLBI Director, Dr. Susan Shurin, to transfer the NGVB from NCRR to NHLBI. Several factors made this transfer appealing, including Sonia's experiences and leadership in the gene therapy arena, that Dr. Cornetta's laboratory was already a core facility in the NHLBI GTRP, and that both the NHLBI and Dr. Cornetta's lab had a track record of anticipating special needs of the gene therapy community. It should be noted that even though the NGVB was transferred to the NHLBI, Sonia ensured that the NGVB continued to provide services to a broad range of researchers, not just NHLBI-funded investigators. Additionally, she was a committed leader of the Trans-NIH Gene Therapy Group, hosting meetings where representatives from Institutes and Centers (IC) across the NIH, including NCRR, then NCATS, could report on their gene therapy projects and learn from one another.

As this brief summary illustrates, Sonia was critically important in establishing, leading, or facilitating most, if not all, of the extramural NHLBI-supported gene therapy programs since at least 1995. The NGVB, CFMGT, and the GTRP remain vitally active programs, and each of these, along with another resource program—the Science Moving towards Research Translation and Therapy (SMARTT) program—is reviewed in more detail in the next section.

Current NHLBI Gene Therapy Programs

The National Gene Vector Biorepository

When established, the goals of the NGVB included the provision of a biologic storage facility for gene vector materials; establishment of a storage archive of materials from human subjects exposed to gene therapy agents; maintaining a pharmacology–toxicology database for gene-vector-related study results and support for pharmacology–toxicology research related to gene therapy; and the development of a coordinating center to facilitate access to gene-therapy-related materials and information.

The current NGVB achieved the intended goals and offers gene therapy researchers a variety of services that can enhance their research. These services span four main areas: (1) a reagent repository, (2) post-trial monitoring services, (3) pharmacology and toxicology resources, and (4) archiving services.

The reagent repository hosts a wide range of plasmids, cell lines, and other reagents submitted by investigators to facilitate access to novel gene therapy reagents. Archiving services are offered free of charge to researchers at academic or other nonprofit institutions who must archive samples to meet FDA guidelines or Institutional Review Board requirements in a clinical trial. The NGVB can archive clinical trial samples collected during the post-trial monitoring phase, materials from pharmacology and toxicology studies that must be maintained under good laboratory practices (GLP) conditions, and reserve or backup clinical-grade vector and master cell banks. Academic investigators conducting clinical trials for which the FDA requires posttrial monitoring for replication-competent viruses can receive testing free of charge. The NGVB will also assist with testing for clonal expansion via linear amplification-mediated polymerase chain reaction (LAM-PCR) and ligation-mediated polymerase chain reaction (LM-PCR) technologies. Building on the former NGVL pharmacology and toxicology database, the NGVB hosts a database of studies used to support FDA applications for gene therapy clinical trials. Also, upon request the NGVB will facilitate letters of cross-reference for investigators so that previously conducted pharmacology and toxicology studies can be used by the FDA when reviewing an investigator's investigational new drug (IND) application.

Additionally, the NGVB offers other helpful resources, such as an online pharmacology–toxicology tutorial, links to various guidance documents and resources, and a relatively new costing tool. This customizable tool was developed collaboratively by staff of the Indiana University Vector Production Facility and the Indiana University Kelley School of Business. The free online tool assists researchers in determining the cost of producing cell and gene therapy products under good manufacturing practices and allows for cost determinations using three different methods (Boeke *et al.*, 2013).

Details on all of the resources offered by the NGVB can be found on the website at www.ngvbcc.org/Home.action and questions may be e-mailed to ngvbcc@iu.edu.

Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases

As described in a recent publication, the CFMGT provides a host of research opportunities with nonhuman primates in

all age groups, from fetal to aged (Tarantal and Skarlatos, 2012). A variety of services are offered to NHLBI grantees, including

- assistance with study development and design;
- systemic or organ-targeted gene transfer protocols (in all age groups);
- cell transplant models (autologous, allogeneic, xenogeneic);
- *in vivo* imaging paradigms (ultrasonography, optical/bioluminescence, positron emission tomography/computed tomography);
- physiologic assessments specific to the heart, lung, blood, and vascular system;
- laboratory procedures (e.g., molecular, cellular, morphometry/morphology, immunohistochemistry, immune, and hematopoietic-based assays); and
- tissue harvests to address biodistribution.

An annual call for proposals is circulated to NHLBI-supported investigators; posted on the CFMGT (www.cfmgt.ucdavis.edu) and the American Society of Gene & Cell Therapy (ASGCT; www.asgct.org) websites; published in *Molecular Therapy*; and presented at various national meetings. Prospective investigators submit Letters of Intent, and those who are selected submit a five-page proposal that is reviewed by a standing Scientific Advisory Committee, which includes leaders in the gene therapy field. Successful investigators can provide their vectors or cells for experiments to be completed by CFMGT personnel; they can receive samples from the CFMGT and run specialized assays in their lab; or they may participate in the study as a visiting scientist at the CFMGT. As investigators discuss their projects with CFMGT personnel, new methodologies and related assays and techniques are developed to accommodate their needs. Investigators and their trainees also have the opportunity for a spectrum of training, ranging from basic laboratory techniques to more sophisticated anatomic, physiologic, cellular, and molecular assessments specific to the monkey model. Studies can also be conducted in accordance with FDA GLP guidelines, and an extensive biorepository of control specimens (e.g., RNA, DNA, cells, tissues) is available to NHLBI investigators.

Innovative aspects of this program include a collaborative team approach; strengths in translational research; unique capabilities in the study of fetal and pediatric nonhuman primate models of human development and disease; and using novel *in vivo* imaging paradigms. The use of *in vivo* imaging has provided new ways to explore long-term gene expression and safety, and to monitor the trafficking and fate of transplanted cells in real time. Since its inception, the CFMGT has supported over 45 studies for NHLBI-funded investigators at academic institutions across the United States, and these studies have been crucial for providing data for new NIH grants and IND submissions. Investigators are encouraged to explore the CFMGT website for additional information.

Gene Therapy Resource Program

Many readers are probably familiar with the GTRP from several past presentations at annual ASGCT meetings and via recent publications (Galis *et al.*, 2013; McDonald *et al.*, 2013). As noted above, in order to provide researchers with

those critical resources identified by the 2005 Working Group, the GTRP was launched in 2007 as a 5-year program composed of four core laboratories and a clinical coordinating center (CCC). This novel program was well received by the community, and under Sonia's leadership it was renewed in 2012 for another 5 years. Dr. Skarlatos was especially proud of the GTRP and was always eager to meet and speak to investigators. Figure 1 shows a radiantly smiling Sonia, along with the team from the CCC, manning the exhibit booth at the 2009 Annual Meeting of the ASGCT in San Diego, CA.

Services offered by the GTRP include preclinical-grade vector production; immunology testing on preclinical materials; pharmacology/toxicology testing; clinical-grade (GMP-grade) adeno-associated virus and lentivirus vector production; and regulatory assistance and partial funding for clinical trials. More detailed information about the GTRP services can be found on the website at www.gtrp.org.

Over the past few years, the GTRP has matured and has clearly demonstrated its place as a translational program. Two of the three clinical trials that are receiving funding support from the GTRP have a long lineage at the NHLBI, with Sonia's involvement all along the way. Dr. H. Kirk Hammond and Dr. Barry Byrne each had program project grants (PPG) for which Sonia was the program officer for many years. These PPG projects progressed and subsequently received support from the NGVL for the preclinical work, as well as for clinical-grade vector production in Dr. Hammond's case. The GTRP was the logical next step for funding assistance for the respective clinical trials. Dr. Hammond's trial, "Ad5.hAC6 Gene Transfer for CHF" (NCT00787059), and Dr. Byrne's trial, "Safety Study of Recombinant Adeno-Associated Virus Acid Alpha-Glucosidase to Treat Pompe Disease" (NCT00976352), are both actively recruiting.

A common misperception about the GTRP is that prospective investigators must have an active NHLBI grant in order to qualify for services. This is not necessarily the case,

but the investigator must be U.S.-based and the proposed work must be geared toward translation, not just purely exploratory or mechanistic in nature. Additionally, the proposed translational work should be related to heart, lung, blood, or sleep disorders, or to a disease with significant clinical manifestations in those body systems. For example, the GTRP is currently providing funding assistance to a clinical trial on Pompe disease, a glycogen storage disease with life-threatening cardiopulmonary complications. If the proposed research does not fit these criteria, it may still be possible to have work done in the GTRP if another Institute or Center (IC) at the NIH can transfer funds to the NHLBI. Given the myriad possible scenarios, interested investigators are encouraged to e-mail any questions about program eligibility to the GTRP CCC at gtrpccc@s-3.com

Science Moving toward Research Translation and Therapy (SMARTT)

The NHLBI leadership recognized that to truly further translational research investigators needed more product development support services. Given her experience in translational research, Sonia was asked to develop such a program. In 2010, the 6-year SMARTT program was launched. SMARTT was designed to accelerate the translation of novel discoveries into successful new therapies for heart, lung, and blood diseases by providing free, confidential, and rapid preclinical development services to investigators. The broad categories of services offered include

- preclinical study planning and regulatory affairs support services;
- GLP and non-GLP pharmacology and toxicology services;
- GMP and non-GMP manufacturing of small molecules and nonbiologics; and
- GMP and non-GMP manufacturing of biologics.

The SMARTT program is composed of a coordinating center and three core laboratory facilities, all of whom can provide investigators with IND support related to their respective areas of expertise. Organizations eligible for SMARTT include academic institutions, not-for-profit organizations and foundations, and small businesses. The proposed work must be within the scope of the NHLBI mission and include an identified lead therapeutic candidate with demonstrated *in vivo* efficacy and a viable IND submission pathway. Two noteworthy exceptions to eligibility to the SMARTT program are projects involving devices and gene-therapy-related projects (for which there is already the GTRP). Additional information about the SMARTT program, including an online application process, can be found on the program website at www.nhlbismartt.org/

Sonia and NHLBI Cell Therapy Programs (PACT, CCTRN, and PCBC)

Sonia was involved with three different NHLBI cell-related programs: (1) the Production Assistance for Cellular Therapies (PACT) program (www.pactgroup.net/), (2) the Cardiovascular Cell Therapy Research Network (CCTRN; <https://ccct.sph.uth.tmc.edu/cctrn/>), and (3) the NHLBI Progenitor Cell Biology Consortium (PCBC; www.progenitorcells.org/).

FIG. 1. The GTRP booth at the 2009 ASGCT meeting in San Diego, California: Manning the booth are, seated on the left, Sonia Skarlatos and, on the right, Meg Diggins. Standing on the left is Eric Daniels, and Sue Sepelak is standing on the right. ASGCT, American Society of Gene & Cell Therapy; GTRP, Gene Therapy Resource Program.

PACT and CCTRN

As the field of cellular therapy moved beyond granulocyte transfusion and bone marrow transplantation, it became apparent that the preparation of cellular products was becoming a science unto itself. The isolation and identification of the desired cell population could take months, and optimization of this process could take a year or longer, not including the potency assays. All of this work is expensive and labor-intensive, requiring staff qualified to perform at the highest technical level. Although these tasks are vital to the production process, they are not hypothesis-driven, so this type of work does not meet the requirements for NIH research project grants through R01 and R21 mechanisms. Recognizing the challenges faced by researchers and clinicians working in the field of cellular therapy, the NHLBI established the PACT program in September 2003 with three cell processing facilities (CPF) and a coordinating center.

PACT provides clinical product manufacturing support to further the mission of the NHLBI in the areas of cardiac, lung, and blood diseases, and it provides broad support of translational research across all disease areas to serve the entire cell therapy community. Access to expertise in project management, regulatory affairs, and quality systems is available through PACT. Education initiatives in PACT include webinars, CFP-hosted workshops, national workshops, and active participation and leadership within the cell therapy community through collaboration with other cell therapy organizations and academia.

In 2005 the NHLBI convened an advisory Working Group to provide the institute with recommendations on the translation of cell-based therapies for cardiovascular diseases. The Working Group recommended the formation of a Cardiovascular Cell Therapy Research Network. Dr. Skarlatos was named as the NHLBI program officer, and the CCTRN was established in 2007 as a 5-year program with five clinical research sites and a data coordinating center. The CCTRN chose three initial multicenter trials with the target population in each to be coronary artery disease patients with left ventricular dysfunction (Ejection Fraction $\leq 45\%$) and explored the use of bone-marrow-derived mononuclear cells (BMMNCs) in the acute and chronic stages of the disease (Simari *et al.*, 2010). Eager to promote the field of cellular therapies beyond the traditional hematopoietic stem cell transplantation studies, Sonia facilitated collaboration between PACT and the CCTRN.

Having experience with providing cell products for both single-center and multicenter trials, PACT worked with the CCTRN to provide BMMNCs for the three clinical trials: Transplantation in Myocardial Infarction Evaluation (TIME), its companion trial Late TIME, and the First Mononuclear Cells Injected in the United States (FOCUS) trial. TIME and Late TIME were designed to evaluate whether autologous BMMNCs could be transplanted and function after acute myocardial infarction, with Late TIME using different postinfarct transplantation time points (Traverse *et al.*, 2011, 2012). These studies required extensive coordination between the CPFs and the research site clinical staff since the bone marrow had to be extracted from the trial participants with enough time to process the cells and have them ready for reinjection during surgery. The FOCUS trial was designed to evaluate the safety and efficacy of BMMNCs in patients with chronic ischemic heart disease with persistent (>30 days) left ventricular dysfunction after acute infarction who had no revascularization options (Perin *et al.*, 2012).

Not only were these trials important to the field of cardiovascular cellular therapy, but they also served as an important paradigm for multicenter cell therapy clinical trials (Moyé, *et al.*, 2011; Buxton and Skarlatos, 2012). In these types of trials, one of the first decisions to be made is whether the cells will be manufactured centrally or locally. Local manufacturing carries the additional burden of ensuring that technical staff are sufficiently trained such that all trial participants receive cells that are equivalent in potency and purity. The TIME, Late TIME, and FOCUS trials had to use local manufacturing since the cells were autologous and could not have an out-of-body time longer than 12 hours. A quality assurance group was established with PACT and CCTRN personnel for these trials in order to train staff, conduct site visits, and review all trial documentation. As part of the review process, this group tracked the times taken for the various components of marrow harvesting, transportation, processing, release testing, randomization, placebo preparation, and return to the clinical center for administration to the trial participant (Richman *et al.*, 2012). Although the technical cell processing procedure takes only 90 min, the total time for processing was approximately 7 hours. Contributing to this were incoming testing and device preparation, release testing, patient randomization, and product delivery. Across the five CCTRN centers, the mean out-of-body time was 9 hours, leaving only a 3-hour window of usable time for the cells. These data led to methods to improve cell delivery in multicenter cell therapy clinical trials. Sonia's vision and leadership were essential to the fruitful collaboration between these two groups and resultant practice improvements in the conduct of cardiovascular cell therapy clinical trials. Although Sonia was not directly involved in the establishment or operations of the PACT program, her involvement played an important contributing role to the competitive renewal and expansion to five CPFs in January 2010.

Additionally, under Sonia's program leadership, the CCTRN was successfully renewed in 2012 as a 7-year program. Currently, the CCTRN is conducting the trial "Clinical and MR Imaging Assessments in Patients with Intermittent Claudication Following Injection of Bone Marrow Derived ALDH Bright Cells (PACE)," and other trials are under development. Details about the PACE trial (NCT01774097) can be found at this link: www.clinicaltrials.gov/ct2/show/NCT01774097?term=PACE&rank=14

Progenitor Cell Biology Consortium

Another program Sonia was involved with is the NHLBI Progenitor Cell Biology Consortium (PCBC) (Buxton and Skarlatos, 2012). Awarded in 2009, this 7-year program was developed through an innovative three-step process that was designed to foster synergy and collaboration among experts of varying backgrounds. The PCBC program consists of nine research hubs across 17 cooperative agreement grants, an administrative coordinating center, and collaborative sites. The goal of the PCBC is to identify and characterize progenitor cell lineages, to direct the differentiation of stem and progenitor cells to desired cell fates, and to develop new strategies to address the unique challenges presented by the transplantation of these cells.

An innovative aspect of this program is that there are annual set-aside funds for competitive internal and external

studies. Ancillary studies are open to investigators not currently participating in the PCBC. These projects must be a collaborative effort between a current PCBC investigator and an outside investigator who brings additional expertise. Preference is given to investigators from institutions that are not currently involved in the PCBC. The funds for these ancillary projects are administered through the Administrative Coordinating Center, led by Dr. Michael Terrin at the University of Maryland, Baltimore. The Request for Proposals is published on the PCBC program website and the NHLBI public website, as well as announced in the NIH Guide, typically with a May application deadline. More information about the entire PCBC program, including these annual funding opportunities, can be found at www.progenitorcells.org

Summary

Dr. Sonia Skarlatos enjoyed a 28-year career at the NHLBI and had many notable achievements. During the last 17 years of her career, she had a particular focus on gene and cell therapy research, serving as the Program Officer for many grants and institute-initiated research programs. Table 1 summarizes the currently active translational research and resource programs for gene and cell therapy researchers that Sonia established, led, or facilitated over the recent years.

The author would like to note that it would have been impossible to speak to all of the researchers and colleagues whose careers were positively influenced by this one truly remarkable individual. However, the people to whom the author did speak to about this article and their work with

TABLE 1. THE NATIONAL HEART, LUNG, AND BLOOD INSTITUTE'S TRANSLATIONAL RESEARCH AND RESOURCE PROGRAMS FOR GENE AND CELL THERAPY RESEARCHERS

<i>Program name</i>	<i>Services and resources offered</i>	<i>Website</i>	<i>Contact information</i>
National Gene Vector Biorepository (NGVB)	Reagent repository Posttrial monitoring for replication competent viruses Pharm/Tox services Archiving services	www.ngvbcc.org/Home.action	E-mail: ngvbcc@iu.edu or Ms. Lorraine Matheson Phone: 1-317-274-4519
Center for Fetal Monkey Gene Transfer (CFMGT)	Study design & development Systemic or organ gene transfer protocols Transplant models Physiologic and laboratory assessments <i>In vivo</i> imaging Tissue biodistribution assays	www.cfmgt.ucdavis.edu/	E-mail: cfmgt@primate.ucdavis.edu
Gene Therapy Resource Program (GTRP)	Preclinical vectors Immunology testing Pharm/Tox testing GMP/Pre-GMP adeno-associated virus & lentivirus vectors Regulatory affairs & clinical trial funding assistance	www.gtrp.org	E-mail: gtrpccc@s-3.org
Science Moving towards Research Translation and Therapy (SMARTT)	Preclinical study planning Regulatory affairs support GLP/non-GLP Pharm/Tox GMP/non-GMP production of small molecules and nonbiologics GMP/non-GMP production of biologics	www.nhlbismartt.org/	E-mail: NHLBISMARTT@nhlbi.nih.gov Phone: 1-919-541-8722
Production Assistance for Cellular Therapies (PACT)	Research- and clinical-grade cell product production Clinical protocol development Project management and regulatory affairs assistance Quality systems expertise Educational resources	www.pactgroup.net	www.pactgroup.net Follow instructions on the "Contact Us" link
Cardiovascular Cell Therapy Research Network (CCTRn)	The PACE trial in peripheral arterial disease is currently enrolling (NCT01774097).	https://ccct.sph.uth.tmc.edu/cctrn/	Contact information for the various research centers: https://ccct.sph.uth.tmc.edu/cctrn/public/home/About_cctrn.aspx
Progenitor Cell Biology Consortium (PCBC)	Annual funding opportunities for ancillary projects	www.progenitorcells.org	www.progenitorcells.org/contact

This table summarizes the translational research and resource programs for gene and cell therapy researchers that were established, led, or facilitated by Dr. Sonia Skarlatos. All of these programs were active at the time of publication, and the website and contact information is shown.

FIG. 2. Sonia and her legacy of the National Heart, Lung, and Blood Institute (NHLBI) programs. This figure shows the currently active translational research and resource programs available to gene and cell therapy researchers that the late Dr. Sonia Skarlatos established, led, or facilitated during her time at the NHLBI.

Sonia on these various programs offered similar comments. They noted how skillful Sonia was at bringing together a group of people with diverse backgrounds and various skill sets and forming an effective team. Moreover, she had a way of making each person feel like an important member of that team. With her kind manner, patient demeanor, and superb organizational skills, she was a true leader.

It has been said that it is not necessarily the number of our days on this earth that makes an impact, rather the quality of our days. Sonia was a genuinely happy person who lived every day to its fullest. As Fig. 2 illustrates, the number of Sonia's days was far too short, but the scope and impact of her work will be manifest for years, if not generations, to come.

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Address correspondence to:

Dr. Cheryl L. McDonald
6701 Rockledge Drive
Room 8114, MSC-7940
Bethesda, MD 20892-7940

E-mail: mcdonalc@nhlbi.nih.gov