PXE Awareness

National Association for Pseudoxanthoma Elasticum (NAPE, Inc.)

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Lee Ducat

Founder and President of NDRI

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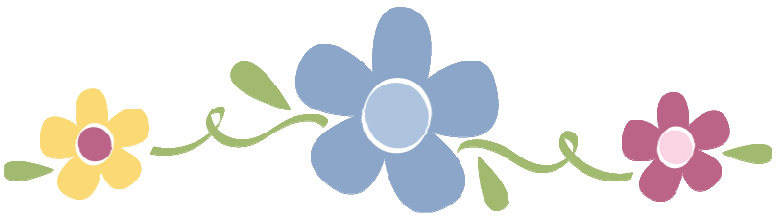

President's Message

NDRI (National Disease Research Interchange) has served the medical research community for thirty years by providing human tissue and fluids for research. Lee Ducat, founder of the Juvenile Diabetes Foundation, was asked by researchers to develop a program for gathering human biomaterials. Her organizational skills, contacts and ability to work with patient advocacy groups, coupled with her understanding of research protocols, made her an ideal candidate for the task. For thirty years NDRI, under her guidance, has demonstrated to the medical research community across the nation the great value of such a program. NDRI has contributed to important discoveries by closely supporting scientists to free their energies for research rather than seeking out needed human biomaterials. Last year the National Institutes of Health awarded $8.5 million to NDRI to extend its efforts to rare disorder research.

When NAPE began to focus on PXE gene identity research, NDRI was focused on disorders affecting huge numbers of people. They would not have been interested in PXE, and at that time we didn't need help. We had Dr. Ken Neldner who had developed the largest caseload of PXE patients in existence. His own research identifying PXE characteristics, published in Clinics in Dermatology, 1988, set the foundation for future research. He easily supplied a study sample of one hundred families with two PXE-affected siblings for the gene project. A lab, established at Harvard by Dr. Klaus Lindpaintner of Roche Genetics, selected Dr. Berthold Struk for the research, with the result we all know - ABCC6 was identified in 2000. And thanks to that discovery, PXE research today is conducted around the globe.

This was the dream of Dr. Neldner, and NAPE will continue to pursue his vision for a treatment and eventually a cure. After a long pioneering career in PXE patient care and research, Dr. Neldner is retired. We no longer can call on him to identify patients who might participate in specific research projects. We have learned much from him and will use that knowledge to continue his work. And now, we have NDRI to coordinate our efforts to support new research. NDRI will work directly with PXE

researchers to develop protocols for supplying needed human samples. They have a network of cooperating labs and hospitals with 24-hour per day - seven days per week service. Their own lab with skilled personnel can assist scientists in various research tasks. NDRI has a proven track record which has resulted for the last 24 years in financial support by the National Institutes of Health. NAPE's Board is delighted to announce our partnership with NDRI which has the potential to encourage new research. Its success depends on our willingness to provide needed human tissue and/or fluids for specific projects. This issue of *PXE Awareness* presents NDRI from its inception in 1980 to its new commitment to add rare disorder research support while continuing existing support programs. Please read NDRI's impressive story, reprinted here from their own newsletter, *The NDRI Interchange*, March, 2010. For more information, check out their website (www.ndriresource.org) and begin to contemplate your role in cooperation with our scientists to make the same kind of difference we made with the gene search. At this moment, NDRI personnel, with assistance from a NAPE PXE researcher, are developing registry requirements for PXE research. Soon we will contact NAPE members with information needed for research participation. NAPE will not give your name or contact information to NDRI. It will be up to each of us to make that contact. Please join with me and NAPE's Board as we take the next significant step in stopping PXE.

Finally, please note our 2010 biennial meeting in Philadelphia this October 22 and 23. Details will appear in the July issue of *PXE Awareness*. An excellent patient-focused program is planned. It will include a presentation by NDRI staff and will provide an opportunity to ask questions. Please join us as we continue our mission to "cope until the cure."

With excitement in our shared future,

Fran Benham, PhD

NDRI - CELEBRATING 30 YEARS 1980-2010
MAKING RESEARCH HAPPEN

30 Years Connecting Scientists with a Continuous, Reliable Source of Human Biomaterials for Research

In 1980, the design of a new paradigm, NDRI, changed the course of scientific research by providing a reliable source of all types of human biomaterials to scientists prepared precisely according to their research protocols. NDRI was the first design and implementation of a national prototype for continuous recovery, preservation and distribution of human cells, tissues and organs accompanied by medical histories. Thanks to NDRI, over 300,000 human biomaterials that once were trashed, incinerated, or stored in formaldehyde became a national resource for researchers on the cutting edge, developing new treatments for diseases that affect millions of people around the world. New findings from research studies using NDRI biomaterials are documented in over 100 new publications each year, totaling several thousands in the last two to three decades. NDRI's contribution to disease research acknowledges one pivotal fact - one of the best ways to study human disease is to study human tissue. "Many diseases especially rare diseases have few or no animal models," explains NDRI Founder and President Lee Ducat. "It became clear to us, early on, that researchers needed our help to answer the big question – does what happen in a mouse or other lab animals happen in human beings?" Before NDRI, research laboratories were struggling to find the human tissues they needed, often dependent solely on what they could negotiate from limited pathological samples obtained at local institutions. Research study designs rarely included human tissues other than skin or blood because on a broader scale, human biospecimens were just not available in reliable numbers. An early advisor and participating NDRI researcher, S. Michael Mauer, M.D., University of Minnesota Medical School, called NDRI "a prototype of unparalleled importance."

NDRI – the Beginning of a New Paradigm for Science

The journey began with a trip Lee Ducat made to St. Louis to visit Paul Lacy, M.D., Ph.D., then Mallinckrodt Professor and Chairman, Department of Pathology, at Washington University School of Medicine. "That is where I first saw what pancreatic islet cells looked like," Lee recalls. Dr. Lacy told her, "We need human pancreas to continue our

islet cell isolation research. If anyone can help us get it, Lee, you can." Was he serious? She knew he was and he needed her help. "Paul Lacy was my teacher and mentor, I felt obliged to try to get him the tools he said he needed to cure diabetes." Lee returned to Philadelphia and began to gather the knowledge she needed for what seemed her biggest challenge. She met with hospital administrators and organ procurement organizations (OPOs) to find out if it was possible to recover discarded human tissue in a viable way. Several meetings with National Institutes of Health (NIH) leadership led Lee to help organize a conference of NIH scientists, who in every discussion group across all disciplines reported that to advance their studies they needed a reliable source of human tissues. Lester Salans, M.D., then Director at the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK), became a key advisor in this early effort. Dr. Salans summarized, "The availability of human tissue for the study of diabetes will permit for the first time, clinical researchers to directly investigate the disease and its complications in man, and to extrapolate findings of basic research in laboratory animals to the human condition." Although NIH leadership recognized the potential value of a prototype for national human tissue collection for research, adequate funding was not available. Lee was successful in securing close to $3 million in funding from Pew Memorial Trust in Philadelphia to design and build the NDRI resource. With that funding, NDRI was founded as a program of the Juvenile Diabetes Foundation in 1980. With the help of NDRI's scientific advisors, systems were designed for researcher application, peer review of research projects and rotation for tissue deliveries. In less than a year, systems put in place were tested when the first tissues were recovered and delivered. A placenta and umbilical cord, from a diabetic mother who called to offer her tissue, were delivered to the lab of Nicholas Kefalides, M.D., Ph.D., and pancreas tissue recovered from a transplant donor was sent to Franz Matschinsky, M.D. for his work at the University of Pennsylvania.

Pioneering in support of islet cell research

NDRI staff and advisors worked with OPOs around the country to target pancreas from organ donors for Paul Lacy, M.D., Ph.D., and David Scharp, M.D., at Washington University in St. Louis, two of the world's recognized leaders in diabetes research. By 1985, these scientists had developed their islet cell isolation and purification techniques using pancreas from NDRI. Their seminal research to isolate and transplant human islets and the first clinical trials in humans forged a new pathway for diabetes researchers in search of a cure. This work would

not have been possible without the pancreas tissue from NDRI. Islet cell transplant research continues at multiple institutions around the world. Hope remains that this research might ultimately lead to a new treatment or a cure for patients with insulin dependent diabetes. Looking back, Paul Lacy, M.D., Ph.D., who became NDRI's Founding Chairman commented, "NDRI has transformed the attitude of medical scientists from ignoring the use of human tissue in research to one of requiring these tissues for the study of human disease. New and important findings would not have been made in the absence of this unique organization." Another early NDRI advisor, Bernard Leibel, M.D., Hospital for Sick Children, Toronto, Canada, reflected, "The NDRI is a concept replacing modeling with reality. For medical science, it offers an unrivaled opportunity."

NDRI systematically continued to build a broad-based national network of tissue and organ procurement sources, each year adding new hospitals, eye and tissue banks and organ procurement organizations (OPOs), and later satellite tissue retrieval centers, recovering an increasing number and variety of human tissues. The team set up a biomaterial preservation and storage facility in Philadelphia and in less than two years had delivered 1,000 tissues for research. NDRI advisor Howard Nathan, now President and CEO of Gift of Life Donor Program, worked with NDRI from the beginning to facilitate the systemized retrieval of non-transplantable organs for research. "I am personally proud of my association with NDRI and grateful for being able to have had the opportunity to contribute to the growth of NDRI over last 30 years as an advisor and through Gift of Life Donor Program's work as a founding site. Giving families the option to donate so they can make a difference in perhaps tens of thousands or millions of peoples' lives is really something that makes families feel that out of a tragedy that, good will come. To be a part of something bigger than what we are, through a group like NDRI is very exciting and very fulfilling in your life's work, and NDRI will be a part of the future in curing disease."

NDRI grew quickly with top scientists on its Board of Directors and with researchers from all over the country requesting tissues. One of the first Board members, Abner Notkins, M.D., now Principal Investigator, Infection and Immunity Branch, National Institute of Dental & Craniofacial Research, has said, "The NDRI has had an enormous impact, and contributed tremendously to the research of thousands of scientists. It is one of the best examples of how the efforts of a handful of private citizens can have a major impact on diseases that afflict millions of people around the world." In discussing his studies on virus

induced autoimmunity, Dr. Notkins, commented, “If it wasn’t for NDRI these studies on human tissue simply would not have been possible.”

NDRI gained support and recognition from national leaders. Senator Arlen Specter became aware of NDRI, a Pennsylvania constituent with offices in Philadelphia, as a new effort to advance research. Senator Specter, who with his understanding of medical research and his support of drug development to find new treatments and cures, has been an advocate of NDRI for over two decades and remains supportive of the progress NDRI has made to bring human biomaterials for study to the research laboratory. A turning point for NDRI was funding from the National Institutes of Health to serve as a resource for NIH scientists. NDRI has received continuous NIH funding support for the last 24 years as part of a “Multi-Institute Initiative” and in 2008 was awarded a five year grant to continue providing a full scope of research biomaterials with core support from NCRR Director, Barbara Alving, M.D., and Program Officer, Rosemarie Filart, M.D. Additional support is from ORDR, the Office of Rare Diseases Research, NEI, National Eye Institute, NIDDK, National Institute of Diabetes and Digestive and Kidney Diseases, NIAMS, National Institute for Arthritis and Musculoskeletal and Skin Diseases, NIAID, National Institute of Allergy and Infectious Diseases and NHLBI, National Heart, Lung and Blood Institute.

NDRI offers customized service to scientists

More than 20,000 human biomaterials of all types come through the NDRI program each year and are matched to the protocols of some 500 researchers at 245 centers. The NDRI database of participating researchers has grown to be the largest in the world of researchers studying human tissue. More than 100 publications each year describe scientific progress conducted using human biomaterials from NDRI. The NDRI repository holds more than 400,000 samples. NDRI has created a unique Online Biomaterials Catalogue, the only one of its kind offering instant access for researchers to the human biospecimens they need from a collection of some 9,000 samples on the Internet. Arthur Rubenstein M.B.B.Ch., Executive Vice President, University of Pennsylvania Health System, Dean of the School of Medicine, has said, “NDRI provides a unique service to investigators all over the world and has become indispensable to many research projects. Its spectacular success exceeds even our most optimistic expectations and is a tribute to the foresight, drive and vision of Lee Ducat its founder.”

In 2010, NDRI remains the leading national organization to connect human tissue, critical clinical data and donor medical histories with the research scientists working on new therapies and cures for human diseases. NDRI has built an impressive list of partnerships working with 200 tissue collection centers around the country that include just about every organ donor organization, hospitals, eye banks and medical centers. NDRI has created programs, which bring *post mortem* tissue to scientists from all over the country directly to their laboratories. NDRI has the talent and "know how" to construct networks of surgical centers for recovery of specific tissues from surgical procedures that scientists require for their studies. As a researcher responder organization, NDRI continues to design new systems and networks to recover biomaterials from specific types of donors with rare, complex and common diseases. NDRI continues to reach for the leading edge in the development of new resources and new technologies to serve scientists nationally.

10 NDRI Today and Dedicated to the Future of Science

Successful specialized programs designed for science in support of stem cell research…

In response to the embargo on human embryonic tissue for stem cell research, NDRI set up the systems to recover alternative resources for stem cell scientists. NDRI's goal in setting up this program was to target adult tissues known to have robust stem cells. Networks were set up to recover bone marrow from vertebral bodies and enlist centers to recover birth tissues including cord blood, placenta and umbilical cord. In addition, NDRI was able to provide isolated adult stem cells, CD34+ cells, CD34+ depleted cells, and mononuclear cells. Umbilical cord blood recovered by NDRI has been used for studies of immune depression, identification of novel tumor antigens, regulation of progenitor cell differentiation, patterns of gene expression, cellular replacement therapy and more. "Myself and a lot of my colleagues really do rely on NDRI to provide those important controls for all those different experiments that we do at the Genome Institute," says David Bodine, Ph.D., Head of the Hematopoiesis Section, National Human Genome Research Institute. "NDRI has been a partner in our research for 15 years. As a matter of fact, I probably would have chosen a different avenue of research, had I not had NDRI to help us along."

NDRI successful collaboration with JDRF in support of diabetes research…

NDRI's national tissue procurement network provides discard transplant pancreas from consented donors, with both Type 1 and Type 2 diabetes, never before targeted for recovery of organs for research. NDRI also provides isolated pancreatic islet cells from normal, Type 1 and Type 2 donors. For the first time, through "nPOD," the Network of Pancreatic Organ Donors with Diabetes, funded by JDRF, NDRI is collaborating to serve scientists with unprecedented access to Type 1 donor pancreas and other organs for study, including from recently diagnosed individuals, as well as long term diabetics. According to "nPOD" Director Mark Atkinson, Ph.D., Professor of Pathology, University of Florida, "A key to the success of 'nPOD' has been our partnership with NDRI. When 'nPOD' started, we had high hopes for what the program would tell us regarding the causes of Type 1 diabetes and guidance to efforts seeking to find a cure for the disease. Two years later, I think even skeptics would be amazed at the progress we have seen with the program." Through this collaboration, NDRI has made it possible for researchers to discover that the pancreas is an organ of remarkable heterogeneity and that insulin positive beta cells may still function in some longterm diabetics. Most recently, as illustrated by George Eisenbarth, M.D., Ph.D., Executive Director, Barbara Davis Center for Childhood Diabetes, two patterns of childhood onset pathology have been defined termed type A (presumably immune mediated) and Type B.

In collaboration with "nPOD," NDRI is working with George King, M.D., Director of Research, Joslin Diabetes Center, to build a registry of some 500 Joslin Medalists, who have lived 50 years or more with Type 1 diabetes, many of whom have escaped serious complications. Through NDRI's Private Donor Program, *post mortem* recoveries of tissues donated by these Medalists are coordinated throughout the country by NDRI's national network of 40 recovery experts. NDRI is the only national program that can coordinate *post mortem* recovery throughout the United States for scientists, no matter where the donation may occur. Studies of the Medalists so far have indicated that as many as 30-40 percent may have beta cells that continue to make insulin. "It is indispensable to the 'nPOD' program to have the NDRI infrastructure and systems to support the Medalist project, to quickly get the project moving," says Dr. King. "It would have been impossible for us to set up this system on our own."

George Eisenbarth, M.D., Ph.D., describes “nPOD” as “A remarkable collaborative effort between ‘Medalists’ who have lived more than 50 years with diabetes and volunteered to provide pancreas for research at the time of their passing away, Dr. King at Joslin, heading the medalist studies, and Lee Ducat, doing what the academic community would have great difficulty organizing, namely, obtaining and rapidly processing the donated pancreas, and ‘nPOD’ providing the web portal to view the pancreas by scientists throughout the world.” This collaboration he says, “is giving us our first understanding that there is tremendous heterogeneity for what we call Type 1 diabetes. Understanding this heterogeneity will certainly impact both diagnosis and therapies of the future.”

In support of cancer research…

NDRI was first to develop a national program to recover cancer tumors with supporting pathological data. Thousands of tumor samples each year are recovered for studies on leukemia, lymphoma, cancers of the liver, prostate, lung, breast, ovaries, uterus, cervix, colon, thyroid, melanoma and brain. Researchers also have access to NDRI’s Comprehensive Pan Cancer Tissue Microarray consisting of 642 unique cases with 522 tumors representing 20 major tumor types and 129 normals in a five slide set providing important information to scientists investigating new ways to detect and treat cancer.

In support of genetic research…

NDRI was first to create a large registry of families for research. In 1988, NDRI established the HBDI, the genetics division of NDRI. HBDI is one of the world’s largest collections of families with Type 1 diabetes, making available to scientists important family history data, cell lines sera, buffy coats and DNA for research.

In support of HIV/AIDS research…

NDRI is the only national tissue resource to provide HIV donor tissue to scientists. With funding from NIAID, the National Institute of Allergy and Infectious Diseases, NDRI created the very first national systems to collect infectious human tissues from both HIV-positive and non-symptomatic HIV donors for scientists.

In support of eye research…

Early on, NDRI designed the systems to retrieve eye tissues for studies of macular degeneration, diabetic retinopathy, glaucoma, cataracts and retinitis pigmentosa, and more. NDRI recovers some 4,000 human eyes and eye parts including retina, iris, lens, aqueous humor, conjunctiva and poles, donated each year for scientists conducting hundreds of studies.

Moving to provide short hours *post mortem* tissues for research studies…

Scientists today are looking for organs and tissues with extremely short *post mortem* times, in many cases, requesting these be delivered fresh with no processing. NDRI has designed systems to recover organs and tissues within 0 to 4 hours *post mortem*. In addition, NDRI is working with OPOs to expand potential tissue recoveries from DCD, deceased cardiac donors. Tissues are collected within short *post mortem* times. These donors are key to expanding the recovery of human liver and multiple other organs maximizing short hour *post mortem* organ recovery for scientists and could potentially provide multiple viable organs for research.

In support of rare disease research…

NDRI coordinates networks to recover human organs and tissues, both diseased and normal, for the study of hundreds of rare and uncommon diseases that affect some 25 million people around the world. With funding from the Office of Rare Diseases Research, NDRI is partnering with a growing network of Voluntary Health Organizations, some 50 presently, to expand and advance rare disease research, building donor and researcher registries and biorepositories. Through its Private Donor Program, NDRI is reaching out to those having surgery or those consenting to *post mortem* donation, helping them understand that we each have the power to impact science during our lifetime.

NDRI's successful collaboration with the Cystic Fibrosis Foundation produces two new drugs…

Working with the Cystic Fibrosis Foundation, NDRI developed systems to recover explanted lungs for CF. Through our donor registry we are able to coordinate the collection of disease lungs that

are removed prior to transplant. Through this effort, NDRI facilitated breakthrough development of two compounds, now in clinical trials, that target the mechanisms at work in cystic fibrosis Eric Olsen, Ph.D., Vice President and Program Leader, Vertex Pharmaceuticals Inc. to predict, “We think we are on our way towards a cure for CF.”

The NDRI Board of Directors is committed and confident that human tissues provided by NDRI nationally and internationally have reshaped the scientific landscape throughout the world, have created a new paradigm and catalyzed a multitude of possibilities for future research. The NDRI Board of Directors advisory to new NDRI initiatives, are under the chairmanship of Meenhard Herlyn, D.V.M., D.Sc., Professor and Program Leader, Molecular and Cellular Oncogenesis Program, and Associate Director for Translational Research, Wistar Institute Cancer Center, and includes, David Bodine, Ph.D., Head, Hematopoiesis Section, National Human Genome Research Institute, NDRI Chairman Emeritus, Hal Broxmeyer, Ph.D., Distinguished Professor, Chairman & Mary Margaret Walther Professor of Microbiology/Immunology, Scientific Director of the Walther Oncology Center, Professor of Medicine, Indiana University School of Medicine, NDRI Chairman Emeritus, D. Walter Cohen, D.D.S., Chancellor Emeritus, Drexel University College of Medicine, Dean Emeritus, School of Dental Medicine, NDRI President and Founder, Lee Ducat, Paul Meltzer, M.D., Ph.D., Advisor to the NDRI Board, Chief, Genetics Branch, CCR, NCI, Ali Naji, M.D., Ph.D., J. William White Professor of Surgery, Director Kidney/Pancreas Transplantation Center, Director of the JDRF-Penn Islet Transplantation Program, University of Pennsylvania School of Medicine, Lou Philipson, M.D., Ph.D., Professor, Department of Medicine, Section of Endocrinology, Diabetes and Metabolism and Director, Kovler Comprehensive Diabetes Center, University of Chicago, R. Paul Robertson, M.D., Past President, American Diabetes Association, President & Scientific Director, Pacific Northwest Diabetes Research Institute, Michael White, member of the JDRF Board of Directors and former JDRF Chairman of Research.

National Association for Pseudoxanthoma Elasticum

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No membership fee is required, although donations are needed to pay operational expenses, including telephone, fax, email, website and newsletter services.

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PLEASE COMPLETE THE SECTION BELOW IF YOU HAVE PXE, THINK YOU HAVE PXE, OR ARE FILLING THIS OUT FOR SOMEONE ELSE

Name: _____ **Phone:** _____

Email: _____ **Fax:** _____

Address: _____

City: _____ **State:** _____ **Zip:** _____ **Country:** _____

Male ❒ **Female** ❒ **Birthdate:** _____ **Age:** _____

I am diagnosed with PXE ❒**Yes** ❒ **No** **Newsletter:** ❒ **Print** ❒ **CD**

Are you legally blind? ❒ **Yes** ❒ **No** ❒ **Email notification**

Do others in your family have PXE? ❒ **Yes** ❒ **No** **If so, who? (Mother, Father, Sibling, etc. & Name)** _____

_____

Please list any medical problem(s) you are experiencing: e.g., eye involvement, skin lesions, heart problems, gastric bleeding, etc., and comments/questions (use another page if required):

_____

_____

_____

Are you willing to be contacted by another who wishes to talk with someone else who has PXE? ❒ **Yes** ❒ **No**

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