



# NCC Collaborator

*Expanding Genetic and NBS Services Through Multifaceted Partnerships*



## The Power of Partnerships

Partnerships take many forms, from a couple gliding effortlessly on the dance floor to brokering a business deal or working together towards mutual goals while freely sharing complementary strengths and resources. True partners share risks and rewards to produce results neither partner could have attained alone.

The Regional Collaboratives (RCs) and the National Coordinating Center (NCC) have engaged in many fruitful partnerships with each other during the past seven years—and they have also partnered with others to attain their goals. In this issue of the *NCC Collaborator* you will read about some exciting and creative partnerships between the RCs and entities outside of the NCC/RC system.

- **NEGC** has partnered with the Vermont Child Health Improvement Program to bring new tools to their QI projects;

- **NYMAC** and the Community-Based Sickle Cell Project of Brookdale University and Medical Center have brought culturally competent sickle cell education to the Brooklyn community;
- **SERC** has engaged in a cluster of partnerships to enhance their work in the areas of long-term follow-up, genetic metabolic nutrition, emergency preparedness and more;
- **Region 4** is expanding its Inborn Errors of Metabolism Collaborative to 13 clinics in 10 states after receiving a \$4.5 million NIH grant;
- The **Heartland RC** jumpstarted its activities related to transition from pediatric to adult care by partnering with D-70 Integrated Community Systems for Youth with Special Health Care Needs state implementation grantees from Kansas and Missouri;
- The **Mountain States RC** is working with the Medical Home Portal to improve services specific to children with heritable disorders—a partnership that grew out of an AAP Medical Home Visiting Professorship award; and

- The **Western States RC** is engaging with academic and health department experts to collect precedent-setting population data on Very Long Chain Acyl-Co-A- Dehydrogenase Deficiency (VLCADD) and improve health outcomes for individuals living with VLCADD.

At the same time, the NCC again used the American College of Medical Genetics (ACMG) Annual Clinical Genetics Conference as a forum for dialogue among the public health and medical genetics communities and underserved populations with special genetics needs. This past March, Vancouver provided the setting for a community conversation, *Screening for Carnitine-Palmitoyl Transferase, Type 1A (CPT1A) in the First Nations Populations of Alaska and British Columbia*, co-sponsored by 'Kloshe Tillicum' British Columbia and Yukon Territories Network Environment for Aboriginal Health Research and the ACMG Foundation. Families and professionals shared scientific knowledge and personal experiences, but it was the poignancy of the contrasting Alaska Native and First Nations family stories that underscored the power of addressing challenges in the delivery of genetic services through partnerships.

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# Screening for Carnitine-Palmitoyl Transferase, Type 1A (CPT1A) in First Nations Populations: A Community Conversation

A Special Satellite Meeting to the  
ACMG Clinical Genetics Conference

**I**n March, the National Coordinating Center for the Genetic and Newborn Screening Service Collaboratives (NCC) partnered with 'Kloshe Tillicum' British Columbia (BC), Yukon Territories Network Environment for Aboriginal Health Research and the ACMG Foundation to sponsor its second special satellite symposium prior to the ACMG Annual Clinical Genetics Meeting. The session, Screening for Carnitine-Palmitoyl Transferase, Type 1A (CPT1A P479L) in the First Nations Populations of Alaska and British Columbia, took advantage of the international setting in Vancouver, BC, to offer meeting attendees a unique opportunity to participate in a community dialogue between genetics experts, families, researchers, policymakers, and primary care providers. This dynamic symposium highlighted differing cultural and national approaches to the CPT1A P479L variant in these two populations.

## Background

CPT1A deficiency is normally known as a rare autosomal recessive long-chain fatty acid oxidation disorder, presenting as hypoketotic hypoglycemia and metabolic decompensation triggered by fasting, which can progress to seizures, encephalopathy, and sudden death. The clinical significance of the P479L variant in the *CPT1A* gene is unclear and remains controversial. Although it reduces CPT1A enzyme activity in cultured fibroblasts, there is measurable residual enzyme activity. This variant is present in First Nations of BC, Alaska Natives and the Inuit of Nunavut and Greenland where the rate of homozygosity has been documented to be as high as 73%.

## Session Format

The NCC's Alaskan and international partners discussed their experiences in recognizing the presence of the common CPT1A P479L variant, methods to understand the underlying prevalence, and whether the CPT1A P479L variant confers risk for infant mortality in Alaska Natives and BC



First Nations. The session began with a brief overview of NBS programs, regional educational systems, and parameters for recognizing homozygosity for the variant. Researchers presented recent findings and outlined current challenges.

### The Alaska Experience

Thalia Wood, MPH, CLS, Children's Unit Manager for the State of Alaska, discussed the history of CPT1A screening and follow-up in the Alaska Native population. Alaska is geographically very large, yet it is home to less than 700,000 people and has approximately 11,000 births annually. The great geographic distances and sparse numbers of people living outside of a few urban areas raise special challenges with regard to access to newborn screening (NBS) follow-up. Alaska contracts with the Oregon Public Health Lab for analysis of its NBS samples, with the expanded NBS panel introduced in late 2003. By January 2004, the first suspected case of CPT1A deficiency was detected in the Alaska Native population by NBS

with blood spot acylcarnitine profiles. By the end of 2004, six more cases were identified and confirmed with DNA markers. These infants were found to carry the same P479L variant common in Canadian and Greenland Inuit populations and in certain BC First Nations populations.

This high incidence of the P479L variant raised a red flag for the Alaska NBS Program about the need for both further research and community education. In response, the NBS program undertook a quality control study to determine the sensitivity of newborn screening by MS/MS to detect infants homozygous for the variant. This demonstrated that in order for MS/MS based screening to have a high sensitivity (>99%), the NBS program would have to use a cut-off with a low specificity (95%), resulting in an unacceptably high false positive rate. Consequently, the NBS program currently detects ~100 (15%) of the estimated 700 affected infants each year. The complete significance of the variant is still being evaluated along

with its possible contribution to infant mortality. With the knowledge that newborn screening is identifying only 15% of affected infants, it was a call to action for the Alaska Department of Health and Social Services and the Alaska Native community to take the approach that every newborn should be treated as potentially affected with the P479L variant. This resulted in a highly successful, collaborative educational initiative.

The initiative began with a more passive and traditional education approach: brochures were sent to all families who had a child diagnosed with CPT1A deficiency. However, when the explanations in the brochures did not adequately fill the needs of many of the families being targeted, the Alaska NBS program explored alternate approaches. Based upon previously successful health-related DVDs, the state received funds from the Western States Genetic Services Collaborative (WSGSC), Norton Sound Health Corporation, and Southcentral Foundation to develop a storytelling-based DVD, *The Other Energy Crisis, CPT1 Deficiency*, to educate families and local community health aide workers (who often provide rural communities



with critical first line medical care) about CPT1A deficiency. In the DVD, family stories are interspersed with medical information provided by Dr. Matt Hirschfeld, a pediatrician with the Alaska Native Medical Center, Dr. David Koeller, a geneticist with Oregon Health and Sciences University (OHSU), and Thalia Wood. The DVD, which is narrated by an Alaska Native, reviews signs and symptoms of CPT1A deficiency. It also emphasizes that most children with this condition are healthy and will grow and develop normally. Many of the children portrayed in the DVD are playing with their friends or eating healthy foods to reinforce the concept that children with CPT1A deficiency only have health concerns when they undergo a prolonged fast.

Providers and families who have evaluated the DVD have been very positive, particularly regarding its effectiveness in educating health aides and other care providers about CPT1A deficiency. In addition, families who viewed the DVD could accurately describe the most important points. This suggests that children in families with accurate knowledge about CPT1A deficiency may receive better healthcare than those who have not viewed the DVD. (See *NCC Collaborator*, March 2010, page 10).

Ms. Wood concluded her talk by showing the DVD to the symposium attendees.

### The BC Experience

Currently, BC does not include CPT1A deficiency in their NBS panel although apparently symptomatic individuals can be tested. Hilary Vallance, MD, from BC Children's Hospital and

Director of the Provincial Newborn Screening Program, presented the research framework used in BC to learn more about the CPT1A P479L mutation. She reviewed the importance of the CPT1A protein in fatty acid oxidation, classic CPT1A deficiency, and the postulated differences with the CPT1A P479L variant.

Graham Sinclair, PhD, also from the Provincial Newborn Screening Program, and Sorcha Collins MSc, from UBC on Vancouver Island reviewed key principles of participatory action research and used large territorial maps to depict the prevalence of the CPT1A variant in BC, Yukon, Northwest Territories, Nunavut and Greenland—a land mass larger than Alaska, and equally sparsely populated. Again, a high prevalence of the P479L variant was found most commonly in coastal regions. A significant association of the P479L variant with infant mortality in high prevalence areas was presented. The reason for the high prevalence of the P479L variant is speculated on as an historical genetic-dietary advantage with a high fat, low carbohydrate marine diet. The speakers emphasized the challenges they are grappling with since the ho-



mozygosity rate is so high in some regions of BC (up to 25%), and whether the association studies provide sufficient evidence to directly implicate the P479L variant in infant mortality. If a risk exists, about 1% of First Nations infants homozygous for the CPT1A variant are at risk of sudden unexpected death. Although NBS would be technically feasible with a combination of acylcarnitine profiling and DNA testing, the net health benefit (balanced against harms) of recognizing those individuals is not clear.

### CPT1A OHSU Study

David Koeller, MD, a medial geneticist at OHSU and the Alaska-Oregon NBS Program, reported on some new research findings on five cases from overnight fasting studies conducted at OHSU to document evidence-based

*Continued on page 13.*



# the new england **negc** genetics collaborative

*Submitted by Monica R. McClain, PhD, Project Manager, NEGC*

## New England Genetics Collaborative Partners with the Vermont Child Health Improvement Program

The collaboration between the New England Genetics Collaborative (NEGC) and the Vermont Child Health Improvement Program (VCHIP) began when VCHIP's Executive Director, Dr. Judith Shaw, was recruited to serve on the NEGC advisory committee. VCHIP is a population-based child and adolescent health services research and quality improvement program housed at the University of Vermont. Its mission is to optimize the health of Vermont's children by supporting measurement-based efforts to enhance private and public child health practice. VCHIP facilitates improvements in care for Vermont's children by:

- Serving as a motivational force for improving the quality of pediatric health care services by providing knowledge, expertise, and continuous encouragement to Vermont's health care professionals.
- Fostering partnerships with private and public organizations.
- Supporting creativity, excellence, and respect in all interactions.
- Promoting innovation and examining unique approaches to support practitioners in their efforts to improve care through measurement-based initiatives.
- Conducting research.



- Disseminating its growing body of knowledge on successful quality improvement initiatives through publications and presentations.

VCHIP supports clinicians in their efforts to enhance care by providing them with tested tools and techniques of quality improvement, and actively helps clinicians incorporate basic quality improvement principles into their busy practices. NEGC has benefited from its partnership with VCHIP primarily through the leadership of Leah Burke, MD, Pediatric Geneticist, University of Vermont Medical Group at Fletcher Allen. Dr. Burke is participating in two of the NEGC Quality Improvement projects: one is for children who are referred with developmental delays; and the second is a metabolic clinics quality improvement learning collaborative. VCHIP has taken the lead in researching and preparing the Institutional Review Board application for the first project, and for providing data entry for both quality improvement projects. Additionally, the Ver-

mont Medicaid program, Green Mountain Care, has provided matching funds to VCHIP that are being used to provide salary support for Dr. Burke's time spent on quality

improvement activities. This partnership has been essential for Dr. Burke's successful participation in the NEGC quality improvement activities.

Both the NEGC and VCHIP hope to pursue additional collaborations in the future, capitalizing on their shared goals to: 1) promote quality improvement to achieve optimal health for children youth, and families; 2) support collaborations among public and private health organizations to facilitate meaningful and sustainable improvements in health delivery systems; 3) share the results of successful initiatives through trainings and publications; and 4) translate new knowledge into practice. The overall outcome of the partnership between NEGC and VCHIP, with their similarly aligned missions and complimentary programs, is improved health for children.

<http://www.negenetics.org/>

*Submitted by Verna DuBerry Ademu-John, MS, Program Coordinator, Division of Pediatric Hematology/Oncology, Brookdale University Hospital and Medical Center*

## Peer Education Spreads the Word About Sickle Cell Disease

In 2005, the Community-Based Sickle Cell Project at Brookdale University and Medical Center in Brooklyn, NY launched a Sickle Cell Peer Educator Training Program to educate high school students about sickle cell disease and trait, and enable them to become peer educators within their schools and communities. Conducted annually since then, NYMAC has funded the training sessions in recent years. Each training session lasts 7 to 8 weeks, with a two-hour module presented each week.

The Community-Based Sickle Cell Project is a collaborative effort of three hospitals (Brookdale, Kings County Hospital Center and SUNY Downstate Medical Center), a community health center/FQHC (Brownsville Multi-Service Family Health Center), and two community-based organizations (Sickle Cell/Thalassemia Patients Network and Caribbean Women's Health Association). All work together to meet the needs of patients and families with sickle cell disease and trait. The Peer Educator Training is offered in partnership with two college-prep, medically-oriented high schools (the World Academy for Total Community Health [WATCH] and the High School for Medical Professions), and strives to increase awareness of sickle cell disease and enhance genetic education and advocacy within the large African American, Hispanic American, and Caribbean immigrant populations in Brooklyn.



Peers at World Sickle Cell Day

Prior to enrolling in the project the students and their parents acknowledge their responsibilities to the program by signing agreement/commitment and consent forms. The Brookdale Sickle Cell Program Coordinator then conducts the student training. Students receive a training manual that includes information about sickle cell disease, genetics and inheritance patterns, and the role genetic counseling can play in understanding this information. Students also learn and practice presentation skills and techniques, and they are required to complete a sickle cell-focused project (e.g., artwork, paper, etc.) and to make a presentation on some aspect of sickle cell disease or trait, demonstrating that they have achieved a basic understanding of sickle cell trait and disease and have acquired the skills to become sickle cell advocates. Pre- and post-training tests show marked

improvements in students' knowledge of sickle cell disease.

More than 100 students have enrolled in the Peer Educator Training Program, with 74 successfully completing six or more training sessions and receiving certificates. These students have conducted outreach at health fairs, blood drives, and other sickle cell awareness activities in their schools and community. They have also participated in paid summer internships, conducting sickle cell outreach and education at community clinics.

We believe that training students to advocate for a disease is empowering and serves as a culturally competent way to increase sickle cell awareness and advocacy in our community.

<http://www.wadsworth.org/newborn/nymac>



# SOUTHEAST NBS & GENETICS COLLABORATIVE

Submitted by Brian L. Pike, PhD, Program Manager, SERC

## SERC: Partnership for a Common Vision

SERC recognizes the wealth of resources beyond our Regional Collaborative structure and strives to partner with outside groups. As a result, SERC has built strong relationships with many organizations, from professional societies to parent organizations and industry groups. Such partnerships provide opportunities to share knowledge, expertise, and resources that further our common vision of improving newborn screening (NBS) and genetics services.

Perhaps SERC's most notable collaboration is our Long-Term Follow-Up (LTFU) Workgroup, which has welcomed expertise from members of Genetic Metabolic Dietitians International, the Society for Inherited Metabolic Disorders, and the American College of Medical Genetics. Workgroup members are working together to improve patient outcomes by developing nutrition management guidelines. The LTFU workgroup has also collaborated with the Public Health Informatics Institute and the National Library of Medicine on developing information system requirements for LTFU programs; this work culminated in a publication in *Genetics in Medicine*.<sup>1</sup> The LTFU workgroup is furthering

"Partnerships provide opportunities to share knowledge, expertise, and resources that further our common vision"



their informatics work by conducting a pilot information technology capacity assessment in conjunction with the Newborn Screening Translational Research Network and is pursuing a PKU ontology project with the Georgia Institute of Technology, Georgia State University, and others.

Other successful collaborations include work led by the Hemoglobinopathy and Medical Home Workgroups. Our Medical Home Workgroup has partnered with the American Academy of Pediatrics, and our Hemoglobinopathy Workgroup continues to work with the CDC on the Registry and Surveillance System for Hemoglobinopathies.

Emergency preparedness (EP) is a top priority for SERC, and a recent collaboration with Region 4's MyEIF (Emergency Information Forms) [formerly MEMSCIS] is promising. SERC's EP Workgroup chairs participated in a MEMSCIS re-branding workshop that led to recommendations for improvement. Discussions with the South Central Public Health Partnership may also lead

to EP continuing education opportunities for healthcare professionals. SERC's EP and Laboratory Performance Workgroups are also partnering with the Association of Public Health

Laboratories for a regional EP session scheduled for SERC's annual meeting, which is held in conjunction with the Southeast Regional Genetics Group.

Finally, SERC has worked closely with experts from many of the aforementioned organizations, industry groups and parent organizations, like PKU Alliance and Family Voices, to create a much-needed patient-based registry, NBS Connect, which is launching this year. SERC also partners with these groups and others to stay abreast of topics of interest to consumers in our region. Their feedback continues to shape our regional activities.

In short, SERC values its partnerships with groups outside of the Regional Collaborative structure. In fact, we believe that they are crucial to the region's success.

<sup>1</sup>Singh RH, Hinman AR. Newborn dried bloodspot screening: Long-term follow-up activities and information system requirements. *Genet Med*2010;12(12):S261-S266.

<http://www.southeastgenetics.org>



# Region 4 Genetics Collaborative

Submitted by Cynthia Cameron, PhD, Director, and Sally J. Hiner BS, LBSW, Coordinator, Region 4 Genetics Collaborative

## Region 4 Expands Partnerships through the Inborn Errors of Metabolism Collaborative

In 2004, the Region 4 Genetics Collaborative established a workgroup to address long-term follow-up of inborn errors of metabolism (IBEM). The group initially defined data elements to track clinical management and health and developmental outcomes for patients with medium chain acyl-CoA dehydrogenase deficiency (MCADD). In 2007, the Health Resources and Services Administration awarded Region 4 a Priority 2 grant to support this project, and, by 2010, data elements for 24 IBEM had been defined and 225 cases entered into the tracking system.

As news of the project’s progress was shared with the Secretary’s Advisory Committee for Heritable Disorders in Newborns and Children, as well as with participants at several national conferences, interested metabolic specialists across the country sought to join the Region 4 project. In 2010, the National Institutes of Health (NIH) announced a grant opportunity to study the natural history of rare disorders, and Region 4 took the lead in establishing partnerships with new clinics to form the Inborn Errors of Metabolism Collaborative (IBEMC).

In April 2011, NIH awarded \$4.5 million to the Michigan Public Health Institute, which houses the Region 4

Genetics Collaborative, for the IBEMC. Susan Berry, MD, lead of the Region 4 Priority 2 Project, and Cynthia Cameron, PhD, Director of the Region 4 Genetics Collaborative, are co-principal investigators for this grant, which will provide the resources needed to support data collection from 13 clinics representing 10 states (see Table 1).

The IBEMC will collect longitudinal data to better define the natural histories and understand the effect of treatment interventions for patients with IBEM, including:

- Investigating the relationship between NBS values, genotype, and early manifestations and complications of IBEM;
- Evaluating the impact of early identification and intervention on IBEM;

- Informing decision making about optimal public health investment in NBS;
- Clarifying the previously undefined natural history of very rare metabolic conditions; and
- Identifying current nutritional and therapeutic interventions for children with IBEM and evaluating their effectiveness.

Based on current caseloads, IBEMC clinics estimate that they will enter data on more than 2,000 patients by 2016. These data will provide a foundation for clinical trials and result in improved treatment for children with metabolic conditions.

<http://region4genetics.org>

INSTITUTION	STATE
Children’s Memorial Hospital	Illinois
Cincinnati Children’s Hospital	Ohio
Nationwide Children’s Hospital	Ohio
Saint Francis Hospital	Oklahoma
Sanford Children’s Hospital	North Dakota
Riley Children’s Hospital	Indiana
University of Illinois	Illinois
University of Michigan	Michigan
University of Minnesota	Minnesota
University of Missouri	Missouri
University of Pittsburgh	Pennsylvania
Waisman Center	Wisconsin
Wayne State University	Michigan

Table 1: The 13 IMEMC partner institutions, located in 10 states.



# Heartland Genetics and Newborn Screening Collaborative

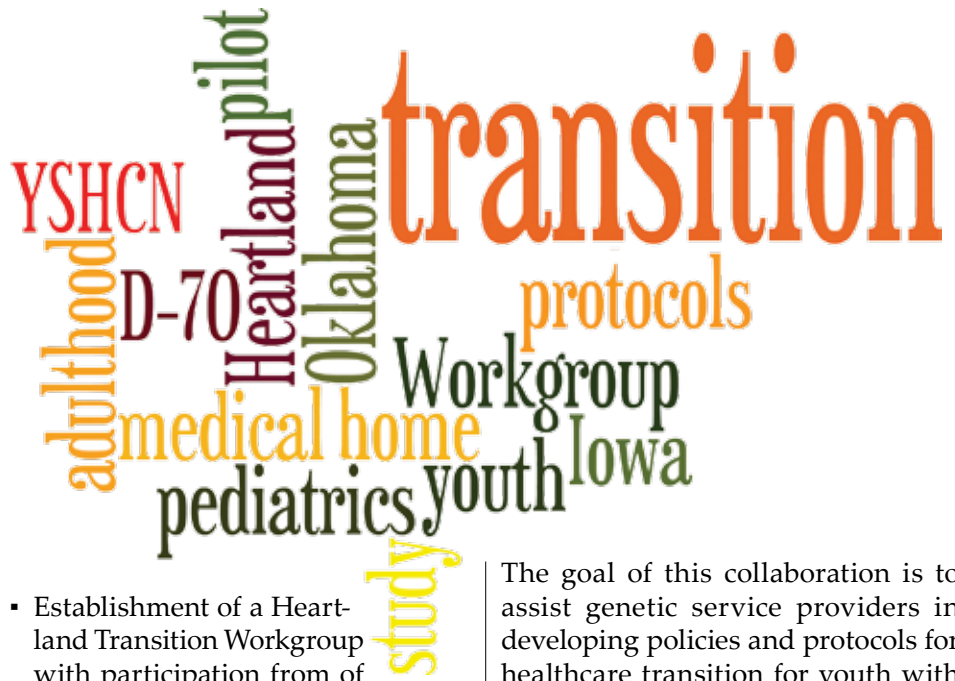
*Submitted by Mary Ann Coffman MS, CGC, Project Coordinator, Heartland Genetics and Newborn Screening Collaborative and Heather Moore, MPH, Project Coordinator, Systems in Sync, Children and Youth with Special Health Care Needs, Kansas Department of Health and Environment*

## Supporting Transition Through Collaboration

*How are transition services for youth with genetic conditions addressed within the Heartland Region? What role do genetic services play in helping adolescents with special health needs transition to adult services?*

These questions led the Heartland Genetics and Newborn Screening Collaborative (Heartland) on a search for current practices in our region. They also led us to discover the HRSA-funded state implementation grants (D-70) for Integrated Community Systems for Youth with Special Health Care Needs (YSHCN) awarded to Kansas and Missouri. These grants support the creation of inclusive community-based systems for YSHCN. Activities that address access to medical home and support for transition to adulthood are central to each of the grants.

A strong partnership between Heartland and the D-70 grantees immediately developed and in April 2010 a meeting was held to address the RC's original questions and identify areas where collaboration would be most effective. At the conclusion of this meeting, the working group recommended that the Heartland focus on the development of a transition model for youth with genetic conditions using medical home principles. This partnership has included:



- Establishment of a Heartland Transition Workgroup with participation from of the D-70 grantees;
- Presentations from the Kansas D-70 staff at the Heartland's 2010 Annual Meeting, held in Des Moines, Iowa in September 2010; and
- Work towards a pilot study/project to address transition services for youth with genetic conditions, described below.

Beginning in the Summer 2011, Heartland will conduct a pilot study with Laura Pickler, MD, at the University of Colorado. Dr. Pickler leads one of three learning collaborative sites for the "Got Transition?" National Health Care Transition Center. Heartland has identified two clinical genetic centers in Oklahoma City (University of Oklahoma Department of Pediatrics, Section of Genetics) and Wichita (Kansas University Pediatric Subspecialty Clinic, Genetic Services) to collaborate with Dr. Pickler's site.

The goal of this collaboration is to assist genetic service providers in developing policies and protocols for healthcare transition for youth with genetic conditions, utilizing medical home model principles.

Heartland's strong and continuing partnership with our D-70 grantee colleagues has opened doors and increased our knowledge about medical transition. It has also accelerated Heartland's medical transition efforts in ways that would not have otherwise been possible.

<http://www.heartlandcollaborative.org/>



*Submitted by Celia Kaye, MD, PhD, PI; Joyce Hooker, Project Manager, and Liza Creel, MPH, Project Coordinator, MSGRCC*

## **MSGRCC Partners with the Medical Home Portal to Improve the Medical Home for Children with Heritable Disorders**

Since early 2010, staff from the Mountain States Genetics Regional Collaborative Center (MSGRCC) have been exploring potential partnerships with the Medical Home Portal, a web-based infrastructure that aims to provide families and professionals with ready access to the reliable and useful information they need to advocate and care for children with special health care needs. MSGRCC sees the Medical Home Portal as a tool that can improve medical and community-based care for newborns and children with heritable disorders. In August 2010, MSGRCC was selected for a Medical Home Visiting Professorship award from the American Academy of Pediatrics National Center for Medical Home Implementation and the National Coordinating Center for the Regional Genetics and Newborn Screening Service Collaboratives. This award gave MSGRCC an opportunity to begin building a strong partnership with the Medical Home Portal, its director, Dr. Chuck Norlin, and primary medical home providers in the eight states comprising the MSGRCC.

On February 24, 2011, MSGRCC hosted its second Medical Home Visiting Professorship Workshop in Phoenix, Arizona, under the leadership of Dr. Norlin, who served as the Visiting Professor. Dr. Norlin facilitated an in-depth workshop that included an overview of the Portal and presentations by Portal partners, including parent representatives and staff from the Utah Food Bank, which provides the Portal with community-based resources from its 2-1-1 telephone information system. Additionally, Dr. Norlin had participants (including physicians, public health leaders, payers, and consumer representatives) work together as state teams to explore the Portal and its many resources. Finally, participants discussed how they could use the Portal in their states to improve medical homes for children with heritable disorders and other special health care needs.

In follow-up to the Medical Home Visiting Professorship Workshop, MSGRCC is working closely with Dr. Norlin to identify opportunities to expand the Portal into other states in the Mountain States Region. This includes identifying state resources and contacts, such as those at state 2-1-1 systems, who can be key state partners. Portal staff members are communicating regularly with the state teams that expressed strong interest in bringing the Portal to providers in their states. MSGRCC intends to work closely with Dr. Norlin and his staff to track those states that do implement the Portal for use in improving care of children with heritable disorders. For more information on the Portal, please visit [www.medicalhomeportal.org](http://www.medicalhomeportal.org).

<http://www.msgrcc.org/>





Submitted by Arthur K. Yu, MS, CGC, VLCADD Project Coordinator, WSGSC

## Public Health-Medical Partnerships Help Study of Rare Genetic and Metabolic Conditions Identified by Newborn Screening

Newborn screening (NBS) is often described to parents as a blood test performed to help identify whether their baby may be affected with a rare genetic/metabolic condition at birth. Although there currently are no cures for these genetic/metabolic conditions, NBS serves an essential public health function because early diagnosis and treatment can help improve the growth and development of affected infants.

For many of these rare conditions (i.e., fatty acid oxidation disorders), treatment recommendations were traditionally based on individual case reports, trial and error, and/or the physician's varying clinical experience. Evidence-based treatment recommendations are often not available and are difficult to develop, given the small number of affected individuals available for research.<sup>1</sup>

To address part of this information gap, the Western States Genetic Services Collaborative (WSGSC) used supplemental funding from HRSA to conduct a pilot project looking specifically at individuals with Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCADD). If left undiagnosed or untreated, VLCADD can result in death.



Establishing the VLCADD project as an RC priority for 2011, the WSGSC is taking advantage of pre-existing partnerships by working closely with NBS program staff from the California Department of Public Health–Genetic Disease Screening Program, the Washington State Newborn Screening Program, and the Northwest Regional Newborn Screening Program. This multi-state, multi-partner collaboration will ensure that the VLCADD project has a sufficiently large study population to produce significant findings.

In addition, the WSGSC developed new partnerships with metabolic genetic specialists from California, Oregon and Washington who are integrally involved in the care of in-

dividuals affected with VLCADD. This includes the recruitment of two University of Washington faculty members, an epidemiologist, Dr. Sverre Vedal, to aid in the statistical analysis, and a metabolic geneticist with a special interest in VLCADD, Dr. Lawrence Merritt III, to serve as principal investigator for the project. The prospective VLCADD study group is predicted to comprise one of the largest study groups to date. Partners hope that by leveraging the strengths and resources of each of the collaborative project team members, this pilot project will be able to compile a robust VLCADD-related dataset and, through analysis, contribute to the development of evidence-based consensus recommendations for the diagnosis and treatment of individuals with VLCADD.

Data collection for the VLCADD project has already begun. Questions or comments regarding this project may be addressed to Arthur Yu at [arthur@hawaiigenetics.org](mailto:arthur@hawaiigenetics.org).

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<sup>1</sup>Solis JO and Singh RH. Management of fatty acid oxidation disorders: a survey of current treatment strategies. *J. Am. Diet Assoc.* 2002; 102(12):1800-1803.

<http://www.westernstatesgenetics.org>

“We carry our babies and bury them, but never stop loving them...please help us so that they do not die.”

Screening for Carnitine-Palmitoyl Transferase, continued from page 5

management in symptomatic children from Alaska with the CPT1A variant. His findings highlighted the importance of remaining vigilant about diet and avoiding fasting.

### Clinical Summary

Laura Arbour, MD, MSc, a medical geneticist with the University of British Columbia and the Vancouver Island Health Authority, reviewed what is known and unknown about the variant; for example, the prevalence is well established. In addition, an association with sudden unexpected death in BC, Nunavut and Alaska has been established, although the contributing factors to infant mortality remain unclear. Possible interacting factors might be prolonged fasting, food security, sleep position, and prematurity. The causes of infant mortality in First Nations and Inuit populations are complex. The association of the P479L variant with infant mortality requires

attention and research is needed to understand the contributing factors to risk and whether screening and/or public health initiatives can make a difference in the prevention of infant mortality.

After these collective comments and presentations, it was apparent that translating the science into the best public health for all is complex and must consider a broad array of issues for practice and policy.

### Family Stories

Lucy Barney, MSN, RN, Provincial Leader, Aboriginal Health, with the British Columbia Ministry of Health Services, Perinatal Services, led the highly interactive Community Conversation that followed. Ms. Barney began by using a schematic of the medicine wheel prepared by Lee-Anna Huisman, MSc, who previously developed a framework for genetic counseling in BC First Nations (see Figure 1). This schematic provided a context for the community discussion on the impact of living with knowledge of the CPT1A variant. She then invited the families in the audience to the microphone to share their stories, worries, and experiences, and to relate them to this framework. The comments shared by the families were both poignant and memorable.

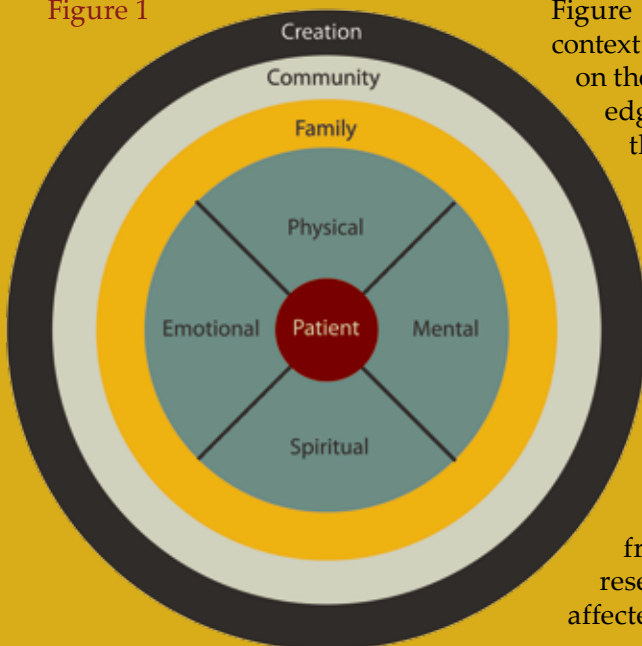
In the audience were two families from Alaska, and approximately 25 individuals from BC. The BC families represented three generations, from affected and unaffected infants and



children, to parents, foster and adoptive parents, and grandparents. All were very open in expressing their needs and experiences, as well as their sense of isolation, desire for more information, and countless pleas for help. While the families from Alaska were consistently informed of the facts and reiterated the sense of empowerment they derived from this, many families and a few community care providers from BC asked repeatedly for help in feeling less disenfranchised and more empathy toward their unmet expectations when seeking help. As one grandmother stated so eloquently, “We carry our babies and bury them, but never stop loving them...please help us so that they do not die.” Another pleaded, “Why are my babies dying? Help me to understand.”

Family members also stated that seeing the DVD produced by Alaska was an eye-opening experience. Family members expressed a need for personalized, culturally sensitive information, and to feel that health professionals were available to communicate with them.

Figure 1



Medicine wheel derived from UBC MSc Genetics Thesis by Lee-Anna Huisman, 2010

Sensing a disconnect and dissatisfaction between the questions families posed and the responses from the panelists, Dr. Arbour assured the BC families that this dialogue would continue in local Victoria and BC communities and that solutions would be discussed. The session concluded with validation of concerns, affirmation of the importance of education, and the empowerment and positive impact that families experience when they have the tools to care for their children. Panelists and audience members alike were impressed by the varying experiences between Alaska and BC, not just in a systemic and programmatic sense, but also in how the knowledge of the presence of the P479L variant impacts individuals at the local level. The symposium was a powerful reminder that understanding the genetics and mechanics of a disorder is only the beginning, and that ensuring family engagement, faith, and trust is fundamental to taking the next steps to successfully managing and preventing the health consequences of a disorder such as CPT1A deficiency.

### Take Home Messages

1. The CPT1A P479L variant affects extended families physically, mentally, spiritually and emotionally. The first two years of life seem to be the hardest for many families. During this time period, families are looking for and eager to receive information and support.
2. The importance of health professional and community health worker education cannot be over emphasized in preventing morbidity and mortality in affected patients.
3. Educated families are empowered when they have simple, understandable information. This gives them a sense of control and allows them to be their own advocates.
4. The unique population characteristics of the P479L variant, including evidence for medical risk and benefit need to be carefully considered when designing effective screening, follow-up, education and management strategies in high frequency populations.

5. Dialogue between Alaska Native and First Nations families, policy makers and their health care providers is crucial as research is translated into broad population management and public health strategies.

6. There is a need for further research to:
  - understand the interplay between other risk factors and the P479L variant;
  - further characterize the natural history of the variant; and
  - study the potential health benefit of the P479L variant

To order a the DVD, contact Thalia Wood at [thalia.wood@alaska.gov](mailto:thalia.wood@alaska.gov)

*Laura Arbour, Judith Benkendorf, Alisha Keehn, David Koeller, Hillary Vallance, Meredith Weaver and Thalia Wood contributed to this article.*

All photographs were taken with permission during the session.

## CPT1A Primer

- Carnitine-palmitoyl transferase type 1A (CPT1A) is a mitochondrial enzyme necessary in the transport of long-chain fatty acids for the production of energy from fat when a carbohydrate source is not readily available.
- In the United States, CPT1A deficiency is part of the uniform core NBS panel. It is not part of the newborn screening panel in Canada, although health care providers may specifically request the test.
- Frequency in First Nations' Communities: In coastal British Columbia (BC) First Nations populations, the amino acid 479 (P479L) variant in its homozygous state has been documented to be as frequent as 25%, up to 50% in some Alaska Native populations, and as high as 73% in Canadian Inuit populations.
- Although only a small proportion of those with the P479L variant come to attention clinically, in all three populations the variant has now been shown to be associated with an increased risk for infant mortality. It is suspected that intercurrent illness may increase risk for hypoglycemia in infants and young children homozygous for the variant, but paradoxically, there is also some evidence the variant may confer a protective effect for adult onset cardiovascular disease and obesity.



# NCC Calendar

## NCC & RC MEETINGS

<b>Mountain States Genetics Regional Collaborative Center (MSGRCC)</b> Annual Meeting	Jul 12-14	Denver, CO
<b>Southeast NBS and Genetics Collaborative/ Southeast Regional Genetics Group (SERC/SERGG)</b> Annual Meetings	Jul 21-23	Asheville, NC
<b>Heartland Genetics and Newborn Screening Collaborative (Heartland RC)</b> Annual Meeting	Aug 24-26	Bismarck, ND
<b>Western States Genetic Services Collaborative (WSGSC)</b> Annual Regional Summit	Sep 12-14	Seattle, WA
<b>Region 4 Genetics Collaborative (Region 4)</b> RC Meeting	Sep 13-15	Lansing, MI
<b>New England Genetics Collaborative (NEGC)</b> Annual Meeting	Nov 15-16	TBD
<b>NCC/RC/GSB PD/PM Annual Meeting</b>	Nov 17-18	Bethesda, MD

## NATIONAL CONFERENCES

<b>Genetic Alliance</b> Annual Conference: 25 Years of Innovation	Jun 23-25	Bethesda, MD
<b>American Public Health Association (APHA)</b> Midyear Meeting : Implementing Health Reform – A Public Health Approach	Jun 23-25	Chicago, IL
<b>Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC)</b> Meeting	Sep 22-23	Washington, DC
<b>National Coalition for Health Professional Education in Genetics (NCHPEG)</b> Annual Meeting: Strategies for Evidence-Based Genetics Education	Sep 26-27	Bethesda, MD
<b>American Society for Human Genetics (ASHG)</b> Annual Meeting in conjunction with the International Congress on Human Genetics	Oct 11-15	Montreal, Canada
<b>Early Hearing Detection and Intervention (EHDI)</b> Partnering for Progress (3 concurrent related conferences)	Oct 26-28	Raleigh, NC

## NATIONAL CONFERENCES, continued

<b>National Society of Genetic Counselors (NSGC)</b> Annual Education Conference	Oct 27-30	San Diego, CA
<b>American Public Health Association (APHA)</b> Annual Meeting and Exposition	Oct 29 - Nov 2	Washington, DC
<b>Association of University Centers on Disabilities (AUCD)</b> Annual Conference and 40th Anniversary Celebration	Nov 6-9	Crystal City, VA
<b>Association of Public Health Laboratories/ Centers for Disease Control (APHL/CDC)</b> NBS and Genetic Testing Symposium	Nov 7-10	San Diego, CA
<b>American College of Medical Genetics (ACMG)</b> Annual Clinical Genetics Meeting	Mar 27-31, 2012	Charlotte, NC



June 2011 Edition Volume 5, Number 2

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The NCC Collaborator is the official newsletter of the National Coordinating Center for the Regional Genetic and Newborn Screening Service Collaboratives (NCC). The newsletter is published quarterly and is available in a portable document file (PDF) via email and at [www.nccreg.org](http://www.nccreg.org). Copyright © 2011 American College of Medical Genetics. The National Coordinating Center is funded by cooperative agreement No. U22MC03957 between the American College of Medical Genetics and the Genetic Services Branch/Maternal and Child Health Bureau/Health Resources and Services Administration.

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