# Critical Connections

*Collaborations among disparate research institutions enhance biomedical research and the nation's health.* **BY LAURA BONETTA**

Little Big Horn College is a two-year community college settled on two acres in a wooded river valley at the heart of the Crow Indian Reservation in south central Montana—a vast, mountainous state with the third-lowest population density in the country. Despite the college's isolated setting, scientists at Montana State University in Bozeman, 200 miles away, are mentoring some of its students on a research project to identify contaminants in the water of the Little Big Horn River that flows through the reservation.

This research effort, one of many across the country, is funded by NCRR's Institutional Development Award (IDeA) program, which aims to increase the research capability of states with historically low success rates of obtaining NIH grants. "We knew that by just supporting peer-reviewed grants to research institutions we would not be effective," says Fred Taylor, NCRR's IDeA program director. "To effect change in a state and make it more competitive on a national level, we needed to reach out to undergraduate universities and other educational institutions and get the community involved."

Through the IDeA program, NCRR supports institutions and communities in 23 states and Puerto Rico with grants that fund multiple areas of biomedical research and reach out to unique populations. Regardless of its actual area of biomedical inquiry, each grant fulfills five main goals to: build and strengthen the research capabilities at participating institutions by hiring staff and purchasing research equipment; support faculty, postdoctoral fellows, and graduate students; provide research opportunities for undergraduate students; develop outreach activities; and enhance the science and technology knowledge of the state's workforce.

## ENGAGING TRIBAL COLLEGES

Little Big Horn College is one of seven tribal colleges in Montana brought together under the IDeA program to collaborate on biomedical research projects with undergraduate and research universities across the state. In the southern portion of the state, along with Little Big Horn College, is Chief Dull Knife College, serving the Cheyenne Tribe. On the northern side are Blackfeet Community College (Blackfeet Tribe), Fort Belknap College

■ Biology teacher Mari Eggers (third from left) supervises students at Little Big Horn College performing research on water quality, one of the IDeA research projects bringing tribal colleges together with Montana universities. Shown in the photo from left to right are Pancho Monroy, Leslie Plain Feather, Mari Eggers, Francesca Pine, Brandon Good Luck, and Candy Felicia.

(Gros Ventre and Assiniboine Tribes), Fort Peck Community College (Assiniboine and Sioux Tribes), Salish Kootenai College (Confederated Salish and Kootenai Tribes), and Stone Child College (Chippewa Cree Tribe). The colleges are each hundreds of miles away from Montana State University and the University of Montana in Missoula, the state's two major research universities.

Because of Montana's large size, few opportunities existed for the faculty and students from different educational institutions to come together. Much of the credit for obtaining participation from tribal colleges goes to Sara Young, outreach coordinator for the Montana program and a member of the Crow Tribe. "It is really important to have someone who has credibility with the tribal colleges," says Young, who had worked on Indian reservations for more than 30 years before joining Montana State University. Young understands the challenges facing Native American students who wish to pursue research careers. All but one of the seven Montana tribal institutions are two-year colleges, which means that to obtain a bachelor's degree, students must leave the reservation. "Most students who live on reservations have very strong family ties," says Young. "It is challenging for a student to move away and not be able to maintain these ties on a daily basis."

Native American students attending a university in Montana often have to deal with feelings of isolation and, in some cases, misunderstanding from a predominantly white faculty and student body. "It is hard to be the only person of color in a class of 200 students," says Young. But there are signs that the research environment, at least at Montana State University, is becoming more welcoming to tribal students. During the summer of 2006, four Native American students conducted research on the Montana State University campus, and all of them are now pursuing bachelor's degrees in health-related fields.

The IDeA program is also helping to establish research projects within the tribal colleges, in subject areas uniquely relevant to the local communities. For the past several years, students at Little Big Horn College have been collecting river water and monitoring its quality. At the same time, researchers at Montana State University have been analyzing the water and fish tissue samples to identify environmental contaminants, such as mercury, pesticides, and pathogens. Students from the tribal college often visit Montana State University to learn these more

PHOTO BY LYNN DONALDSON

sophisticated laboratory techniques and to carry out the analyses themselves.

"They were really interested in having students involved in basic water quality assessment," says Montana State University professor and microbiology department head Timothy Ford, who directs the NCRR-funded program and serves as the primary mentor for the Little Big Horn College project. "That comes from a strong perception on Crow and other reservations that the water is contaminated and a source of disease." The perception is based, in part, on Montana's history of mineral and energy exploration and indiscriminate use of pesticides and other chemicals in agriculture, coupled with anecdotal reports of cancer clusters, stomach problems, and other ailments among those living on reservations.

To help prioritize these concerns in relation to contamination, an environmental health steering committee was formed on the Crow Indian Reservation made up of community members, utility managers, and tribal health representatives. "What we have done with Crow, we will begin to expand to other reservations," says Ford. Already IDeA funding has been used to hire new faculty and to provide mini-grants to six tribal colleges in the state. The increase in faculty means that science instructors have some time to devote to research projects and to pursue further research training.

Other projects supported by the IDeA program in Montana include studies of microbes involved in human disease, such as *Candida albicans* and hantavirus, and those that threaten Montana's abundant livestock and wildlife, such as the chronic wasting disease agent. For each project, the primary investigator is at one of four baccalaureate schools, and the primary mentor, an NIH-funded scientist, is at Montana State University or the University of Montana. One of the biggest payoffs so far, according to Ford, has been a "change in culture" at both the tribal colleges and the undergraduate institutions. "We talk to the deans and presidents, and they are ecstatic about the way undergraduates are exposed to research," he says.

### CONNECTING UNIVERSITIES TO RURAL CLINICS

On the other side of the country, the IDeA program in West Virginia is also enabling critical connections among different institutions and facilities and between mentors and students. Along narrow roads, nestled among the tall peaks of the Appalachian Mountains, the Tug River Health Association has, for many years, been providing health care to residents of the coalfields of southern West Virginia. The small rural clinic, a three-hour drive south of the state's capital, is also participating in a major research effort to identify the genetic underpinnings of heart disease.

The NCRR-funded Appalachian Cardiovascular Research Network project "is a unique research collaboration that includes major research universities, undergraduate institutions, major hospitals, and rural clinics," says Gary Rankin, the grant's principal investigator at Marshall University, located in Huntington. "And it involves all kinds of individuals, from students to molecular biologists to clinicians." It focuses on heart disease, a health problem that is highly relevant to West Virginians. According to statistics released by the U.S. Centers for Disease Control and Prevention in February 2007, the West Virginia population has a high prevalence of obesity, diabetes, and smoking-related illnesses. In fact, the state has the highest proportion of people with heart disease in the nation.

Although heart disease is caused by a mix of genetic and environmental factors, knowing which genes make it more likely for a person to develop the condition could help identify at-risk individuals. "We want to understand a person's susceptibility to disease long before it develops," says Donald Primerano, a professor at Marshall University and the program's director. "These individuals could be advised, for example, on what diet could be beneficial to them."

Those who are eligible to participate in the study have abnormal levels of fats, or lipids, in their blood. "To find out if they want to participate, we either call them or ask them during a regular visit to their physician," says Primerano. Patients are recruited at three major centers (Marshall University, West Virginia University, and Charleston Area Medical Center), as well as from three small rural clinics spread out across the state, extending the program's reach.

The research effort has already had some success in identifying genes involved in obesity-associated cardiovascular disease. For that study, researchers analyzed the sequence of DNA nucleotides within several genes already known to predispose people to heart disease and compared the sequences in overweight and obese individuals to those in normal-weight individuals. They found three genes that differ between the two groups and thus may play a role in obesity-associated cardiovascular disease. An abstract describing the work was presented at the annual meeting of the American Society for Human Genetics held last October in New Orleans (www.ashg.org/cgi-bin/ashg06s/ashg06).

Two more ambitious projects are now under way. Researchers are trying to identify variations in genes involved in two common conditions leading to heart disease that seem to run in families: familial combined hyperlipidemia and familial

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hypertriglyceridemia. This time, the scientists are scanning the entire human genome to identify telltale variations between genes, rather than focusing on a set of known candidate genes.

The two projects take full advantage of the resources at the collaborating institutions. Blood samples collected at the clinics are sent to Marshall University, where DNA is isolated from them. The DNA is then sent to Fairmont State University or West Liberty State University—two undergraduate institutions—to determine the nucleotide sequences of specific genes in each DNA sample. The sequence data are then analyzed at Marshall and West Virginia universities using bioinformatics tools to find significant associations between specific sequences and symptoms of heart disease. "The network helps with patient recruitment, but it also helps us bring together people with different expertise, which you need for these types of studies," Primerano says.

■ Biology professor Mark Flood is heading a project to identify variations in genes involved in heart disease. He is shown in his lab at Fairmont State University in West Virginia with Sarah Dodson, assistant professor of biology (standing), and students (left to right) Contessa Hill and Bonnie Freeman.

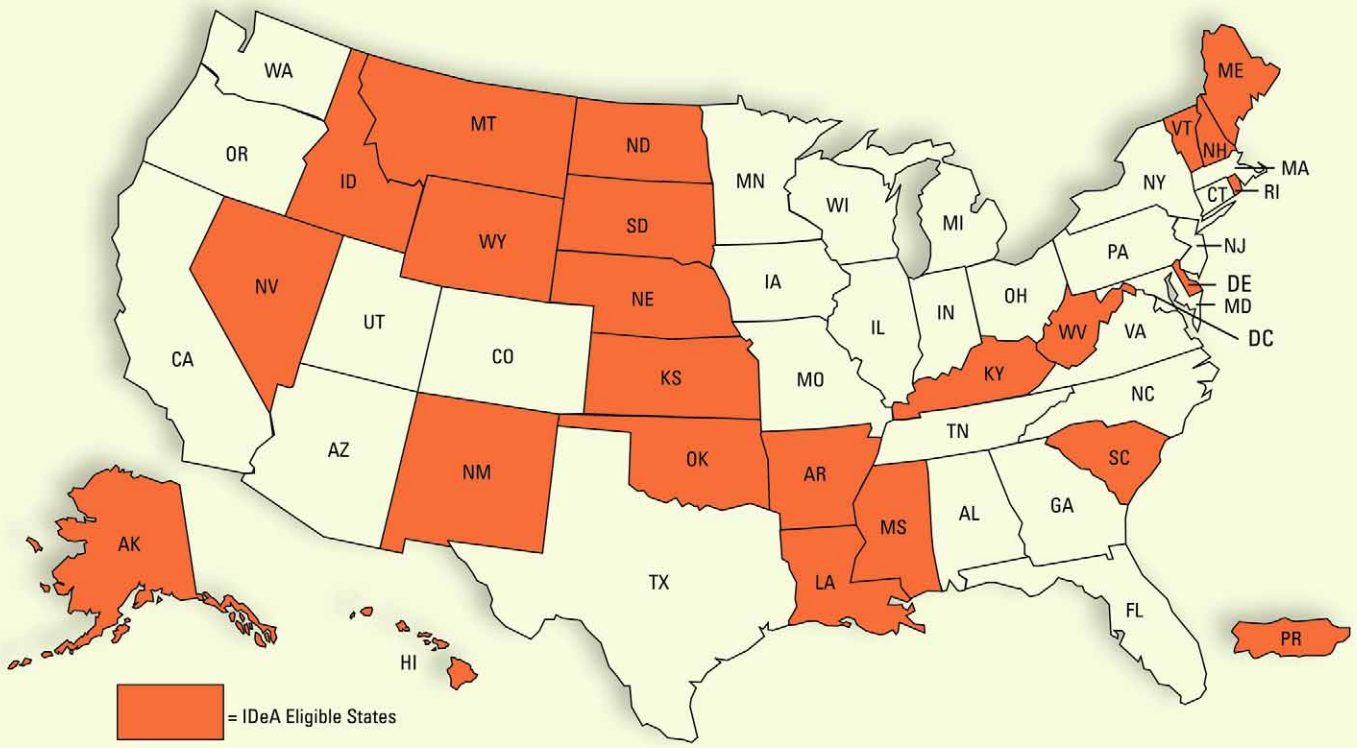
PHOTO COURTESY OF FAIRMONT STATE UNIVERSITY

Mark Flood, an investigator and professor at Fairmont State University, a three-hour drive from Marshall University, directs the familial combined hyperlipidemia study. "We would not have access to patient populations if we did not have these collaborations with Marshall and West Virginia University," says Flood. "My campus has 7,500 undergraduate students; we don't have a medical school or any chance to obtain funding for this kind of research unless we collaborate with investigators from larger institutions."

One thing that makes the Appalachian population particularly well suited for these studies is that, in addition to the high prevalence of heart disease, individuals tend to live close to other family members. As a result, it is relatively easy for researchers to obtain DNA samples from several related individuals within a family, something that greatly aids genetic analysis. "We recently recruited a 22-member family at West Virginia University," says Primerano. So far, the familial combined hyperlipidemia project has recruited about 50 participants, out of a possible 200 that will be needed to complete the study.

IDeA funding was used to buy specialized equipment at Fairmont—a pyrosequencer and several polymerase chain reaction (PCR) machines—and to hire another faculty member, relieving some of Flood's teaching duties and freeing up more time for research. Students are also reaping the benefits. Since the start of the program, Flood has had 10 undergraduate students working in his lab, learning to do PCR and DNA sequencing. "We are seeing some successes with them getting into medical and graduate school or obtaining jobs in the biotech industry," says Flood, adding that students are keen to work on the project because, for the first time, they are seeing the importance of their research to the health of their community.

Another outcome of the IDeA funding is that there is now an office of grants management at Fairmont. "We are seeing many more regional and national grants being submitted by our faculty, and our president has set aside money specifically to support undergraduate research," says Flood.




**NCRR's Institutional Development Award (IDeA) program** provides research opportunities, science education, and economic development and extends high-speed connectivity to grantee institutions to facilitate research collaborations. Twenty-three states and Puerto Rico participate in the program.

### LINKING RESEARCHERS THROUGH "VIRTUAL" NETWORKS

Many IDeA states face the challenge of rural or isolated locations. To overcome the distance between institutions and enhance the research capacity in the state, Louisiana State University (LSU) in Baton Rouge constructed a network to encourage partnerships. The network uses cutting-edge technology, called Access Grid, so that research groups at different sites can interact over high-speed Internet connections. For example, using audio and video conferencing, people can meet "virtually" for lab meetings, classes, and mentoring. The effort is led by Harold Silverman, a professor at LSU in Baton Rouge, and his team of faculty and staff. "One reason for having the Access Grid is that we have programs running at bigger institutions that we thought some of the smaller institutions could take advantage of," says Silverman. "We also wanted to be able to move large packets of real-time data between researchers and to facilitate collaborations."

The project had an interesting start. The State of Louisiana had set aside some money from the 1997 tobacco settlement to create health centers of excellence. The LSU main campus in Baton Rouge and the LSU Eye Center decided to spend the money to build an Access Grid network. "The process was working nicely," recalls Silverman. "So, when we saw the initial NCRR call for creating networks, we thought it would be a good chance to bring the primarily undergraduate institutions onto the grid."


Access Grid, funded by the IDeA program, enables research groups at different sites in Louisiana to interact over high-speed Internet connections. The network has been particularly helpful to researchers who were displaced because of Hurricane Katrina.

PHOTO COURTESY OF LOUISIANA STATE UNIVERSITY

When Silverman and his colleagues began building the physical infrastructure for the Access Grid, most campuses had little or no equipment in place to support the effort. Today the Access Grid links four large research centers—two medical schools in New Orleans, including Tulane University; one in Shreveport; and the LSU main campus—and four primarily undergraduate institutions—Southern University, a historically black university in Baton Rouge; the University of Louisiana in Monroe; Louisiana Tech University in Ruston; and Louisiana State University in Shreveport.

In 2006, the governor of Louisiana pledged more than $40 million over 10 years to support the Louisiana Optical Network Initiative (LONI), a high-capacity network connecting mainframe computers at Louisiana's major research universities. "LONI is required for computational and informatics advances to drive research," says Silverman. "IDeA funding and collaboration were a nucleus for these advances in Louisiana."

Sumeet Dua, an assistant professor of computer science at Louisiana Tech University in Ruston, found a mentor at LSU in New Orleans, 300 miles away. Together, Dua and Hilary Thompson, associate professor in the Department of Public Health at LSU, are developing new bioinformatics tools to analyze the expression of all genes in the eye to identify patterns associated with loss of vision and other disease states. When Dua joined the program in 2002, his university did not yet have an Access Grid node. "That is something I helped establish," he says. "The Access Grid has given us unique opportunities. I can work with leading mentors around the state and beyond without leaving my institution."

Thompson and Dua were able to continue their collaboration, even when Thompson was displaced from his laboratory in New Orleans for several months as a result of Hurricane Katrina. This was possible through the Access Grid communication between Louisiana Tech and Baton Rouge, where Thompson had temporarily moved. Based on the research he has carried out so far and the equipment he has been able to purchase with IDeA funding, Dua says he is now in a position to apply for more NIH grants.

"The barriers to collaboration tended to be distance and a lack of understanding of the roles and missions of other institutions and what constraints they work under," says Silverman. Putting the network together forced university administrators and information technology specialists to visit each others' institutions and communicate, both in person and by using the virtual connection. The process has, in turn, enabled a greater understanding among institutions. "The evidence of success is when you can transfer what we have done to the political realm of the state," says Silverman. "When the governor jumps on board and says, 'I would like to continue putting money in to build the network,' the small steps we took initially among a few institutions have now multiplied."

■ Sumeet Dua, assistant professor of computer science at Louisiana Tech University, discusses data with student Pradeep Chowriappa. High-speed Internet connections funded by the IDeA program link together researchers and students at eight Louisiana research centers and undergraduate institutions.

Louisiana, Montana, and West Virginia illustrate the diversity of the IDeA programs. Each is facing unique challenges and developing different strategies to overcome them, but the grantees are making strides. "In the future, we hope to see these states participate fully in the research endeavor and successfully compete for NIH funding across the board," says NCRR's Taylor. "We would like to see pipelines established to produce homegrown researchers. Our goal is to address the health disparities of the local populations in IDeA states and, ultimately, improve the health of the nation." ■

**TO LEARN MORE:** For more information about the IDeA program, visit the NCRR Web site at www.ncrr.nih.gov/resinfra/ri_idap.asp.

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