Winter 2009

Innovators *at* Heart

A publication for those who support heart-related research, education, and care at the University of Minnesota

Band-Aids and guardian angels

Research findings show promise for repairing and protecting the heart

Ask Joseph Metzger, Ph.D., what he and his colleagues do for a living and he's likely to reply, "We're in the business of fixing hearts."

If his research findings are any indication, business should soon be thriving.

"Fixing hearts is what I think about all day, every day, 365 days a year," says Metzger, chair of the University of Minnesota Medical School's Department of Integrative Biology and Physiology. "My colleagues and I take a basic science approach to the problem—how we might apply modern technologies to improve the functionality of the diseased heart."

A native of Minnesota, Metzger previously worked at the University of Michigan Medical School in Ann Arbor, where he directed its Center for Integrative Genomics. Now back in Minnesota, he hopes to expand and perfect some of his most promising research.

Two research projects in particular are captivating the interests of clinicians, scientists, and patients alike.

In the past few years, Metgzer has designed and tested what he calls a "molecular Band-Aid." It's a chemical that seeks out tiny "microcuts" in the heart muscle. When injected into the bloodstream, the molecular Band-Aid finds these microcuts and then protects those areas from bacteria and other harmful substances so that the muscle can function normally.

Metzger has studied the potential of this therapy in large animals and hopes to begin clinical trials in humans soon.

He believes the molecular Band-Aid could be used to help repair weakened heart muscle in people who have inherited diseases such as muscular dystrophy and in the elderly.

Metzger and his team also are investigating a new therapeutic technique using what he calls a "guardian angel" protein that would be delivered to damaged heart muscle via genetic engineering.

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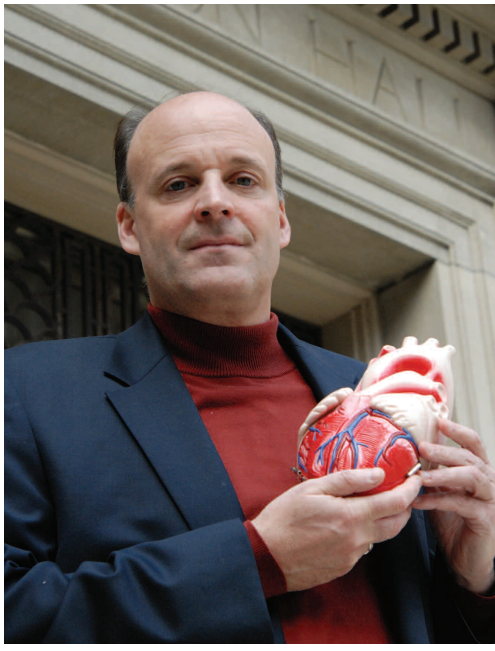
Photo by Jerry Vincent



Minnesota native and leading scientist Joseph Metzger, Ph.D., brought his innovative heart therapy research to his home state in 2008.

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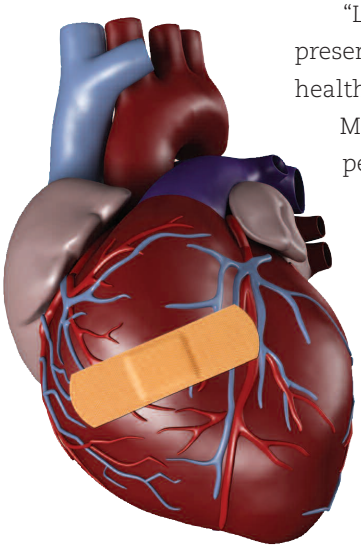
Band-Aids and guardian angels continued from cover



"Like a guardian angel, the protein is always present but not active when the heart muscle is healthy and working well on its own," explains Metzger. "But when the heart muscle's performance is rapidly declining, the guardian angel protein activates and begins to improve functionality."

The degree to which it improves heart muscle function is proportional to the degree of dysfunction: the greater the severity of a person's disease, the more the guardian angel protein would be activated. Because the therapy only works when needed, Metzger expects that it would cause few, if any, side effects.

Compared with the molecular Band-Aid, the guardian angel technology is a longer-term project because Metzger and his team must design the substances that can deliver the new genetic "blueprints" to damaged heart muscle. But Metzger is optimistic.

"In five years, we've taken the guardian angel protein from test-tube experiments to correcting heart disease in small animals," he says. "Major advances are occurring every month in the biomedical field, and we believe that this therapy could have profound effects in restoring the function of the heart."

Metzger, who holds the Maurice Visscher Land-Grant Chair in Physiology, says he's very happy to be home and to bring his research to Minnesota.

"There is renewed vigor of leadership here to be setting the pace in cardiovascular research and medicine," he says. "The University has developed a vision and is committed to building resources and programs to make it a top-notch institution in the field. It's exciting to be part of that effort."

Reap the benefits of leaving a legacy gift from retirement accounts

Retirement accounts are typically set up to allow people to save money on a tax-deferred basis during their working years. Over time, the value of a retirement account may increase beyond what the owner needs in retirement.

But leaving an IRA or other retirement account in estate plans for a loved one can have serious tax consequences, causing double taxation of the assets.

That's why many donors have found that using retirement plan assets to make a gift to charity can be an ideal way to leave a legacy. When a person names the Minnesota Medical Foundation as beneficiary of a retirement plan using a beneficiary designation form, the individual's estate receives a charitable estate tax deduction for the full value of the account. Because the foundation is a tax-exempt charity, no income taxes are due on the donated assets.

Making a gift of retirement assets doesn't require an attorney's services. Donors may simply fill out a beneficiary designation form with their account custodian or retirement plan administrator.

Here's some sample language for your beneficiary designation form to make a gift of retirement assets to heart research, education, or care at the University of Minnesota through the Minnesota Medical Foundation:

"_____ percent (_____%) of my IRA account at [name of custodian], Account Number _____ , shall be distributed to the Minnesota Medical Foundation, 200 Oak Street SE, Minneapolis, Minnesota 55455 (federal tax ID 41-6027707) free of trust [optional: for specific program, research, department, or fund]."

For more information, contact the Minnesota Medical Foundation at 612-625-1440, 800-922-1663, or giftplanning@mmf.umn.edu, or visit ***www.mmf.umn.edu/giftplanning****.*

Major grant funds stem cell research collaboration

Most major medical discoveries don't happen in a single lab; they result from close collaboration across multiple institutions. That's why it was big news when University of Minnesota researchers learned in October that they had received a seven-year collaboration grant to help develop the high-potential field of stem cell therapy.

With the grant from the National Heart, Lung, and Blood Institute (NHLBI), University researchers will partner with a research team from the University of Wisconsin–Madison to understand how and when stem cells commit to becoming a certain type of blood cell.

"What we want to know is, how do various stem cells decide to become blood or heart or blood vessels? How can we enhance that process so it becomes highly efficient and produces a large number of those cells?" says Daniel J. Garry, M.D., Ph.D., executive director of the Lillehei Heart Institute and leader of the University research team.

The collaboration award provides each institution with $750,000 per year and brings together researchers from the heart, lung, blood, and technology research fields. Scientists from partner institutions will meet several times a year to exchange ideas and discuss how they can accelerate one another's work.

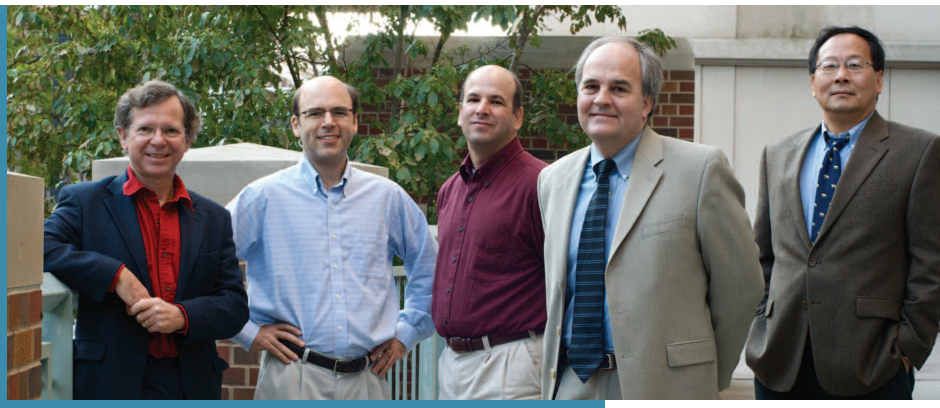
Jonathan Slack, Ph.D., director of the University's Stem Cell Institute, was a pivotal partner in identifying ways to leverage the University's strengths to make a standout grant application, Garry says.

"This was a golden opportunity for us," Slack says. "We already had expertise in embryonic stem cell/iPS cell biology, hematopoietic development, cardiac development, decellularized organs, cell transplantation, and imaging technology—in other words, all the technology required."

Philanthropy is another reason behind the University's grant success. Last year the Engdahl Family Foundation funded an interdisciplinary study by cardiology professor Jay Zhang, M.D., Ph.D., and stem cell scientist Dan S. Kaufman, M.D., Ph.D., aimed at identifying which factors are important in promoting cardiac regeneration. That study provided preliminary data that made the University a strong contender for the NHLBI grant, Garry says.

"Gifts that support novel research ideas often set the table for our scientists to later earn much larger grants from agencies such as the NHLBI," he says. "A gift to start-up research like this often gets a huge return on the donor's investment."

And thanks to the exchange of tools and information through the NHLBI-funded collaboration, the return on investment is only likely to grow.



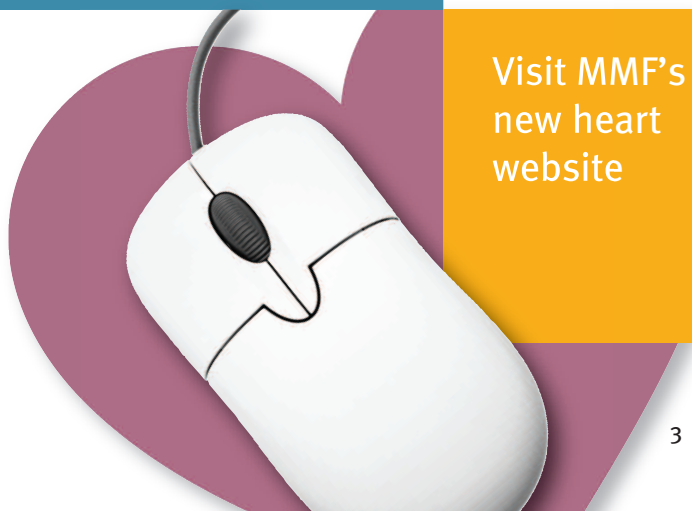
Six University researchers will benefit from the NHLBI grant, including (from left) Jonathan Slack, Ph.D.; Michael Kyba, Ph.D.; Dan Kaufman, M.D., Ph.D.; Daniel Garry, M.D., Ph.D.; Jay Zhang, M.D., Ph.D.; and Doris Taylor, Ph.D. (not pictured).

Photo by Richard Anderson

Visit MMF's new heart website

Learn more about heart research, education, and care at the University of Minnesota on the Minnesota Medical Foundation's (MMF's) new website. MMF raises millions of dollars each year to support health-focused research, education, and care at the University. Our new website features heart-related patient stories, exciting research news, and ways to give and get involved.

Check it out at **www.mmf.umn.edu/heart/**, or to receive e-updates on the latest heart news from the University, join our mailing list at **www.mmf.umn.edu/subscribe**.



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Rita Perlingeiro, Ph.D.

Putting some muscle into her research

For years, Rita Perlingeiro, Ph.D., has been looking for ways to use embryonic stem cells to improve muscle function. Now the University of Minnesota researcher's findings could advance new therapies for muscular dystrophy, a devastating disease characterized by progressive degeneration of the muscles that control movement.

In a study published in the October issue of *Experimental Neurology*, Perlingeiro and her team showed that transplanting embryonic stem cells that have "specialized" into skeletal muscle stem cells into mice with Duchenne muscular dystrophy can restore function to defective muscles.

Making muscle cells from embryonic stem cells in a Petri dish isn't easy to do, says Perlingeiro, an associate professor in the Division of Cardiology who also conducts research aimed at generating new cells to help the heart and blood vessels repair themselves. "We were seeing that muscle cells were inefficiently produced, and not enough of them were being produced to make muscle," she says.

But using a gene called PAX3, Perlingeiro essentially "instructed" embryonic stem cells to make muscle cells instead of other cell types.

Once enough muscle cells were produced, Perlingeiro's team injected them into the injured muscles of mice that have muscular dystrophy. Upon transplantation, the cells not only helped to grow muscle tissue but also improved muscle function. The strategy has proved effective for Duchenne and other forms of muscular dystrophy.

"The most exciting thing about this work is that what you are doing might help someone," Perlingeiro says.

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