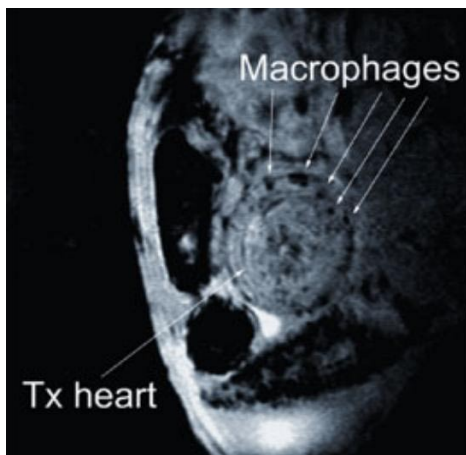


## Carnegie Mellon Develops Non-invasive Technique To Detect Transplant Rejection at Cellular Level Research Could Revolutionize Care of Transplant Patients



PITTSBURGH-Carnegie Mellon University scientist Chien Ho and his colleagues have developed a promising tool that uses magnetic resonance imaging (MRI) to track immune cells as they infiltrate a transplanted heart in the early stages of organ rejection. This pre-clinical advance, described in an upcoming issue of the Proceedings of the National Academy of Sciences (PNAS), ultimately could provide a noninvasive way to detect transplant rejection in patients.

"We have reported for the first time the ability to monitor single immune cells in a live animal using MRI. This could revolutionize the management of transplant patients," said Ho, professor of biological sciences at the Mellon College of Science.

"Successful translation of this work to the clinic ultimately will reduce the number of biopsy procedures and should greatly improve the quality of life for cardiac transplant patients, especially children," added Ho, who directs the Pittsburgh NMR Center for Biomedical Research. "Perhaps most importantly, this advance will allow doctors to provide highly personalized care that could prevent transplant rejection."

Organ transplantation is the preferred clinical

approach to treat end-stage organ failure, but transplant patients face a lifetime of immunosuppressive therapy and the risk of losing the new organ due to rejection. Physicians typically monitor patients for organ rejection following a heart transplant by performing frequent heart biopsies for the first year. Heart biopsies are invasive procedures that involve threading a catheter through the internal jugular vein to the heart's right ventricle and snipping out several tiny pieces of tissue. A pathologist then tests the tissue to identify the presence of immune cells (such as macrophages) as well as other pathological changes in the transplanted heart tissue that indicate the graft is being rejected by the body's immune system.

These procedures are costly, uncomfortable and must be repeated annually to monitor and treat any rejection. Biopsies also are problematic, according to Ho, because they do not look at the whole organ. By only sampling several small areas, a biopsy may miss the area of the transplanted organ where immune cells are gathering—one of the first signs of rejection.

Ho's novel approach investigates transplant rejection non-invasively by observing macrophage accumulation in heart tissues using MRI.

"We were able to use MRI to visualize individual macrophages. By tracking individual cells, we also were able to observe, for the first time, that rejection progresses from the outside of the heart to the inside," said Ho. "Up to now, this phenomenon hasn't been observed in pre-clinical or clinical research because biopsy samples are very limited in location and size."

The reported findings also have broader implications for biology and medicine, according to Ho.

"We now have the ability to visualize non-invasively and with sensitivity individual cells and their movement to targeted sites. Our new approach offers almost unlimited potential for monitoring cell therapies, such as those using stem cells, and for tracking cellular and developmental processes," Ho said.

For the research reported in PNAS, Yijun Wu, research biologist at the Pittsburgh NMR Center for Biomedical Research, tagged macrophages with

nanometer (USPIO)- or micrometer (MPIO)-sized paramagnetic iron oxide particles, which are very sensitive to the magnetic fields used during MRI. Wu injected the MPIO or USPIO particles into rats that had received heart transplants three days earlier. Macrophages, which typically ingest foreign materials inside the body (bacteria, for example), incorporated the particles. Using MRI, the researchers then are able to track tagged macrophages that infiltrate transplanted hearts. The locations of the tagged macrophages are highly defined and appear circular in shape, said Wu. (See image below.) This finding indicates that the new, real-time tracking method is very good at pinpointing exactly when and where rejection is taking place.

Chien Ho and his colleagues are using a heterotropic cardiac transplantation model in rats (above) to develop a non-invasive, MRI-based method to monitor organ rejection. NMR Center scientists label immune cells with MRI contrast agents and track their accumulation at the rejecting graft (dark spots), which is an early sign of organ rejection. (Photo courtesy of Chien Ho, Carnegie Mellon University)

The researchers used a heterotropic heart model to study organ rejection. In this model, a rat receives a second functional heart, which is grafted into its abdomen. The rat's native heart functions normally. In this way, the researchers can study how a transplanted heart changes through sequential stages of rejection while the rat stays healthy. This aspect of the research was conducted primarily by Qing Ye, a research biologist at the Pittsburgh NMR Center for Biomedical Research.

Ho's team at the Pittsburgh NMR Center for Biomedical Research is now pursuing research using larger animal models. They are collaborating with researchers at the University of Pittsburgh School of Medicine, including Dr. David Cooper, professor of surgery in the Thomas E. Starzl Transplantation Institute; Dr. Jeffrey Teuteberg, assistant professor of medicine at the Cardiovascular Institute, Heart Failure/Transplantation; and Dr. Fernando Boada, associ-

ate professor in the Department of Radiology.

The research is funded by the National Institute of Biomedical Imaging and Bioengineering, the National Center for Research Resources, the National Heart, Lung and Blood Institute, as well as the Health Research Formula Funds of the Pennsylvania Commonwealth University Research Enhancement Tobacco Settlement.

Established in 1986 and funded continuously since 1988 by the National Institutes of Health, the Pittsburgh NMR Center for Biomedical Research is dedicated to enhancing molecular, cellular and functional imaging using small animals. The center, sponsored jointly by Carnegie Mellon and the University of Pittsburgh, makes major contributions to the rapidly growing field of nuclear magnetic resonance in biology and medicine.

The Mellon College of Science at Carnegie Mellon develops innovative research and educational programs in a range of scientific, interdisciplinary areas. For more information, visit [www.cmu.edu/mcs](http://www.cmu.edu/mcs).

-- by Lauren Ward, Carnegie Mellon

University 412-268-7761

**Education:** Williams College (BA), Yale University (Ph.D.),

Massachusetts Institute of Technology (post-doctoral training)

**Honors:** John Simon Guggenheim Fellowship; Elected to membership in the Academia Sinica, Taiwan; named Alumni Professor of Biological Sciences at CMU; National Heart, Lung and Blood Institute MERIT award

**Professional/academic achievement:** on advisory committees at various universities and Institutions such as NIH, NSF, Stanford University, Univ. of Pennsylvania, Baylor College of Medicine, etc.

Invited to give talks at national and international scientific meetings.



Dr. Chien Ho

## PAAYPE April Dinner Club

**Thursday April 20 7:00 PM @ My Ngoc (2120 Penn Ave., Strip District. 412-765-1150)**



This month the PAAYPE dinner club returns to the Strip District at My Ngoc, A combination Vietnamese, Thai and Chinese (with the menu clearly divided). While we won't get to see Lucy making Bahn mi outside, we should find fine dishes indoors. Contact Louis (lluang@paaypa.org) to RSVP by Monday April 17th. PAAYPE - Pittsburgh Asian American Young Professional Association

Contact us at: [info@paaypa.org](mailto:info@paaypa.org)

## Asian American authors

There is another Asian American author who will be having book signings in Pittsburgh in late April and through May. If you would be interested in going to book signings or meet the author events, contact Louis at [lluang@paaypa.org](mailto:lluang@paaypa.org). Particularly if you are a reader of romance novels. More info to come.

## Anne Akiko Meyers violin recital and possible meet-the-artist

**Tuesday, April 25, 8:00 PM (6:00 dinner) at Katz Performing Arts Center (Squirrel Hill)**

Come join PAAYPE and hear Anne Akiko Meyers perform. The San Diego native Japanese-American violinist will be performing a mix of classical and contemporary pieces. If there is

sufficient interest we may be able to arrange for a meet-the-artist session. Contact Louis at [lluang@paaypa.org](mailto:lluang@paaypa.org) if interested. In particular, if you would be interested in taking part of the meet-the-artist it is important to contact Louis soon since we would only have the session if there is sufficient interest. We will have dinner together in Squirrel Hill then go to the concert.

## New Moon Orchestra Inaugural Concert

**Sunday April 23rd 2pm @ Carnegie Music Hall (Oakland)**

[www.newmoonorchestra.org](http://www.newmoonorchestra.org)

New Moon Orchestra is Pittsburgh's only Eastern Music Orchestra, with a current focus on traditional Chinese music. New Moon Orchestra will perform its full program on April 23rd at 2pm, assisted by internationally acclaimed soloists Baohui Chen and Youliang Zhou. Also, enjoy the unique New Moon Marketplace, a gathering of local Pittsburgh Chinese artists, jewelers, and food vendors, both prior to and after the show.

If you are interested in attending the Inaugural Concert with PAAYPE, please contact Louis at [lluang@paaypa.org](mailto:lluang@paaypa.org) by April 20th.



## Silk Screen Asian American Film Festival – May 12–20, 2006.

[www.silkscreenfestival.org](http://www.silkscreenfestival.org)

Silk Screen is looking for volunteers! Pittsburgh's first and only Asian American Film Festival is only weeks away. Final preparations are in full swing. However, volunteers are needed for

everything from selling festival passes to the movie screenings and the gala event, to helping with registration and gala set-up, to planning dinners or events with visiting movie stars and movie directors!

If you wish to be a part of this exciting, historic week-long event for Pittsburgh, please email Jessica at [jlee@paaypa.org](mailto:jlee@paaypa.org).

## Annual Asian Heritage Day at the History Center Highlights Diversity of Asian Culture

**Authentic Asian Musical and Dance Performances Among the Day's Activities**

April 7, 2006, PITTSBURGH □ The Senator John Heinz Pittsburgh Regional History Center will celebrate its annual Asian Heritage Day on Saturday, May 6, from 10 a.m. to 3 p.m.

Asian Heritage Day showcases the customs, cooking and ways of life of Asians from nations such as India, Bangladesh, Korea, Indonesia, Japan, Philippines, China and Thailand.

Visitors will be encouraged to try their hand in Asian arts, sample an array of ethnic dishes, purchase unique gifts, and enjoy authentic musical performances and dances. Members from various local ethnic organizations will lead the activities throughout the day.

The festivities are presented in partnership with the Asian Heritage Committee of the Federal Executive Board. In addition to the day-long ethnic activities, the History Center will be selling tickets for "Silk Screen," an Asian American film festival being held in Pittsburgh May 12-20.

Asian Heritage Day is free with paid admission to the History Center. For additional information, contact Nancy Cain McCombe at 412-454-6411 or [ncmcombe@hswp.org](mailto:ncmcombe@hswp.org).

The Senator John Heinz Pittsburgh Regional History Center is an affiliate of the Smithsonian Institution and the largest history museum in Pennsylvania. The Western Pennsylvania Sports Museum is a museum within a museum, comprehensively presenting the region's remarkable sports story through hundreds of artifacts and interactive experiences for visitors of all ages. The History Center and Sports Museum are located at 1212 Smallman Street in the city's Strip District, and are open every day from 10 a.m. to 5 p.m. Regular admission includes both the History Center and Sports Museum: \$7.50 for adults, \$6 for seniors over 61, \$5 for students with ID, \$3.50 for children ages 6-18, and free to members and children under 6. More information is available at [www.pghhistory.org](http://www.pghhistory.org).

