Runners, Walkers, Volunteers, and Supportive Bystanders Needed!!!

Come join us on the beautiful Stanford campus on September 21st at 9:00 a.m. for the third annual **RACE AGAINST PULMONARY HYPERTENSION**.

One of our core missions at the Vera Moulton Wall Center is to raise awareness about pulmonary hypertension and help support research, which we hope will lead to a cure for this debilitating disease. This 5k fun run/walk is a great way for the pulmonary hypertension community--patients, friends, family, and healthcare providers--to help. Proceeds from the race will benefit the Ewing Family Fund for Pulmonary Hypertension Research at Stanford.

We gratefully acknowledge the support of our corporate sponsors Actelion Pharmaceuticals, Accredo Therapeutics, JIBE Marketing, e-Agency, Studio 1.2.0.4, Andronico's Market, Hobee's California Restaurants, and Starbucks Coffee (University Avenue). If you or your company are interested in corporate sponsorship, there is still room for your support.

For additional information contact the Wall Center at 800.640.9255. To register on-line or make a donation visit www.raceforph.org or www.active.com (keyword: PH race).

Hope to see you in September!

VMWC calendar of events

september
Race Against PH - 5K Run/Walk
Sunday, September 21, 2003; 9:00 am
PH Support Group Tuesday, September 2
Clinical Conference Monday, September 8

october
PH Support Group Tuesday, October 7
Clinical Conference Monday, October 13 & 27

november
PH Support Group Tuesday, November 4
3rd Annual Evans Family Lecture
Guest Lecturer: Shaun R. Coughlin, M.D., Ph.D.
Director, Cardiovascular Research Institute,
Professor of Medicine and Cellular and Molecular Pharmacology, UCSF
Thursday, November 6; 8:00 - 9:00 am,
Fairchild Auditorium
Clinical Conference Monday, November 10 & 24

december
PH Support Group Tuesday, December 2
Clinical Conference Monday, December 8

january
PH Support Group Tuesday, January 6
Clinical Conference Monday, January 12 & 26

february
PH Support Group Tuesday, February 3
Clinical Conference Monday, February 9 & 23

march
PH Support Group Tuesday, March 2
Clinical Conference Monday, March 8 & 22

monthly
PH Support Group *1st Tuesday of each month*
12:00 - 1:00pm
Moderator: Martha Russell, LCSW
Please RSVP to 650.724.9255
Clinical Conference *2nd & 4th Monday of each month*
1:00 - 2:00pm (Lunch served)
Please call 650.724.9255 for room location

Lucile Packard Children's Hospital
STANFORD UNIVERSITY MEDICAL CENTER

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Stanford University Medical Center

NEW OPTIONS NEW HOPE
WALL CENTER UPDATE
Fall 2003
VERA MOULTON WALL CENTER FOR PULMONARY VASCULAR DISEASE AT STANFORD

The Third Annual Dunlevie Family Lecture in Pulmonary Medicine:

Richard C. Trembath, M.D., F.R.C.P.

BMPR2:
Genetic Key to PPH

Geneticists are the locksmiths of the medical world, using genes as keys to unveil the mysteries behind disease. Richard C. Trembath, M.D., F.R.C.P., Professor of Medical Genetics at the University of Leicester in the United Kingdom, discussed his discovery of the genetic key to primary pulmonary hypertension (PPH) at the third annual Dunlevie Family Lecture at Stanford University Medical Center.

Trembath's interest in the pathogenesis of human disease was firmly established during his undergraduate days at Guy's Hospital Medical School. His general medical training was followed by clinical training in diabetes and endocrinology at St. Bartholomew's Hospital, as well as genetic research in diabetes at the Institute of Child Health. Today, he is an internationally renowned leader in the field of medical genetics who has published more than 100 papers and abstracts. In addition to his research in pulmonary vascular disease, Trembath and his team are also concerned with conditions such as partial lipodystrophy, a disease in which abnormal fat deposits develop under the skin.

In his opening remarks, Trembath stated that a patient named Nicola first piqued his interest in the genetic causes of PPH in 1992. The newly married Nicola asked Trembath if he believed she was likely to develop PPH, since three of her sisters had already died from the disease. She was also concerned about the possibility of transmitting the gene for PPH to the children she planned to have. When Trembath attempted to research the answers to Nicola's questions, he noted his efforts took only a "second" because there was "virtually nothing known" about the genetic causes of PPH.

After assembling Nicola's extended family history, Trembath found what he now maintains is a classic case of familial, or inherited, PPH: more than 40 members within her family appeared to be at 50-percent risk of inheriting the gene to develop the disease. By referring to the family histories of other PPH patients, Trembath and his colleagues identified a region on chromosome 2 that cosegregated with PPH in the majority of the families they investigated. However, the team was still left with a fairly large area in which the gene could reside, since more than 100 different locations within that region were potential candidates to carry the gene.

A fortuitous clinical observation freed Trembath from the painstaking work of sifting through all 100 locations. He discovered that in the mid-1980s, one New Zealand family contained two girls who had been diagnosed with PPH and passed away; an extended family member had died from the condition as well. When Trembath visited New Zealand to research the case, he learned many members of the same family had suffered from another inherited vascular disorder: hereditary hemorrhagic telangiectasia, or HHT. Trembath then realized a direct connection exists between PPH and HHT, since the same two genes on one chromosome 2 interval can be identified in both diseases.

Upon further study of the same chromosome 2 interval, Trembath identified the presence of a third gene-bone morphogenetic protein receptor type 2, (BMPR2), a gene that is known to aid in lung development. Thanks to the human genome project, Trembath and his team were able to isolate the gene in 24 hours, gather their initial patient data, and confirm that the BMPR2 gene had undergone a mutation in one of their patients. Additional research by both Trembath and scientists at Vanderbilt University further substantiated these initial results.

Trembath observed that while the discovery of BMPR2 created an opportunity to better understand familial PPH, the breakthrough also had implications for

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The Vera Moulton Wall Center for Pulmonary Vascular Disease at Stanford

Lucile Packard Children's Hospital and Stanford Hospital and Clinics are one of the few combined centers in the United States currently offering diagnostic and advanced therapeutic services to both adults and children with pulmonary hypertension. In the fall of 2000, through the generous gift of an anonymous donor, the Vera Moulton Wall Center for Pulmonary Vascular Disease at Stanford was established.

The Wall Center seeks to serve as a leader in both the clinical treatment and research of pulmonary vascular disease, while also providing advanced training opportunities for researchers and clinicians. The *Wall Center Update* is published biannually in the spring and fall.

For Information, Consultation, or Referral:
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Living Positively
with Pulmonary Hypertension

Mari Matsumura lived the typical, active life of a 17-year-old in Kamakura, Japan. She was a member of the tennis team and had big dreams of becoming an astronaut or ecologist. So it seemed strange when climbing the stairs grew increasingly difficult. At times, Mari experienced dizziness, shortness of breath, and irregular heartbeats. Her friends also noticed that Mari's skin often looked blue during tennis practice.

Then one day, Mari fainted in school. She quickly went to a local doctor, who took an electrocardiogram (EKG) of her heart. As he reviewed the test results, Mari knew the doctor's furrowed brow was a sign of something very wrong. The doctor referred her to a local cardiologist, who subsequently admitted Mari to the hospital for further testing.

"That was when I was the most afraid," Mari remembers, "because they don't keep you in the hospital that long unless your condition is serious." She received a heart catheterization and a CT scan of her chest. Luckily, the cardiologist was then able to accurately diagnose Mari's condition as pulmonary hypertension (PH).

"The doctors kept telling me what the statistics were in terms of survival, but that didn't bother me," recalls Mari. "What frightened me was the thought of never being active again. The only image I had of sick people was one of confinement in bed and total dependence on others."

Mari received another referral to a PH specialist in Tokyo, who strongly urged her to go on Flolan—a medication that must be continuously infused into the bloodstream. Mari would have to wear Flolan around her waist in a pump, which would send the drug inside her body via a permanent chest catheter. She felt overwhelmed at the thought of the treatment. Mari wondered how a person could live indefinitely with a catheter in her chest: swimming would be out of the question, and even her daily bathing routine would have to be modified.

Mari and her mother on a recent visit to Japan.

Once Mari's parents heard the diagnosis, they thought of Stanford University Medical Center. Mari's father had attended the Stanford Graduate School of Business years before, and he knew of the University's reputation as a leader in cutting-edge medical care and research. Despite her doctors' cautious words against flying, Mari traveled across the Pacific Ocean for a consultation at Stanford.

"It felt completely different to be seen by the doctors at Stanford," Mari says. Ramona Doyle, M.D., Co-Director of the Vera Moulton Wall Center for Pulmonary Vascular Disease at Stanford and Medical Director of the University's Heart and Heart-Lung Transplantation program, had an entirely different philosophy towards treatment than Mari's doctors back home. While her other doctors simply told Mari she needed Flolan, Dr. Doyle explained *why* she needed Flolan and suggested additional treatment options. "I really appreciated the way the treatment was logically explained to me. It made sense," notes Mari. "The most important difference was Dr. Doyle's encouragement to do what I could and listen to my body." After returning to Japan and beginning Flolan treatment, Mari and her entire family eventually made the decision to move to California, where they could be closer to Stanford.

Now a 20-year-old university student, Mari has transitioned to life in the United States, becoming proficient in a new language and making new friends. She credits the Wall Center doctors and staff for motivating her to live positively and encouraging her to watch her diet, maintain her weight, and exercise regularly. The combined efforts of Mari and her doctors have paid off: her pulmonary pressures, which used to be over 100, were down to 50 on her last echocardiogram. Mari's improved health has allowed her to continue to do the things she enjoys most, such as watching movies, chatting with friends, and taking walks.

"I guess I can't be an astronaut anymore; I don't think my lungs can handle the altitude changes," jokes Mari. However, she still dreams big dreams of entering the medical field one day. Above all, Mari is happy that she can keep pursuing her goals—even if it means wearing a pump every day.