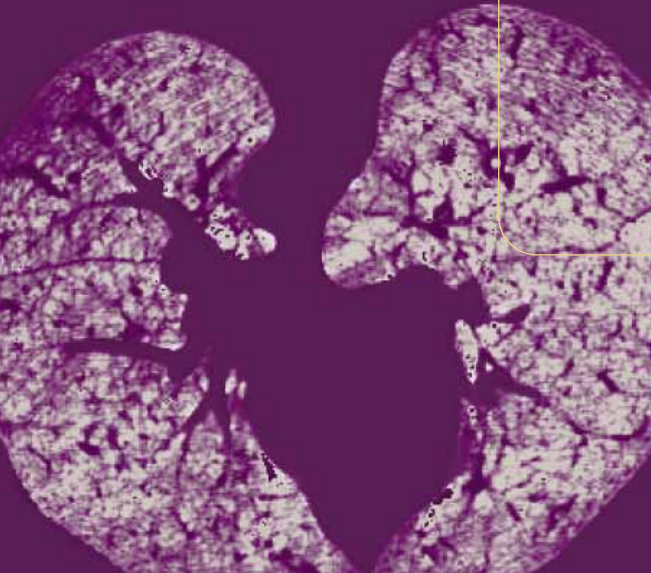
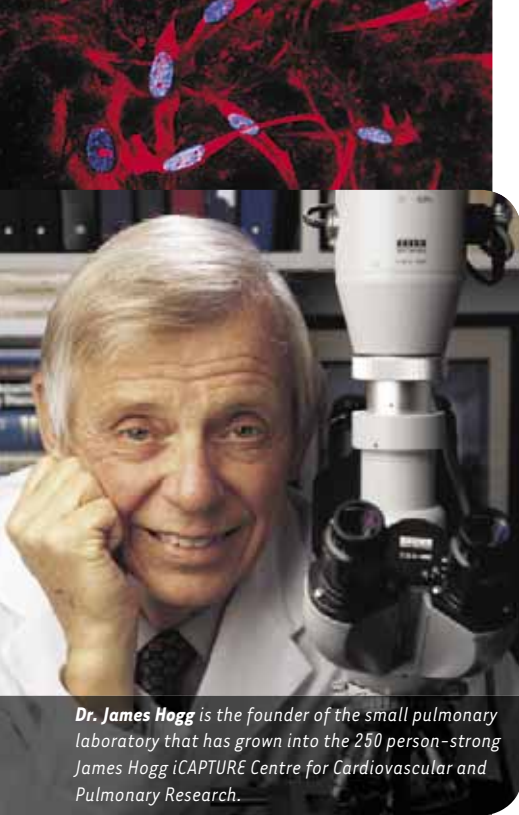




from
molecules
to **miracles**

Every newborn is a miracle, but baby Eleanor's mother Huiling Hu is a miracle too. Just days after giving birth to her daughter, Huiling felt feverish and sore. She was found to have sepsis, an often-fatal, overwhelming infection that affects the heart, lung and blood vessels. Her blood pressure dropped dangerously and her body failed to produce the hormone vasopressin. iCAPTURE researchers Drs. Jim Russell and Keith Walley were on hand at St. Paul's Hospital when Huiling was admitted. iCAPTURE's clinical trial of synthetic vasopressin allowed Huiling to receive this experimental treatment. It helped save her life, and gave baby Eleanor her mother back.





Dr. James Hogg is the founder of the small pulmonary laboratory that has grown into the 250 person-strong James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research.

iCAPTURE's Current Partners

Canada Foundation for Innovation
British Columbia Knowledge
Development Fund
Providence Health Care,
St. Paul's Hospital
University of British Columbia
St. Paul's Hospital Foundation
Heart and Stroke Foundation
of BC and Yukon
BC Lung Association
GlaxoSmithKline
IBM
Michael Smith Foundation
for Health Research
Canadian Institutes of Health Research
Canada Research Chairs
National Institutes of Health (USA)

Year Three in Review: 2002-03

A hidden gem gleams behind the red brick walls on Burrard Street — a place where scientists strive to make a difference for patients by changing molecules into miracles. In the past three years, the iCAPTURE Centre on the St. Paul's Hospital campus of the University of British Columbia has taken great strides in establishing itself as a world class cardio-pulmonary-critical care research facility. In the past year, new imaging and molecular tools purchased with \$21 million in funding from the Canada Foundation for Innovation (CFI), the BC Knowledge Development Fund (BCKDF), and other key partners have allowed the 26 principal investigators to accelerate their work.

Recently renamed **The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research** after its founding scientist, iCAPTURE's health researchers focus on discovering how gene variations interact with environmental factors to cause diseases of the heart, lung and blood vessels. These disorders are the leading cause of decreased quality of life and premature death in men and women in our communities. iCAPTURE's new office and educational space on Burrard West was completed in early spring, and laboratory renovations were completed in October 2003 for an official opening on December 3rd, 2003. At a recent retreat the group embraced six priorities for the future: to Discover, Synergize, Attract, Communicate, Translate, and Sustain their research.

discover

Discoveries happen when people with good ideas and collaborative energy have access to the best available technology. In the past year, researchers have completed the design phase to create a new database for the iCAPTURE Registry of patient tissues, data, and images. Core 1, the **Molecular Phenotyping Laboratory** where genes and proteins are analyzed, acquired new equipment such as the Laser Capture Microdissection system to sample tiny pieces of tissue. Core 1 researchers collaborate with clinician investigators to bring bench-top research to the bedside of patients with hypertension, sepsis, asthma, cystic fibrosis, atherosclerosis, heart failure, and emphysema.

Core 2, the **Laboratory for Ultrastructural Imaging**, purchased new equipment that offers researchers the ability to see, for example, individual molecules in the muscle surrounding blood vessels and airways. Using these strategies, scientists have revealed important new information relevant to high blood pressure and asthma. Core 3, the **Laboratory for Dynamic Cellular Imaging and Biophysics**, is where living cells and tissues can be seen in real time. The two-photon confocal laser microscope purchased with CFI funding is the only instrument of its kind in Canada. Researchers have observed that bone marrow stem cells can migrate to the heart and apparently transform into heart muscle cells after damage. Also in the last year, Core 4, **Organ Pathophysiology and Imaging**, installed a Siemens Computed Tomography (CT) scanner and a General Electric Magnetic Resonance Imager (MRI). These new instruments allow iCAPTURE investigators to test their hypotheses in living patients.

synergize

Synergy characterizes the collaborative relationships on which iCAPTURE's success is built. From the first breath of life in every grant application to the success in the laboratory or clinic, iCAPTURE is a model of synergy and partnerships: between Providence Health Care, VGH and UBC; between laboratory science and clinical science; between students and researchers. In the past year, the CFI infrastructure support has enabled iCAPTURE to pursue major national and international proposals with a diverse group of co-investigators.

These include:

- A CFI application involving the University of Toronto and the University of Montreal to create a cross-Canada cardio-pulmonary research database accessible by all researchers;
- The iQ Engine project with IBM researchers including Barry Robson, an IBM distinguished engineer, UBC Computer Science researcher Raymond Ng, CMMT's Wyeth Wasserman, and UBC statistician Reuben Zamar, to design new ways of analyzing diverse biologic data;
- A major Genome Canada project to identify the genes that modify the severity of cystic fibrosis in collaboration with Dr. Lap-Chee Tsui and investigators at the University of Toronto's Hospital for Sick Children; and
- A CIHR-funded Interdisciplinary Health Research Team award to study gene-environment interaction in heart, lung and blood vessel diseases for \$2.7 million over five years.

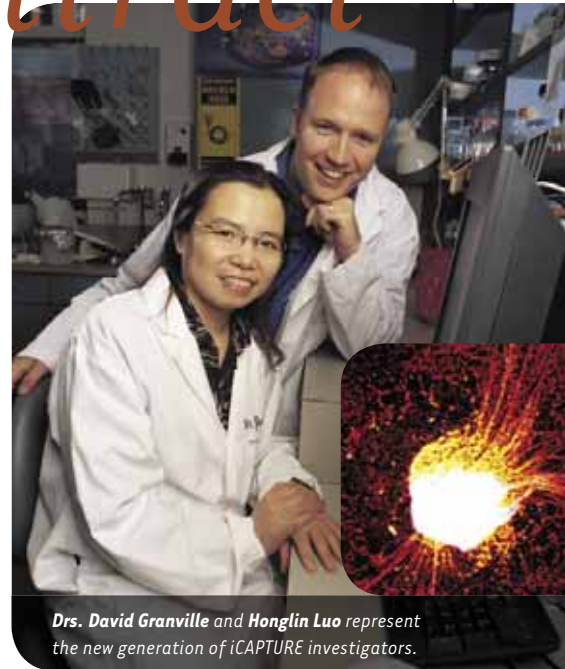


attract

iCAPTURE's new infrastructure, its renovated laboratory space, and successful grant applications have allowed it to proactively recruit top scientists from Canada and around the world. Recruits for 2002-03 include new Canadian Research Chair **Dr. David Granville**, a cell biologist and repatriated Canadian back from the Scripps Research Institute in the USA; **Dr. Tom Podor**, a confocal microscopist from McMaster University; **Dr. Honglin Luo** a molecular biologist from the University of Washington in Seattle; and **Dr. Harvey Coxson**, a home grown expert in lung imaging. In addition to new full time faculty members, a multi-national and talented group of post-doctoral fellows, research associates and graduate students have enriched the laboratory.

The iCAPTURE Centre's ability to attract outstanding post doctoral fellows was greatly enhanced by a CIHR-HSFC Strategic Training Grant entitled "IMPACT: Integrated and Mentored Pulmonary and Cardiovascular Training." The objective of IMPACT is to enhance the trans-disciplinary training environment for post-doctoral fellows to nurture the next generation of investigators. This award provides \$300,000 support per year for six years.

In other news, the UBC Faculty of Medicine has assigned additionally one Tier 1 and two Tier 2 Canadian Research Chairs to the iCAPTURE Centre. Active recruitment of three outstanding scientists is in progress. Tier 1 Chairs provide \$170,000 per year for salary support for the duration of the candidate's appointment. Tier 2 Chairs provide \$85,000 per year for 10 years. These Chairs represent \$5 million in long-term faculty support. In partnership with GlaxoSmithKline and the St. Paul's Hospital Foundation, a \$2.5 million endowment has also been established for a professorship in COPD (Chronic Obstructive Pulmonary Disease) research. Active negotiations with an excellent candidate are in progress.



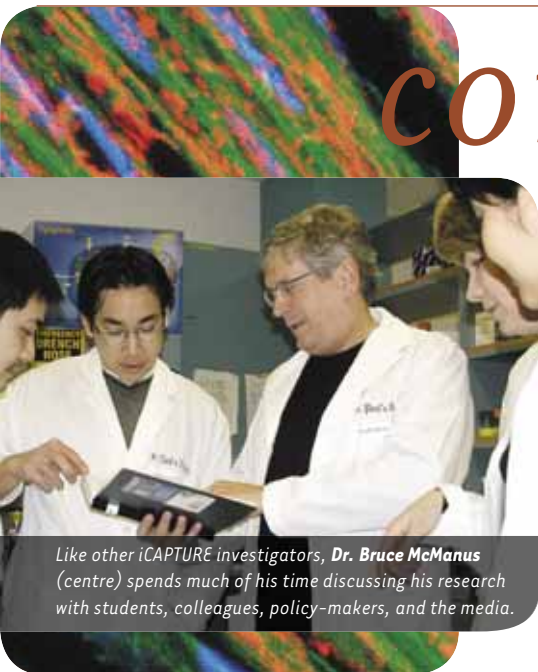
Drs. David Granville and Honglin Luo represent the new generation of iCAPTURE investigators.

communicate

The primary avenue for communication of research is the peer-reviewed biomedical literature. In 2002-03, iCAPTURE investigators published 168 papers (listed on www.icapture.ca).

Public interest in the iCAPTURE Centre continued throughout the year, spurred by the worldwide press release about the IBM / iCAPTURE iQ Engine Project. iCAPTURE appeared in local and national media including the Vancouver Sun, CTV News, CBC, and The Globe and Mail. iCAPTURE's close relationship with the St. Paul's Hospital Foundation continued as staff hosted numerous tours for donors, local business professionals, and the public.

On December 6, 2002, iCAPTURE's newly conceived "Alan Bernstein Distinguished Lectureship" was delivered by its namesake, internationally renowned researcher and leader Dr. Alan Bernstein, head of the Canadian Institutes for Health Research (CIHR). The Lectureship serves to highlight scientific achievements, celebrate health research in the Vancouver community, and provide trainees a learning opportunity. In February 2003, the second annual "Frontiers in Cardiovascular Science Conference" was held. This is a joint initiative between iCAPTURE, UBC, Hope Heart Institute, and the University of Washington. Themes included blood vessels in health and disease, cell signals in cardiovascular disease, and myocardial injury and repair. iCAPTURE also hosted an international young investigators meeting for the study of airway disease.



Like other iCAPTURE investigators, Dr. Bruce McManus (centre) spends much of his time discussing his research with students, colleagues, policy-makers, and the media.

translate

In medical science and health research, the term "translate" means changing knowledge into practice, a goal of every project undertaken at iCAPTURE. For example, groundbreaking work by **Dr. McManus** and colleagues has revealed the potentially adverse effects of an effective weight loss drug on heart valves in patients, forming the basis for development of a safer therapy for obesity. **Dr. Sandford** and colleagues have demonstrated which genes predispose some infants to develop allergy and asthma. **Drs. Russell** and **Walley** are investigating how variations in gene sequences affect the outcome of individual patients with critical illness. **Dr. van Breemen's** team is working with human blood vessels to determine ways to reduce blood vessel blockages and cardiac tissue death. **Dr. Paré's** team is developing predictors of lung disease susceptibility and progression that can be applied in a clinical setting. Each principal investigator at iCAPTURE focuses his or her work on questions that will eventually benefit patients with heart, lung and blood vessel diseases.



*Each new hypothesis born in the iCAPTURE laboratory has the ultimate goal of helping real people like **Huilin Hu** and her daughter, **Eleanor**.*

sustain

To view a complete listing of grants, publications and biographies for 2002/03, visit the iCAPTURE Centre website at www.icapture.ca



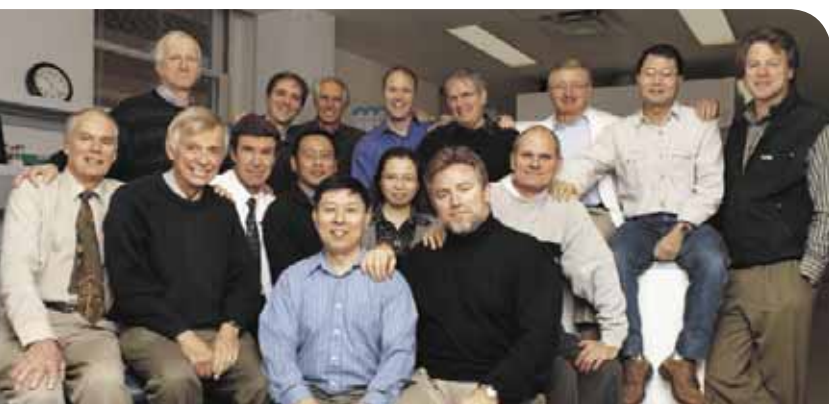
iCAPTURE's efforts to win infrastructure awards and research grants are crucially assisted by administrative team members like **Sandie Gillis**.

Infrastructure support is vital to sustaining iCAPTURE's work. Providence Health Care, the organization that includes St. Paul's Hospital and its Foundation, has provided iCAPTURE with outstanding support from day one. iCAPTURE has built on this support by obtaining additional infrastructure monies from BC's Michael Smith Foundation for Health Research (MSFHR). iCAPTURE also recovers costs for many of the services it can now offer because of its new technology and personnel.

Major Awards and Grants

Ultimately, it is peer reviewed and industry supported operating grants that fund the actual research projects and personnel awards that secure our researchers and trainees. iCAPTURE investigators have been very successful in competing for such awards in 2002-03. A full listing of all grants and awards is available on iCAPTURE's website. Here are some highlights:

- MSFHR grant for research unit support for five years at \$250,000 per year;
- \$400,000 from CANARIE to build and populate a genomic and environmental database;
- **Dr. David Granville** received a Tier 2 Canada Research Chair Award in cardiovascular biochemistry;
- **Dr. Chun Seow** received a CIHR/BC Lung Investigator Award to further his research on how smooth muscle contributes to asthma;
- **Drs. Walley, Dorscheid, Granville** and **Sandford** were honored with MSFHR salary support awards;
- **Dr. Honglin Lou** won a St. Paul's Hospital Foundation—CIHR New Investigator Award;
- **Drs. Saren Azer** and **Harvey Coxson** received the highly competitive Parker B. Francis Fellowship in Pulmonary Research;
- **Dr. Bruce McManus** was elected as a Fellow in the Royal Society of Canada in the Canadian Academy of Science and as a Fellow of the International Academy of Cardiovascular Sciences;
- **Dr. James Hogg** was honoured with the 2002 Henry Friesen Award from The Canadian Society for Clinical Investigation and The Royal College of Physicians and Surgeons of Canada and the 2004 Chugai Award for Excellence in Mentoring and Academic Scholarship;
- **Dr. Peter Paré** received the Jacob Churg Distinguished Researcher Award and the Joseph R. Rodarte Award for Scientific Distinction; and
- **Dr. Stephan van Eeden** was honoured with the William Thurlbeck Distinguished Researcher Award.



Sixteen of iCAPTURE's 26 principal investigators, from left to right:

Back Row: Jiri Frohlich, John Hill, Casey van Breemen, David Granville, Bruce McManus, Bob Schellenberg, Chun Seow, Jim Russell.

Front Row: Peter Paré, Jim Hogg, Stephan van Eeden, Xiaodong Wang, Decheng Yang, Honglin Luo, Tom Podor, Keith Walley.

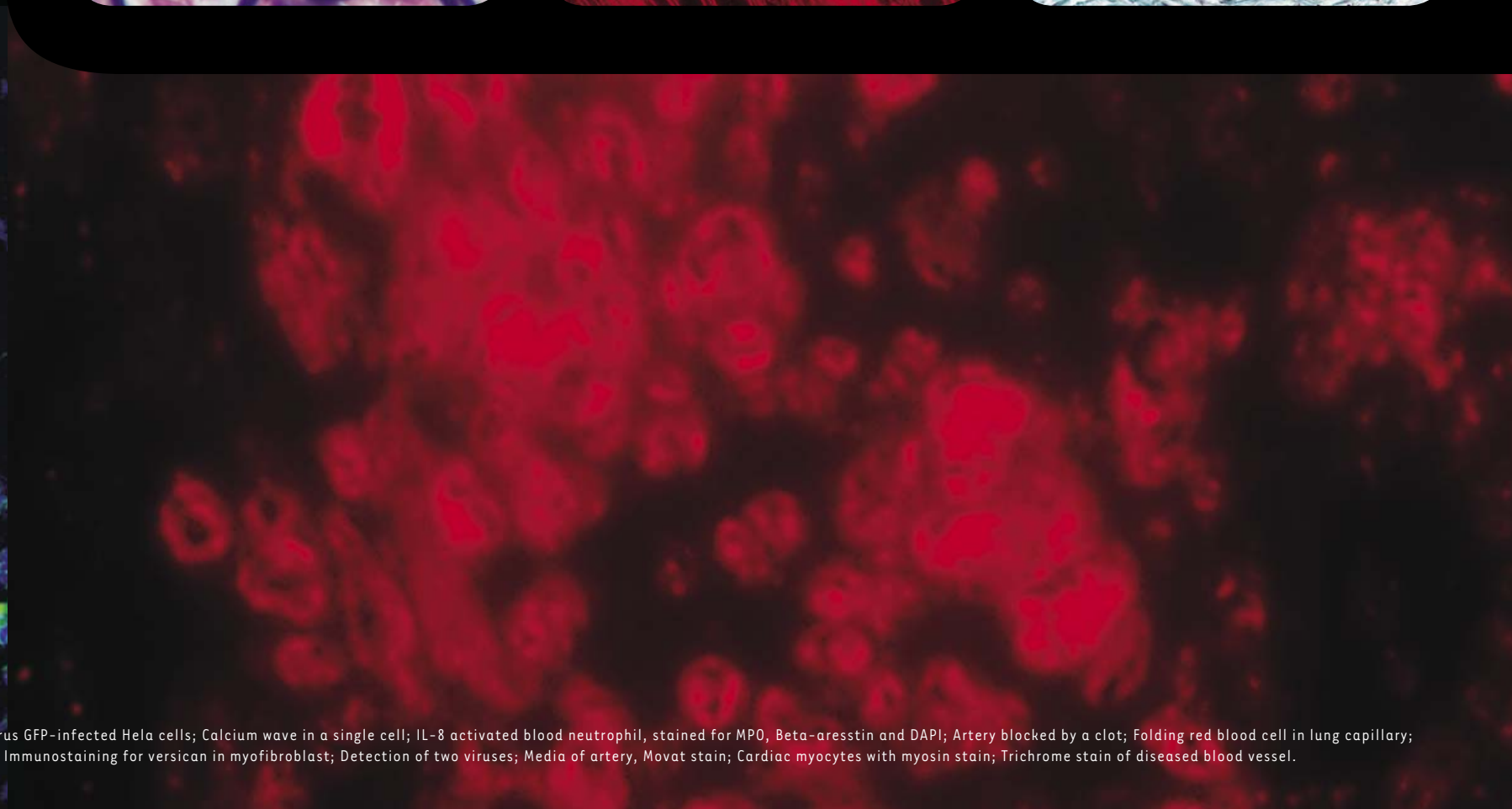
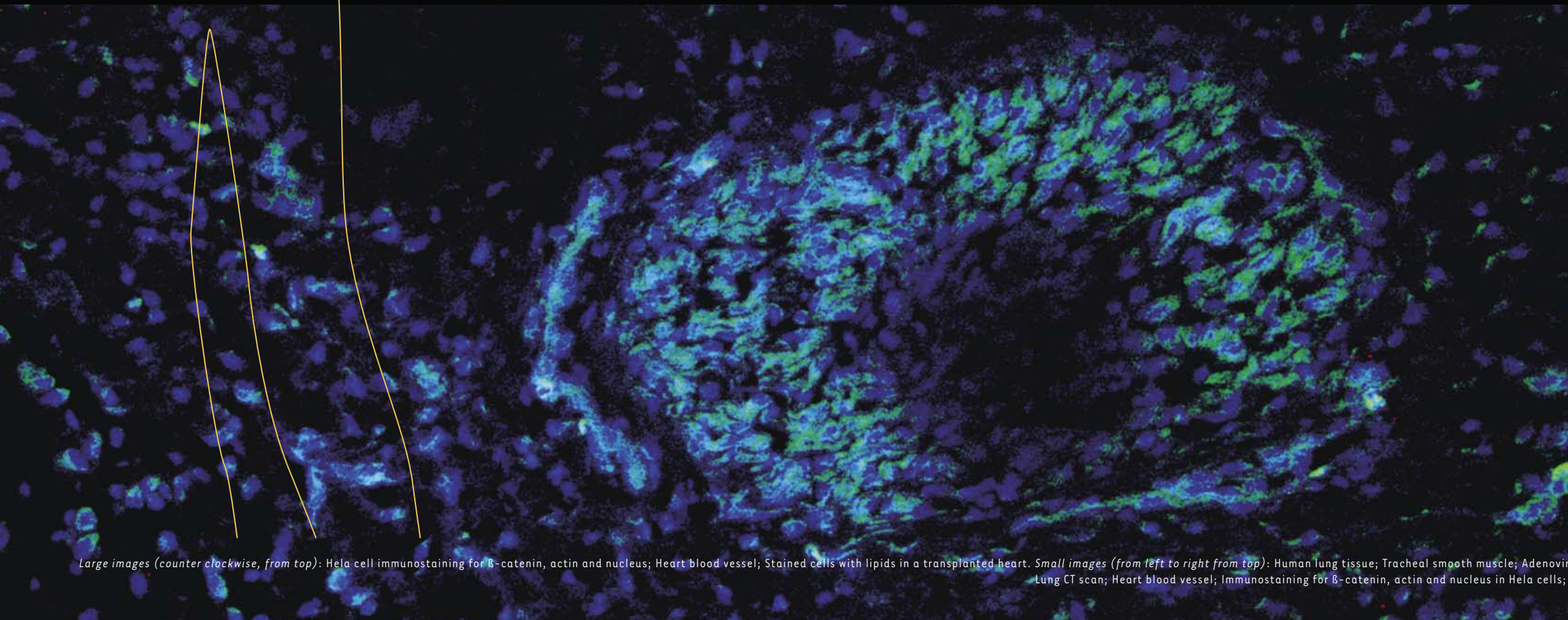
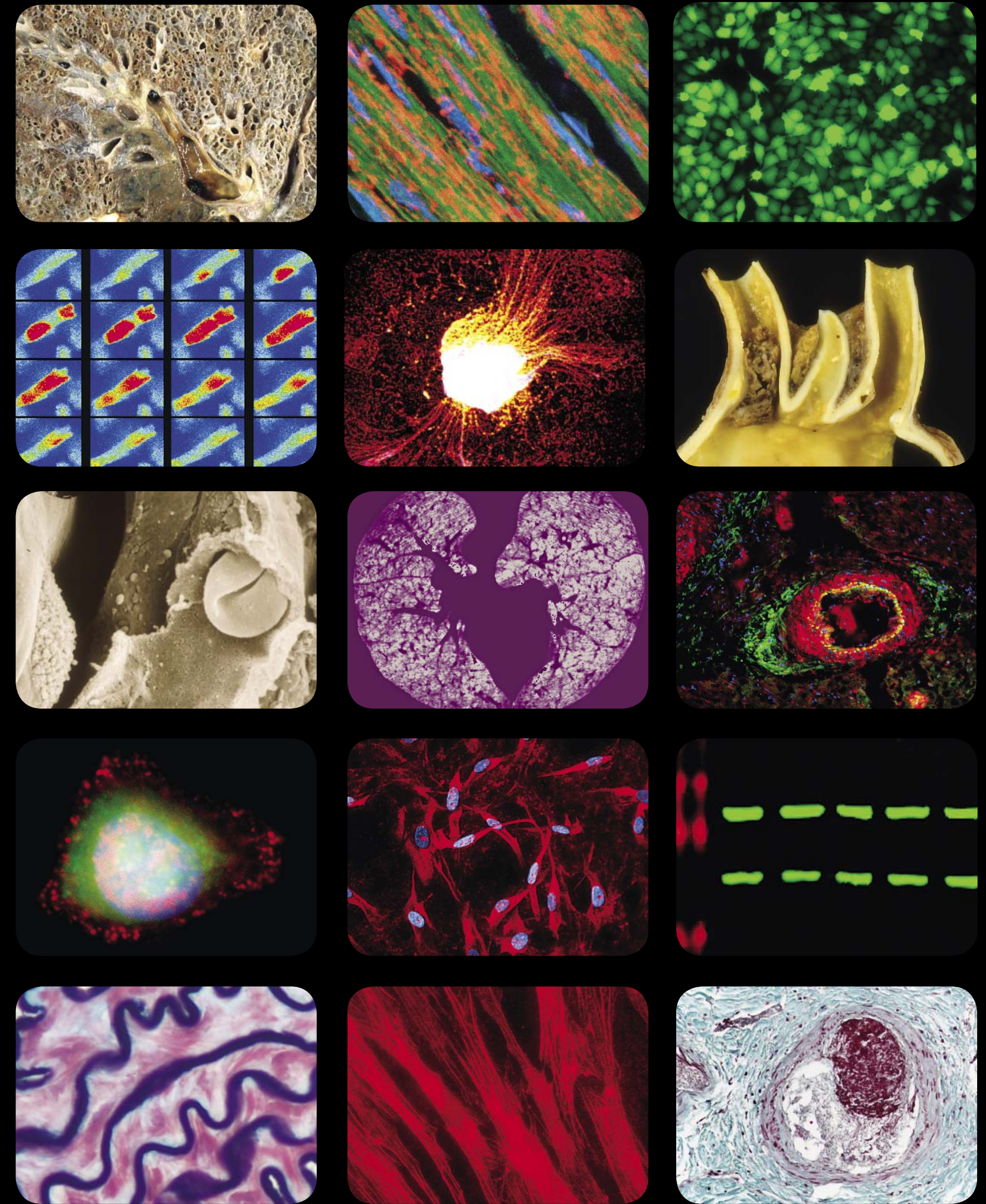
Absent: Mike Allard, Tony Bai, Harvey Coxson, Del Dorscheid, Shizu Hayashi, Richard Hegele, Issy Laher, Andy Sandford, David Walker, Pearce Wilcox.

Private Support of iCAPTURE's Research Worldwide disability from heart, lung and blood vessel diseases continues to rise. The death rate from these diseases still leads all others in the world. iCAPTURE's recent competitive successes with infrastructure funding aren't sufficient to maintain a highly technical and expertly-staffed laboratory. The Centre must continue to raise funds in the private sector. iCAPTURE encourages corporate, private and individual donors to look into iCAPTURE's research, its people and their capabilities with the help of the St. Paul's Hospital Foundation (604 682 8206 / 1 800 720 2983, www.helpstpauls.com) or the UBC Development Office (604 682 8900 / 1 877 717 GIVE, www.supporting.ubc.ca).

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iCAPTURE Imaging, Cell Analysis, and Phenotyping Toward Understanding Responsive, Reparative, Remodeling, and Recombinant Events

“The real voyage of discovery
 consists not in seeking new landscapes,
 but in having new eyes.” — *Marcel Proust*



Large images (counter clockwise, from top): Hela cell immunostaining for β -catenin, actin and nucleus; Heart blood vessel; Stained cells with lipids in a transplanted heart. *Small images (from left to right from top):* Human lung tissue; Tracheal smooth muscle; Adenovirus GFP-infected Hela cells; Calcium wave in a single cell; IL-8 activated blood neutrophil, stained for MPO, Beta-aresstin and DAPI; Artery blocked by a clot; Folding red blood cell in lung capillary; Lung CT scan; Heart blood vessel; Immunostaining for β -catenin, actin and nucleus in Hela cells; Immunostaining for versican in myofibroblast; Detection of two viruses; Media of artery, Movat stain; Cardiac myocytes with myosin stain; Trichrome stain of diseased blood vessel.