Toronto Academic Health Science Network

University Health Network

Toronto General Hospital Toronto Western Hospital Princess Margaret Hospital

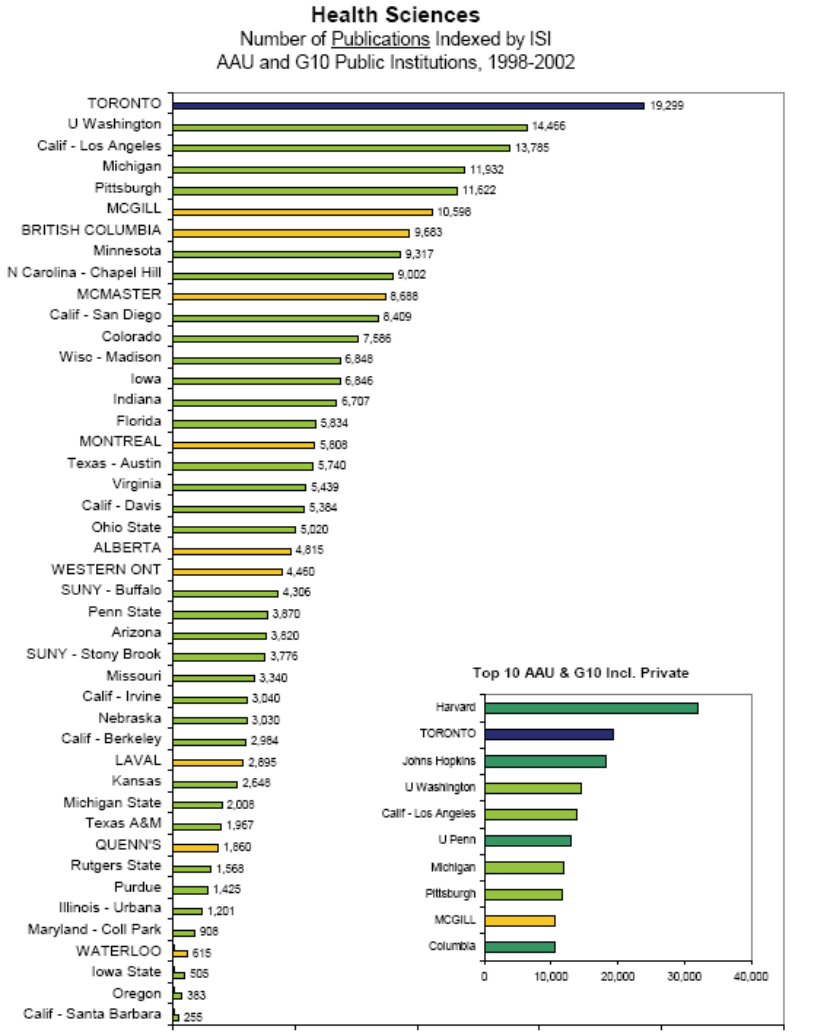
Saving Lives and Creating Jobs

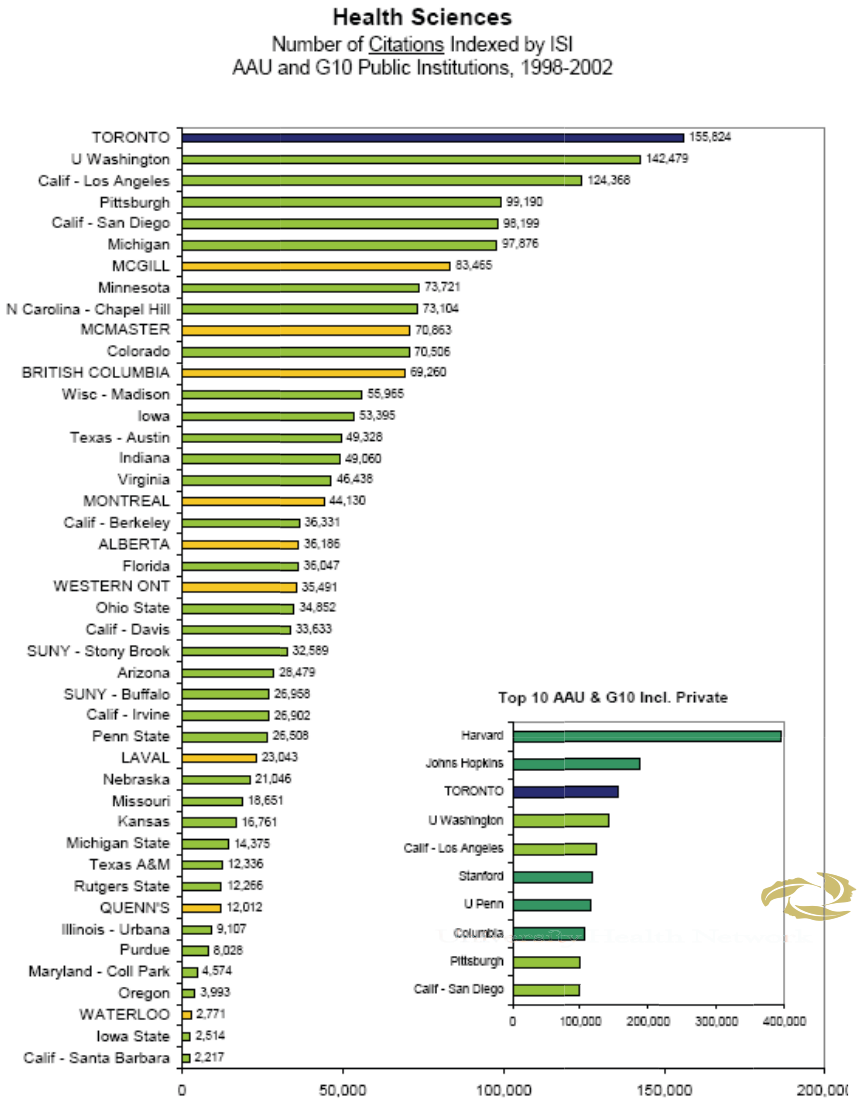
Bob Bell

Breakfast with the Chiefs,

April 2010.

Toronto Produces Outstanding Health Research

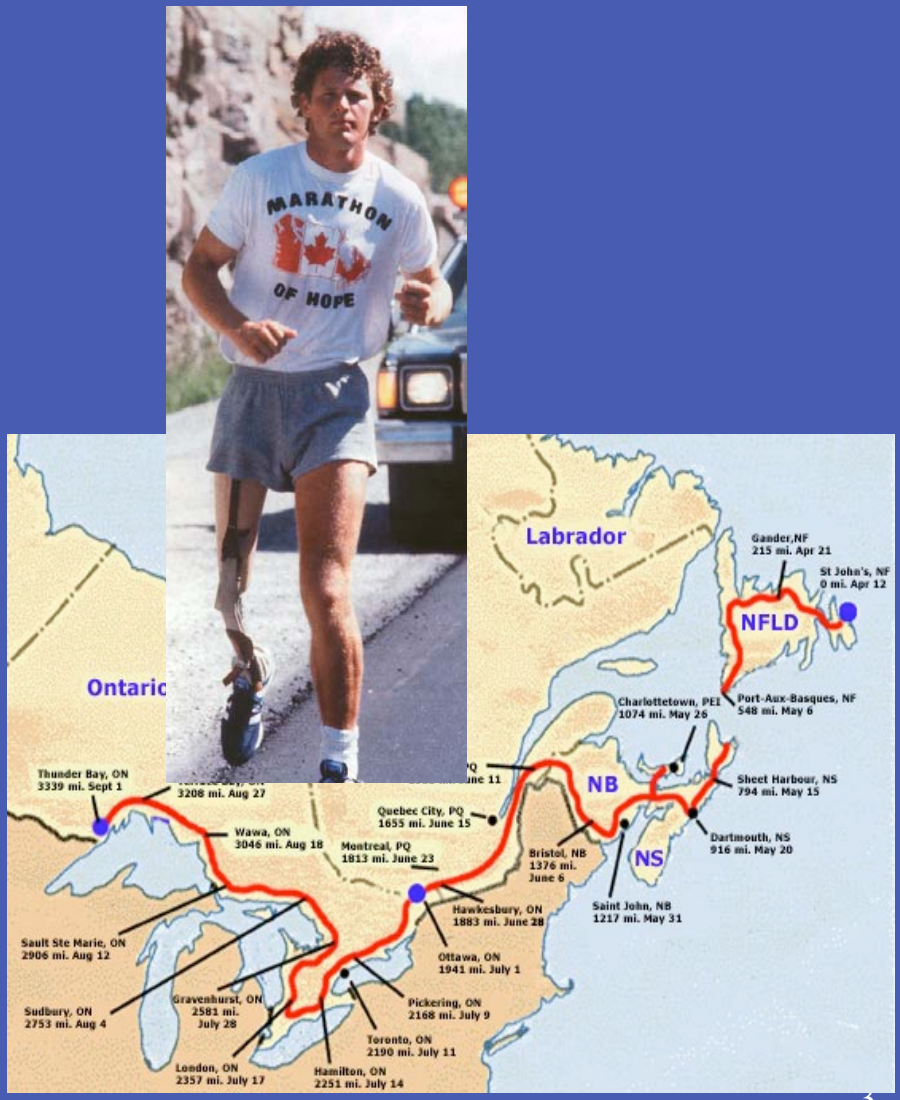




Our Patients have much better outcomes because of TAHSN

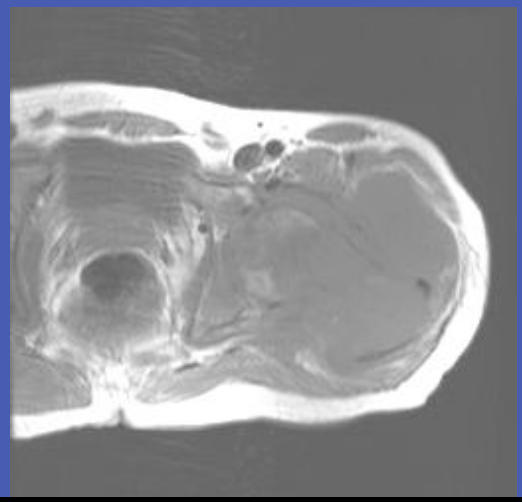
- In 1980 Terry Fox ended his Marathon of Hope in Thunder Bay suffering from spread of osteosarcoma (bone cancer) to his lungs

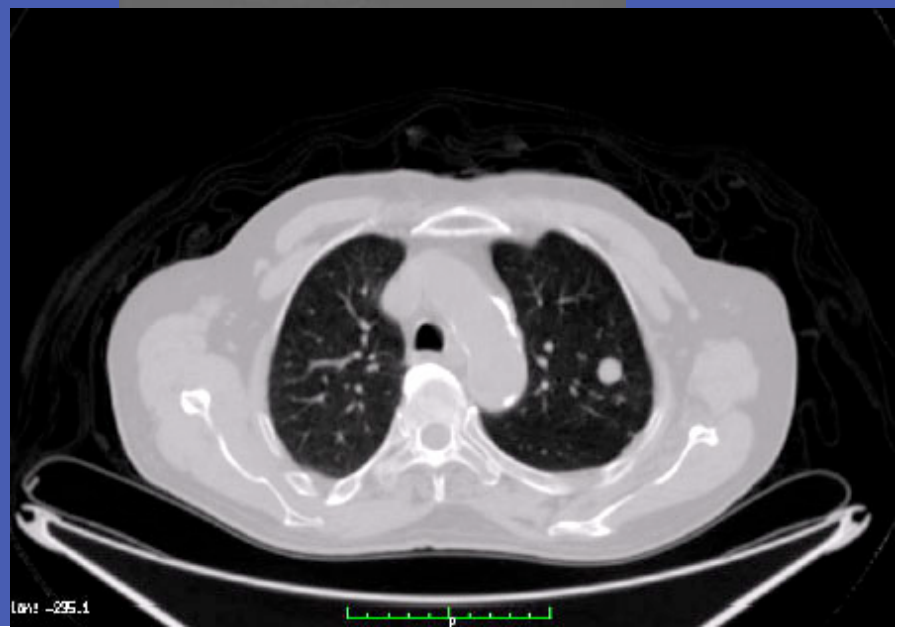
- At that time 90% of osteosarcoma patients required amputations and 85% died of lung metastases



Three Problems with Osteosarcoma in Early 1980's

- Tumours were generally too large to remove without leaving cancer cells behind in leg
- If bone cancers were resected rather than amputated there was no method to replace the bone/joint defect
- Cancer spread to lungs





The Toronto Sarcoma Team

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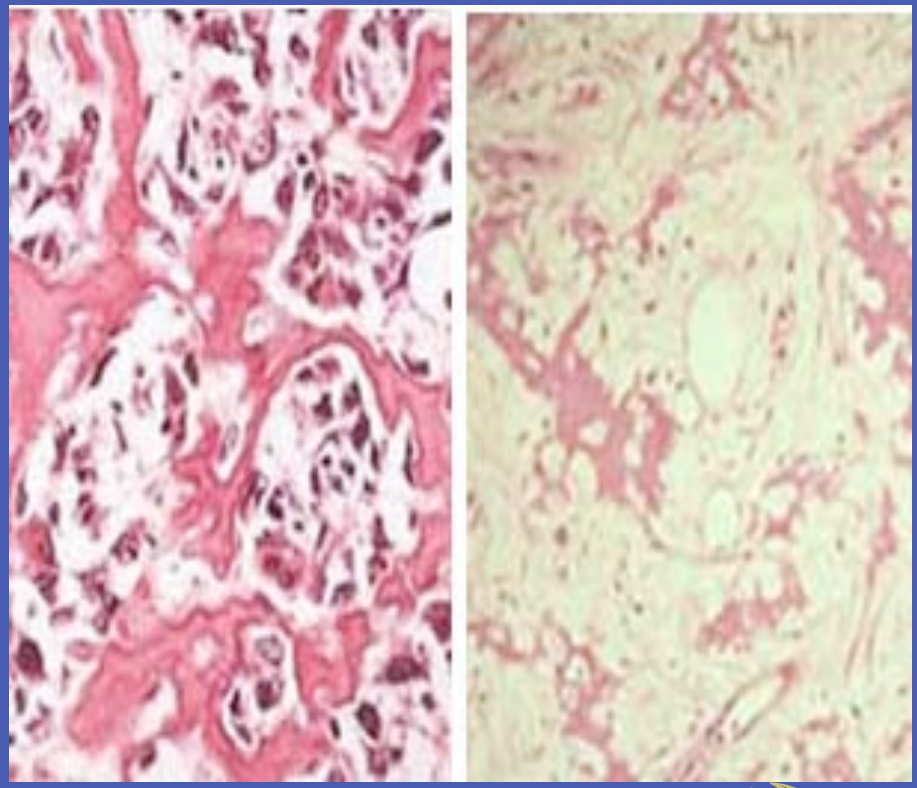
1983- MIOS Study at Boston Children's and Stanford Changed the Treatment of Bone Cancer

- Al Goorin at Boston's Children's Hospital showed that multi-agent chemotherapy dramatically reduced the risk of lung metastases
- Suddenly bone cancer patients had hope

Effect of doxorubicin on local recurrence following marginal resection in the MGH-OGS murine model.

- After demonstrating success of chemo on reducing spread of disease to lungs
- Toronto researchers showed that chemo given prior to surgery killed cancer cells and allowed tumour resection without amputation



Before chemo After chemo

Amputation Not Needed after Chemo: What Could Replace the Bone Defect?

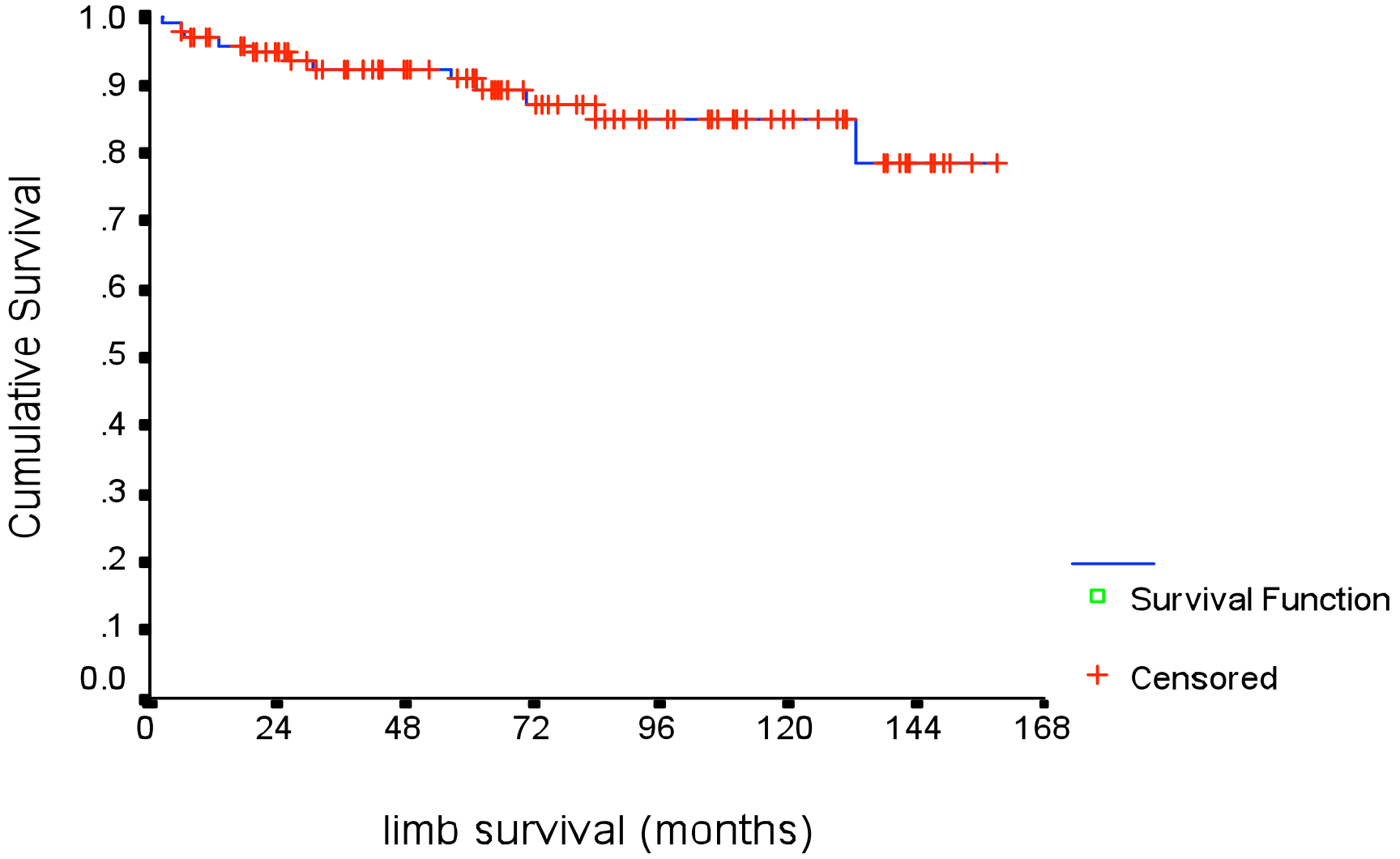
- 1980's - Mount Sinai Hospital and Massachusetts General Hospital became expert in the use of bone transplants in the treatment of bone cancer
- These offered excellent early results but broke down after 2-5 years
- Other centres used cemented metallic prostheses - but these broke down after 2-7 years

The Development of Bone In-growth Metal Prostheses to Replace Bone Cancers

- A collaboration between Austrian and Toronto hospitals resulted in the development of a metal bone and joint replacement with a surface that allowed in-growth of bone into the metal without cement

Limb survival

entire sample (n=99)



Failure Beyond Ten Years Is Usually Related to Prosthesis Fracture

- Most patients have virtually normal function with bone in-growth artificial bone and joint past ten years
- Approximately 10% of patients sustain fractures in their prosthesis

Toronto Hospital Collaboration with Industry Has Resulted in a Substantially Improved Prosthesis

- Identification of fracture risk
- Collaboration in design of new prosthesis
- Development of prosthesis and instrumentation in hospital labs and surgical skills centre

Lung Metastases

- Despite success of chemotherapy in curing 75% of patients, 25% develop lung metastases
- Multiple trials with different chemo show no improvement
- Can biological agents improve these results?

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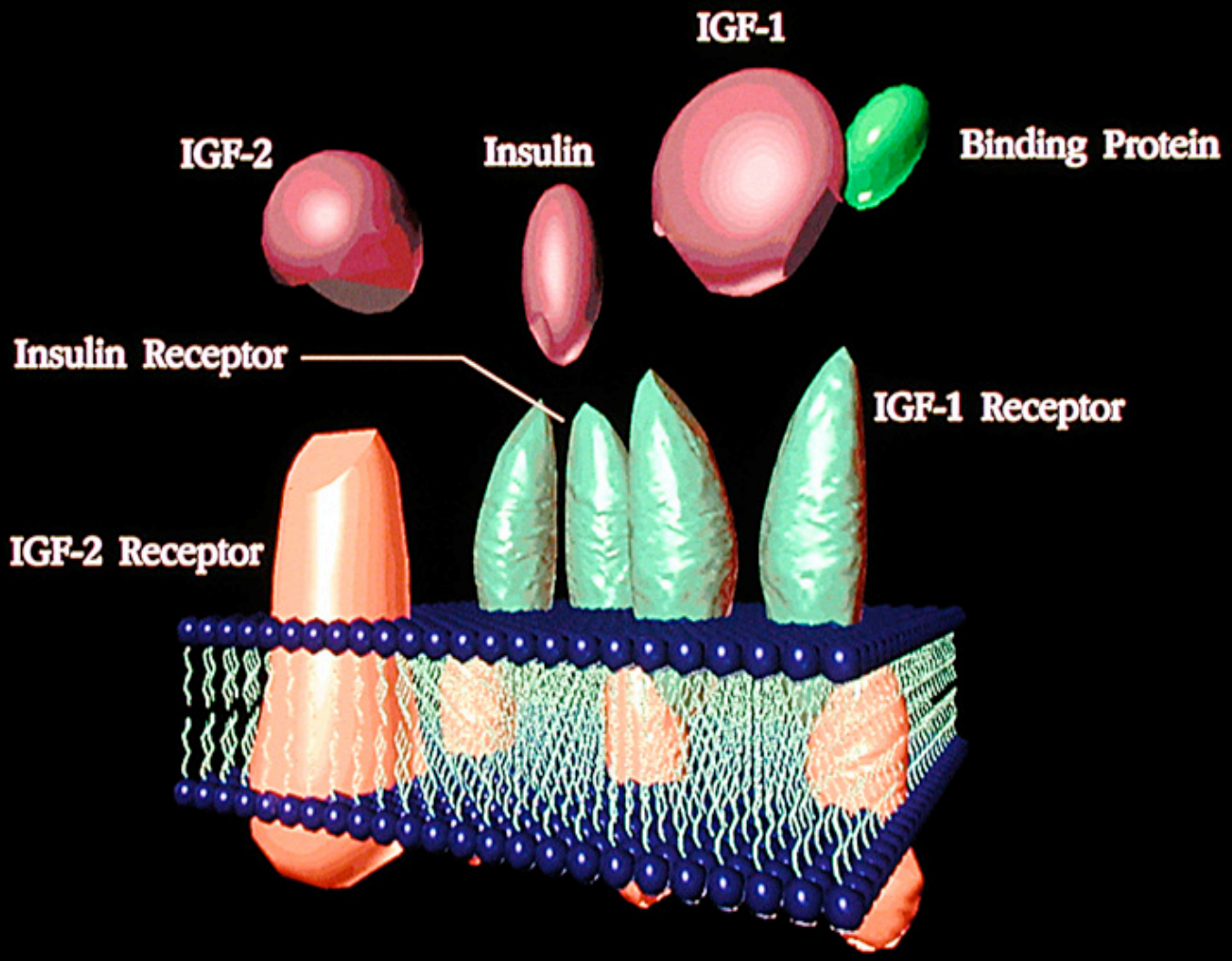
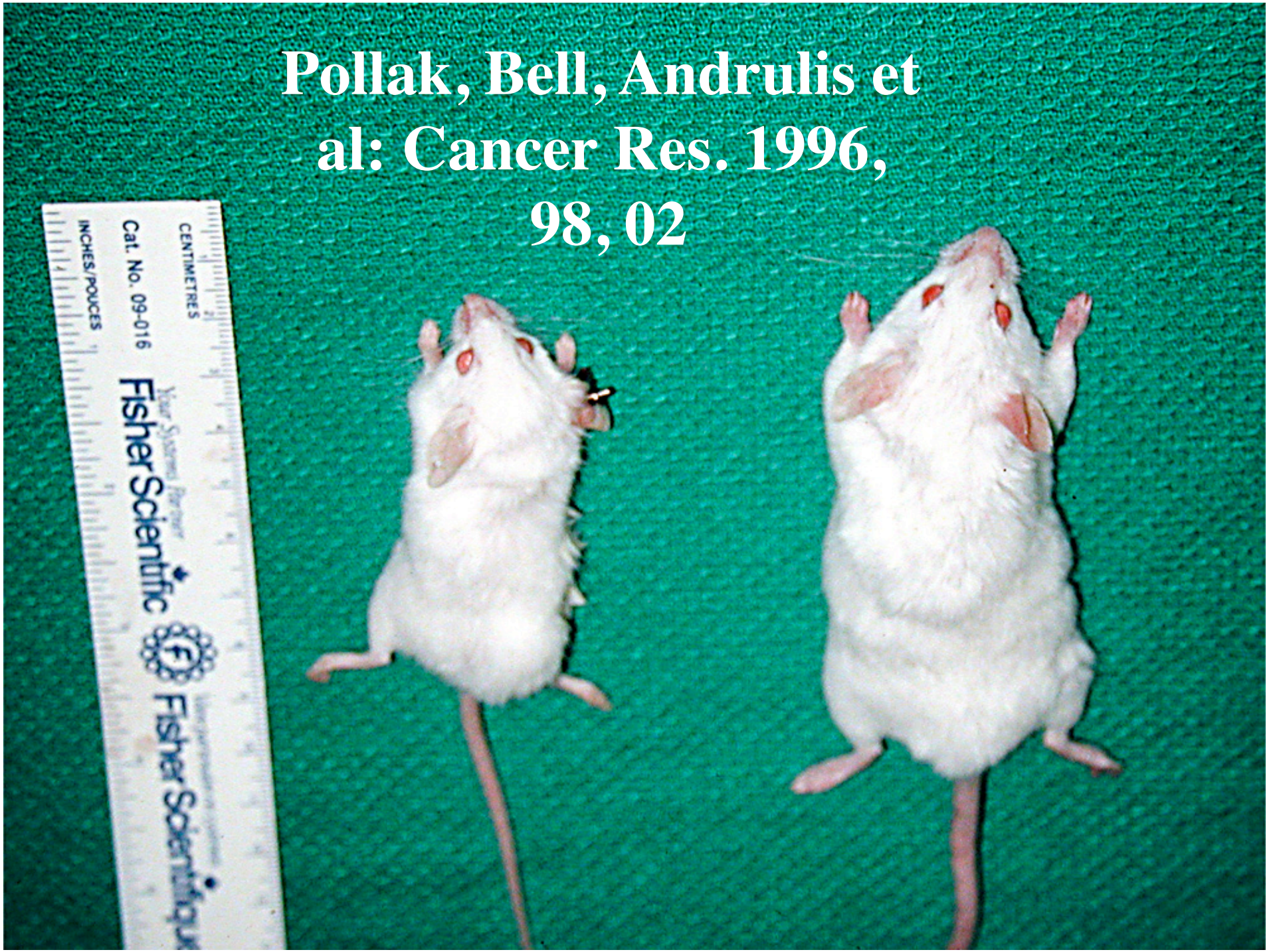
The Insulin-Like Growth Factor Family




Pollak, Bell, Andrulis et al: Cancer Res. 1996, 98, 02
CENTIMETRES
INCHES/POUCES
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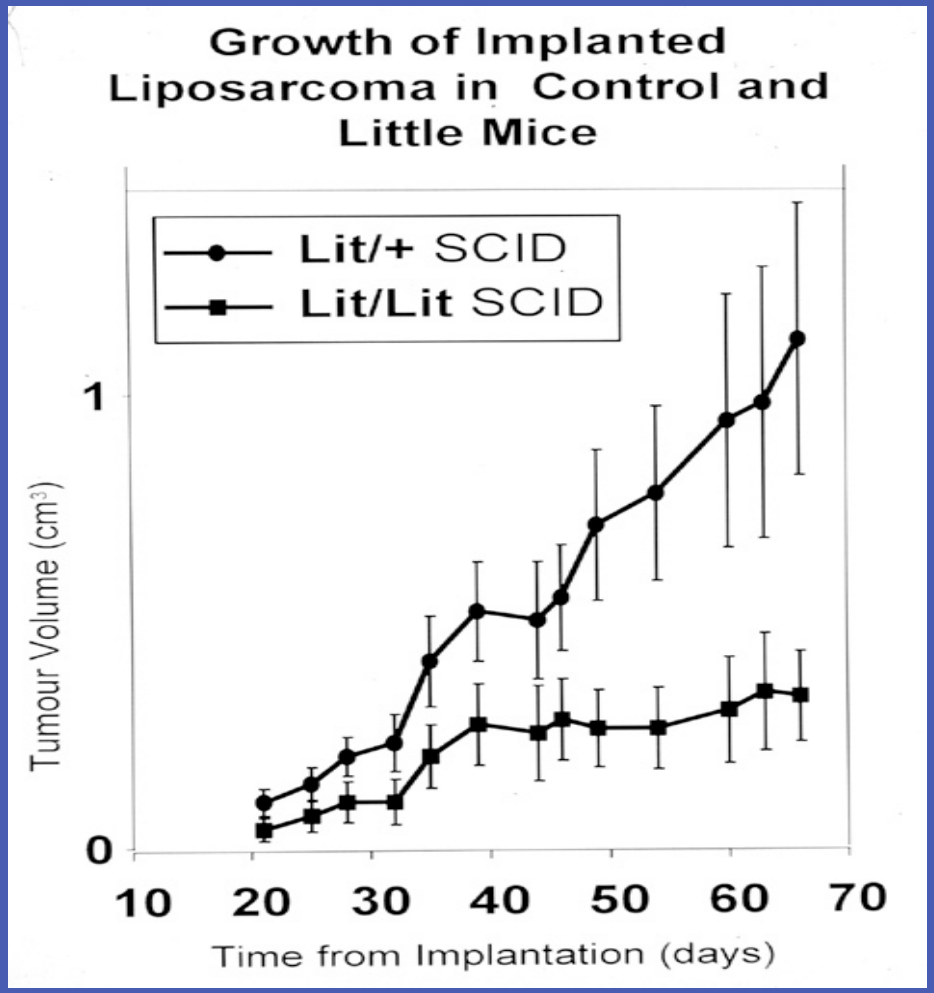
Little Mice Had Slower Tumour Growth and Less Lung Disease



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IGF Inhibitors are Currently in Clinical Trials

- TAHSN identifies molecular abnormalities that are associated with cancer
- Molecular inhibitors tested in human tumour transplants in mice
- Inhibitors now being tested in patients

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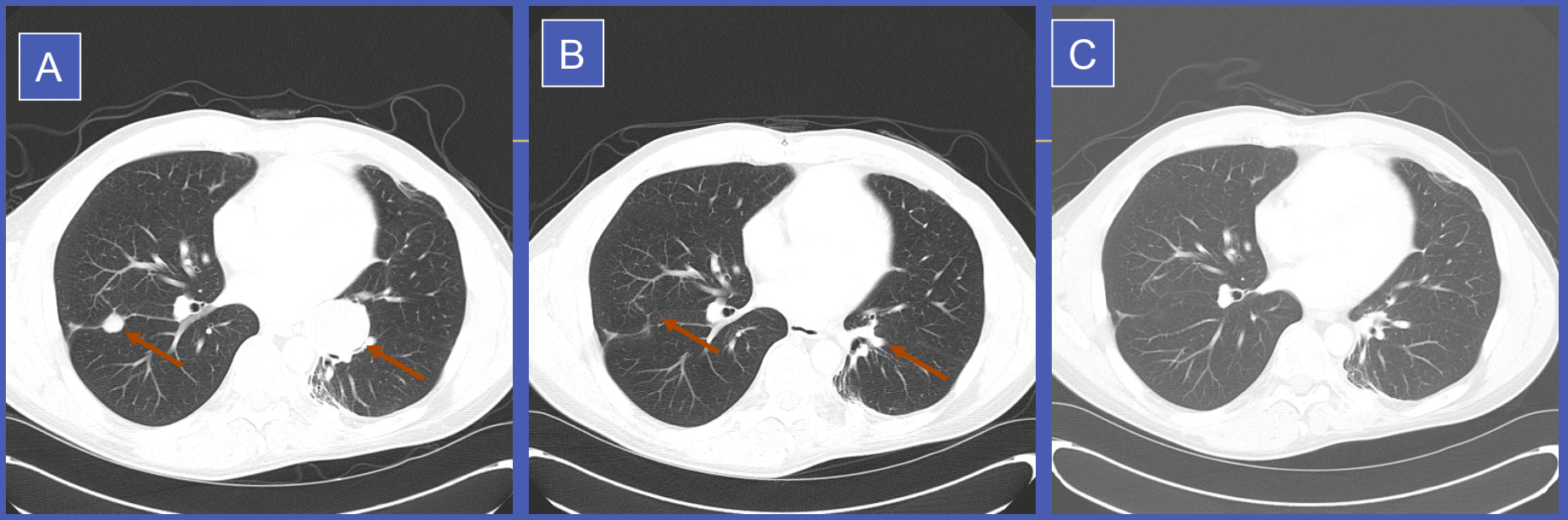
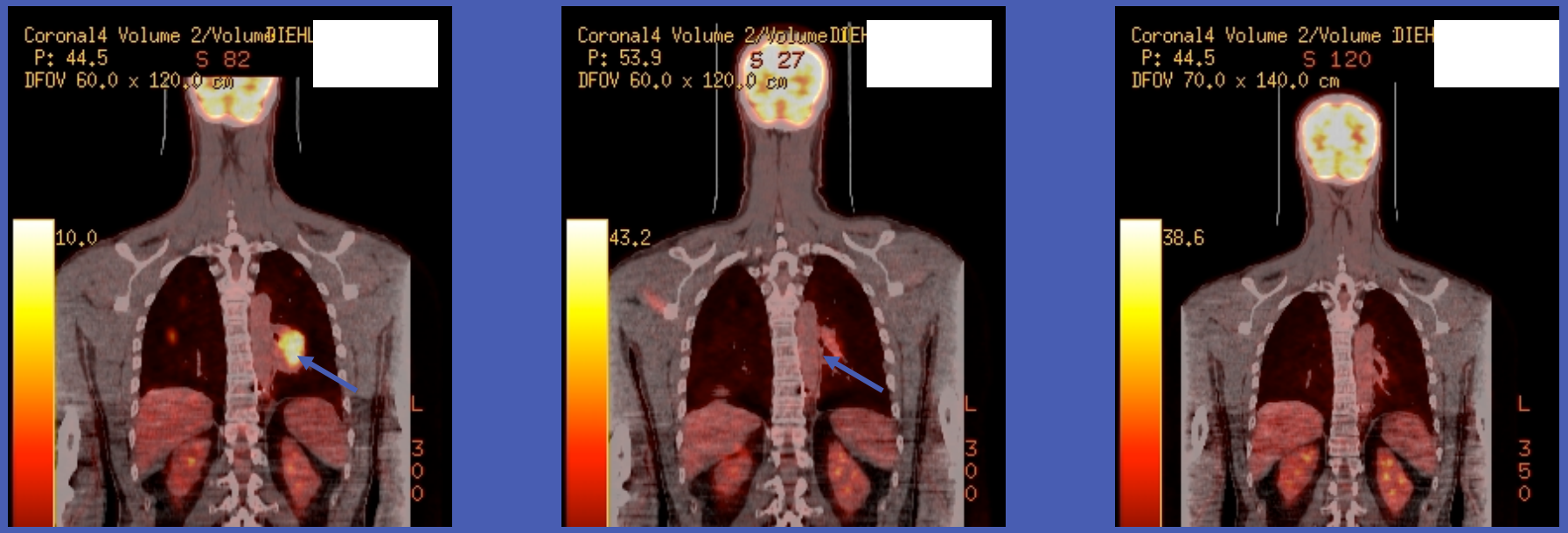
44 year old farmer with third systemic relapse of Ewing's sarcoma





Technology and Discovery

Antonie Philips van Leeuwenhoek

1632 - 1723

…cloth merchant in Amsterdam - magnifying glasses mounted on a small stand used by textile merchants, capable of magnifying to a power of 3.
Improved lens to 300-500X and exposed the field of micro-biology.

Commerce,
Technology, Discovery
Science

(in that order)

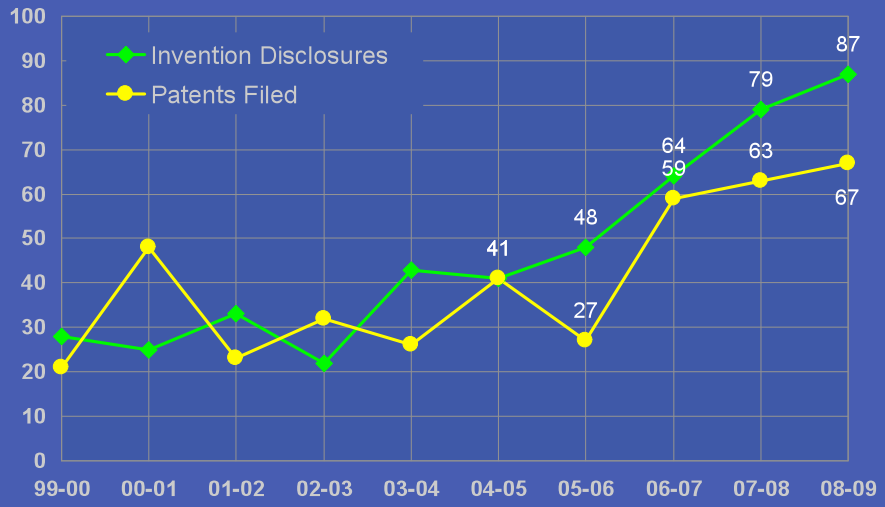
A Collaboration with the Engineering and Physical Sciences at the University of Toronto

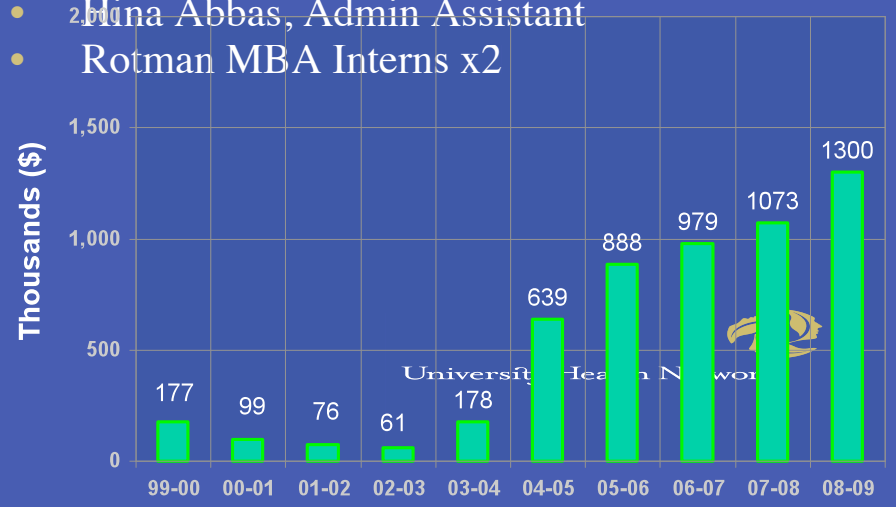
Engineering at U of T is ranked #1 in Canada and 10th overall in the world by the 2008 U.S. *News & World Report and Times Higher Education-QS World University Ranking*

Network

UHN's Technology Development and Commercialization Office – Largest in Canada

- Brian Barber, Ph.D., Director
- Frank Rossetto, Ph.D.,J.D. Dep Dir. & Legal Counsel
- Mark Taylor, P. Eng. M.Sc. MBA, Senior BDO
- Patricia North, LL.B., LL.M. Contracts Specialist
- Thomas Parsons, M.Sc., Senior BDO
- Martin Haardt, Ph.D., BDO
- Rahbar Rahimpour, Ph.D., MBA, Senior BDO
- Yuan Lew, M.Sc. MBA, BDO
- Joe Miller, B.Sc, BDO
- Cheryl Adamo, MA, Compliance Officer
- Vishan Sivagnanam M.Sc., Research Clerk
- Hina Abbas, Admin Assistant
- Rotman MBA Interns x2





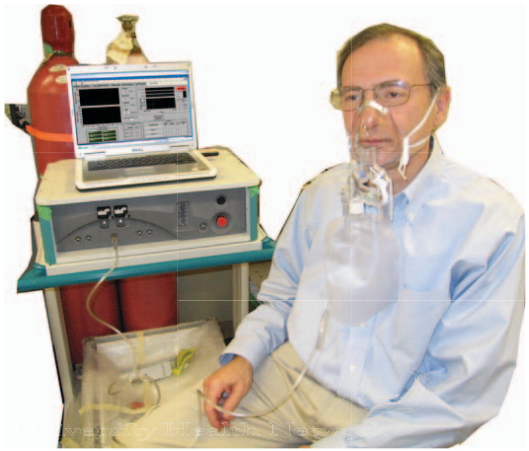
Thornhill Research Inc.

- MOVES™ - Transport Life Support System
  - ICU functionality in a portable integrated system
  - Status:
    - $12MM in development contracts from US military
    - FDA submission June 2009
    - $20MM procurement contract scheduled for late 2009
- DuoCheck™ Patient Safety System
  - Reduces drug error on the operating room
  - Enables simple anesthesia record charting

Thornhill Research Inc.

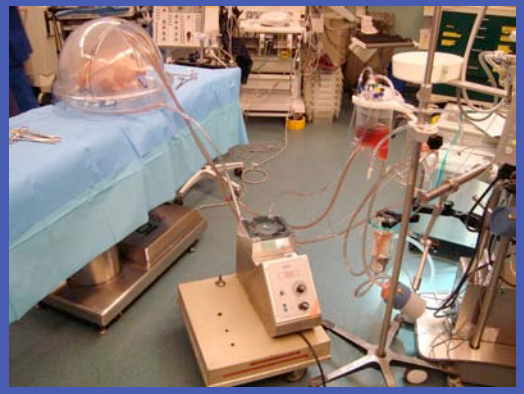
- Accu-Fick™ Non-Invasive Cardiac Output
  - First non-invasive device for both spontaneously breathing and ventilated patients
  - Status:
    - Pilot studies complete (130 patients)
    - Refinement and clinical studies ongoing

- RespirAct™ Neuro-imaging Device
  - Able to accurately manipulate brain blood flow to enhance vascular reactivity measurement
  - Improves stroke diagnosis and management
  - Status:
    - Studies under way at UHN, Duke University, University of Nottingham (UK), Montreal Neurological Institute (McGill), Hospital for Sick Children, University of Montreal, University of Colorado, Presbyterian Hospital (Dallas), University of Otago (NZ)



The Future of Innovation: Ex Vivo Lung Conditioning

- 70% of potential lungs from organ donors are damaged
- TGH research showed that ex vivo treatment can “reclaim” half of discarded lungs
- Following first patient applied in 16 further cases within 6 months
- Will double lung transplant rates



Univers

$26M in 2008- $130M in 2010

agios

Cancer Metabolism
Targeting the Achilles' Heel of Cancer

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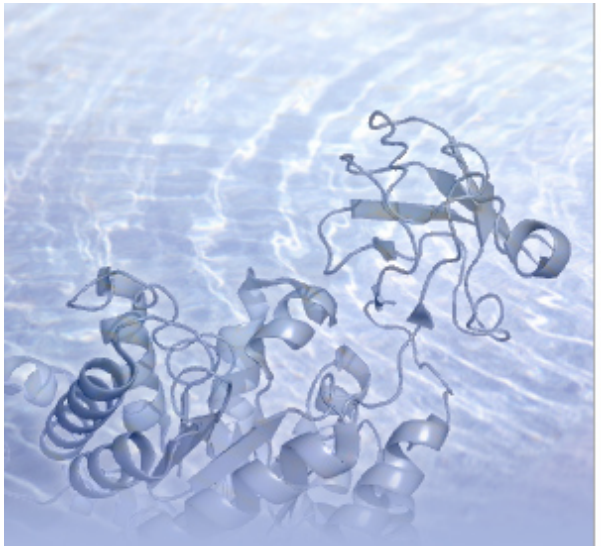


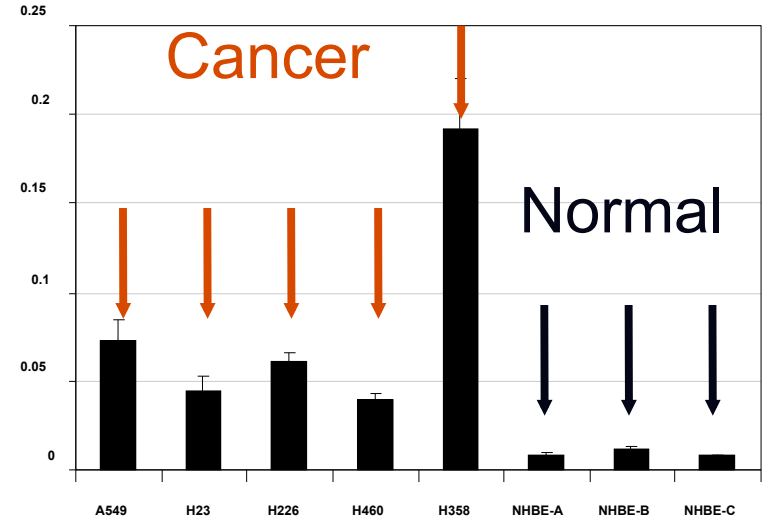
Agios is a biopharmaceutical company at the forefront of one of the most exciting new areas of cancer research: cancer metabolism. Cancer metabolism represents a breakthrough understanding of how cancer cells become addicted to using more nutrients than normal cells to ensure their survival and growth.

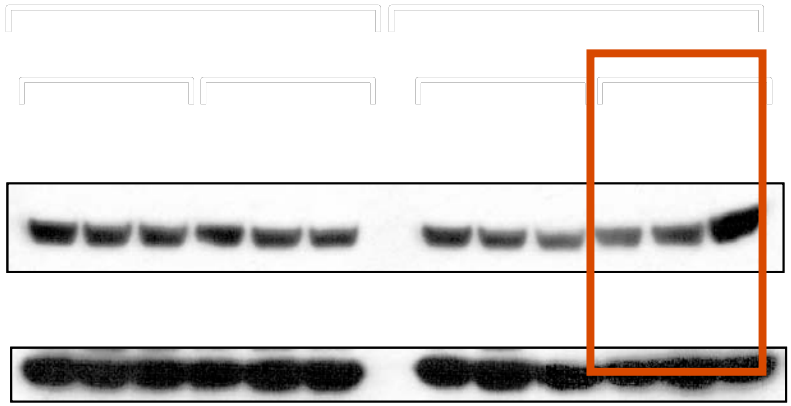
Agios Pharmaceuticals is developing a deep pipeline of drug candidates that disrupt the growth and survival of cancer based on unique insights of the founder, scientific advisory board as well as building on decades of research in the fields of oncology and metabolism.

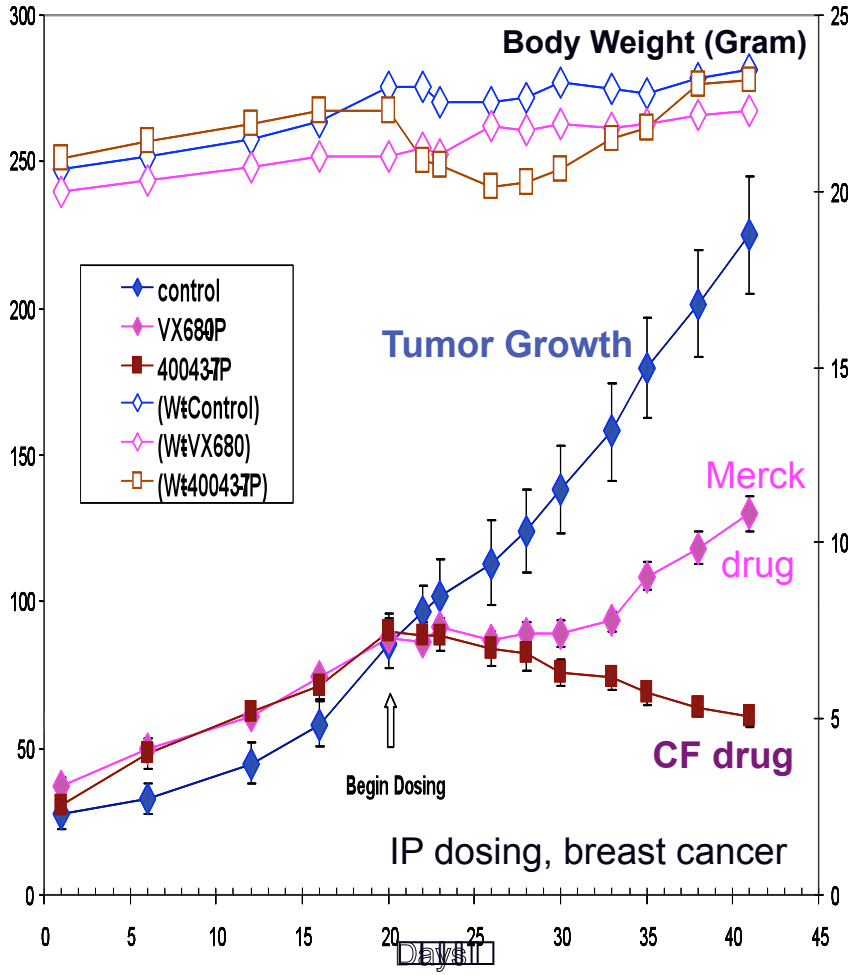
Campbell Family Drug CFl20

Up-regulated in Cancer cells in Low Oxygen

Regression of Human Cancer in Mice







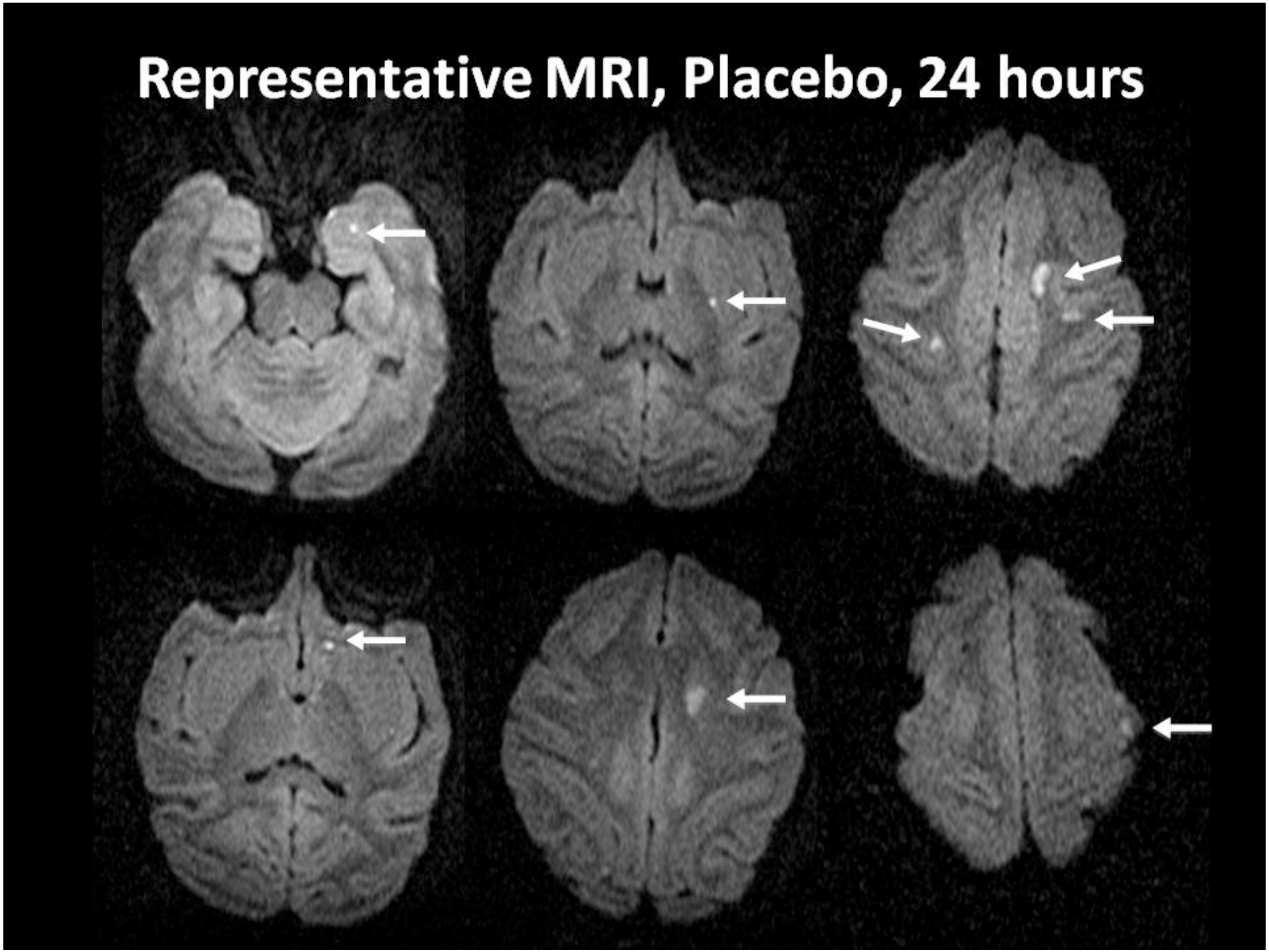
REPORTS

Treatment of Ischemic Brain Damage by Perturbing NMDA Receptor–PSD-95 Protein Interactions

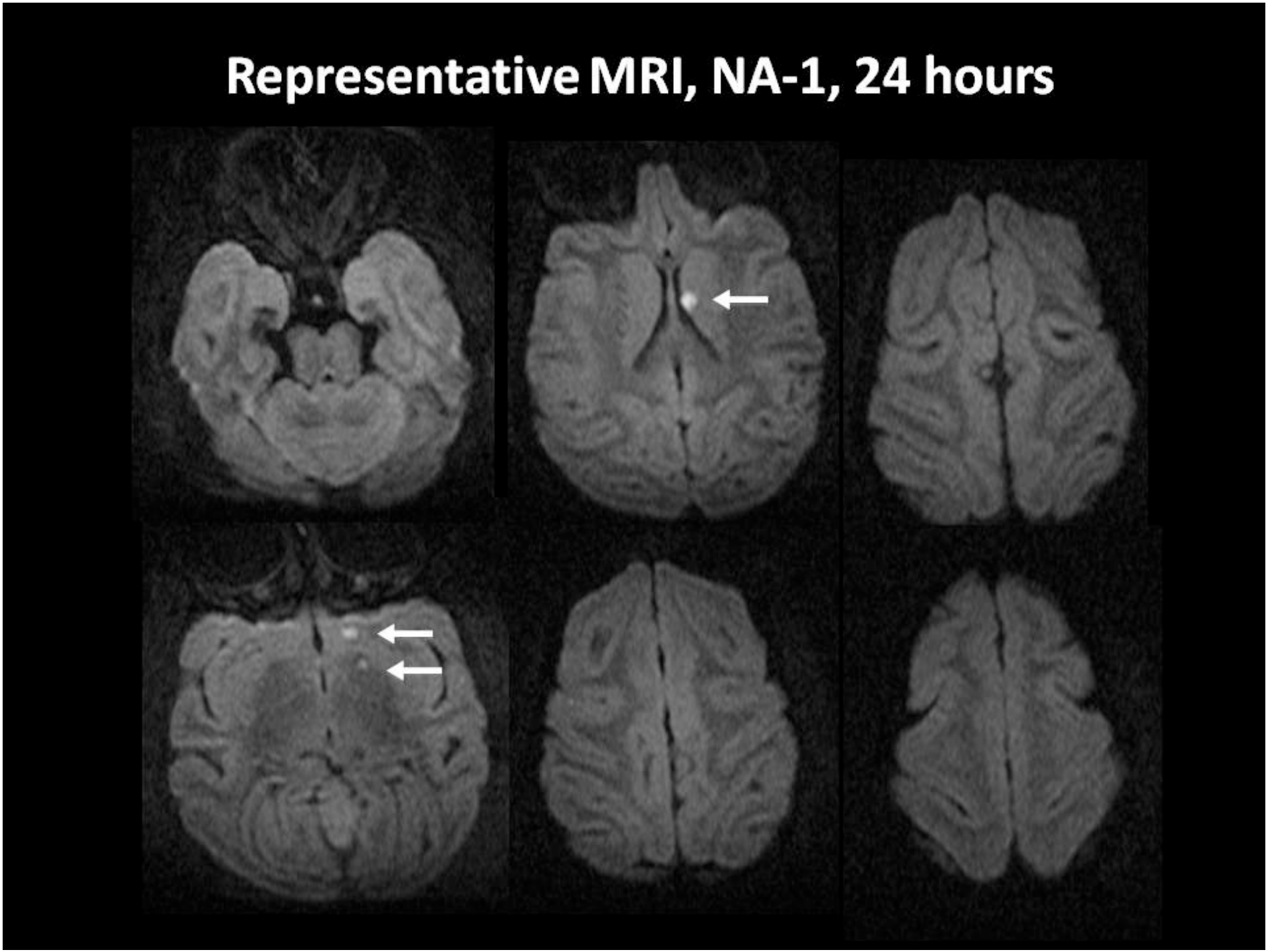
Michelle Aarts,[1*] Yitao Liu,[2,3,4*] Lidong Liu,[2,3,4] Shintaro Besshoh,[5] Mark Arundine,[1] James W. Gurd,[5] Yu-Tian Wang,[2,3,4] Michael W. Salter,[3,6†] Michael Tymianski[1,6,7†]

N-methyl-D-aspartate receptors (NMDARs) mediate ischemic brain damage but also mediate essential neuronal excitation. To treat stroke without blocking NMDARs, we transduced neurons with peptides that disrupted the interaction of NMDARs with the postsynaptic density protein PSD-95. This procedure dissociated NMDARs from downstream neurotoxic signaling without blocking synaptic activity or calcium influx. The peptides, when applied either before or 1 hour after an insult, protected cultured neurons from excitotoxicity, reduced focal ischemic brain damage in rats, and improved their neurological function. This approach circumvents the negative consequences associated with blocking NMDARs and may constitute a practical stroke therapy.

25 OCTOBER 2002 VOL 298 SCIENCE www.sciencemag.org


Representative MRI, Placebo, 24 hours

Representative MRI, NA-1, 24 hours



NA-1 Trials

- **Drug currently in Phase IIIb randomized trial across Canada**
- **Market potential for all cardiac bypass patients**
- **Market potential for all aneurysmal coilings**
- **Market potential for early management of strokes**

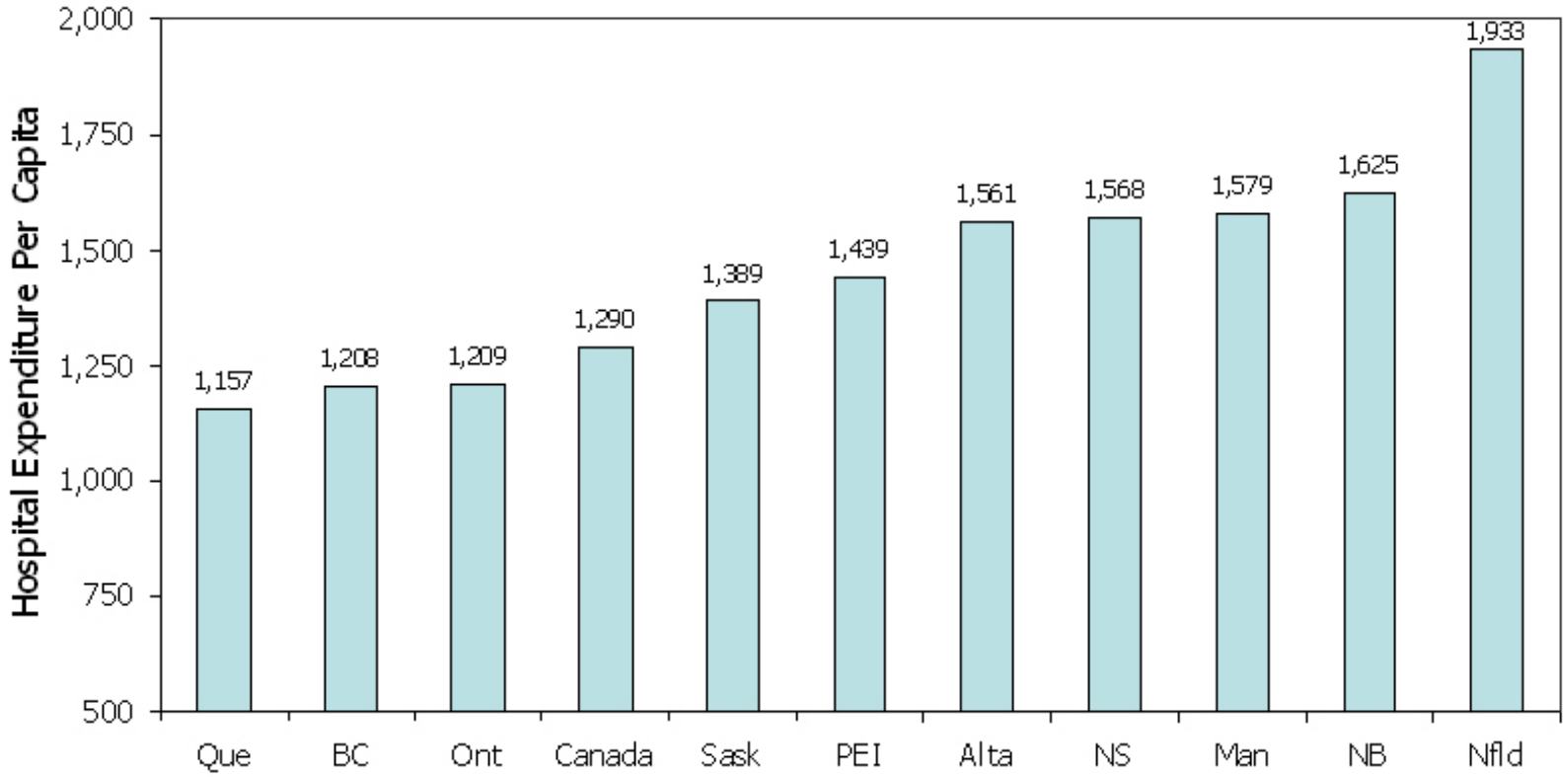
MaRS:
The Economy of the Future?

MaRS Innovation

- U of T, Ryerson, OCA and ten affiliated hospitals have joined to combine technology transfer
- Science convergence and commercialization centre
- Focus on international market sensitivity and selection of best projects
- User friendly approach to venture capital

The Ontario Advantage

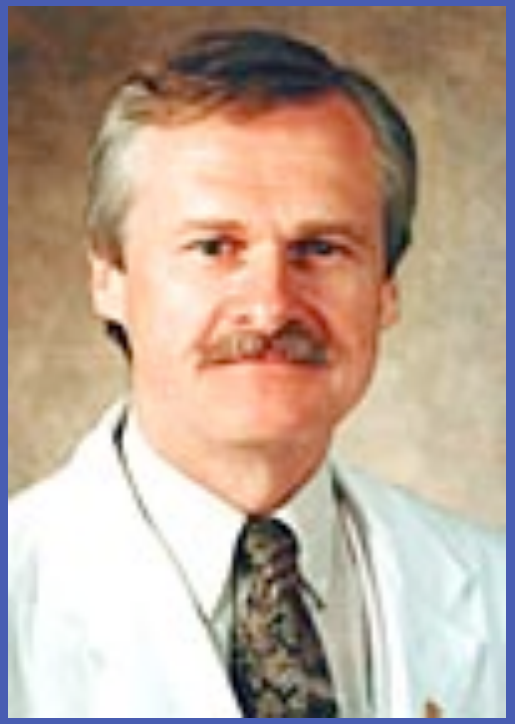
Hospital Expenditure per Capita by Provincial Governments, by Province, 2008



Source: National Health Expenditure Database, Canadian Institute for Health Information, 2008.
Notes: Data for 2008. Canada average includes the territories.

Evidence that Reduces Costs and Improves Outcomes

- Research showed that OR communication impacted safety
- Checklist developed to improve communication
- International study by WHO using UHN checklist
- Checklist saves lives and money



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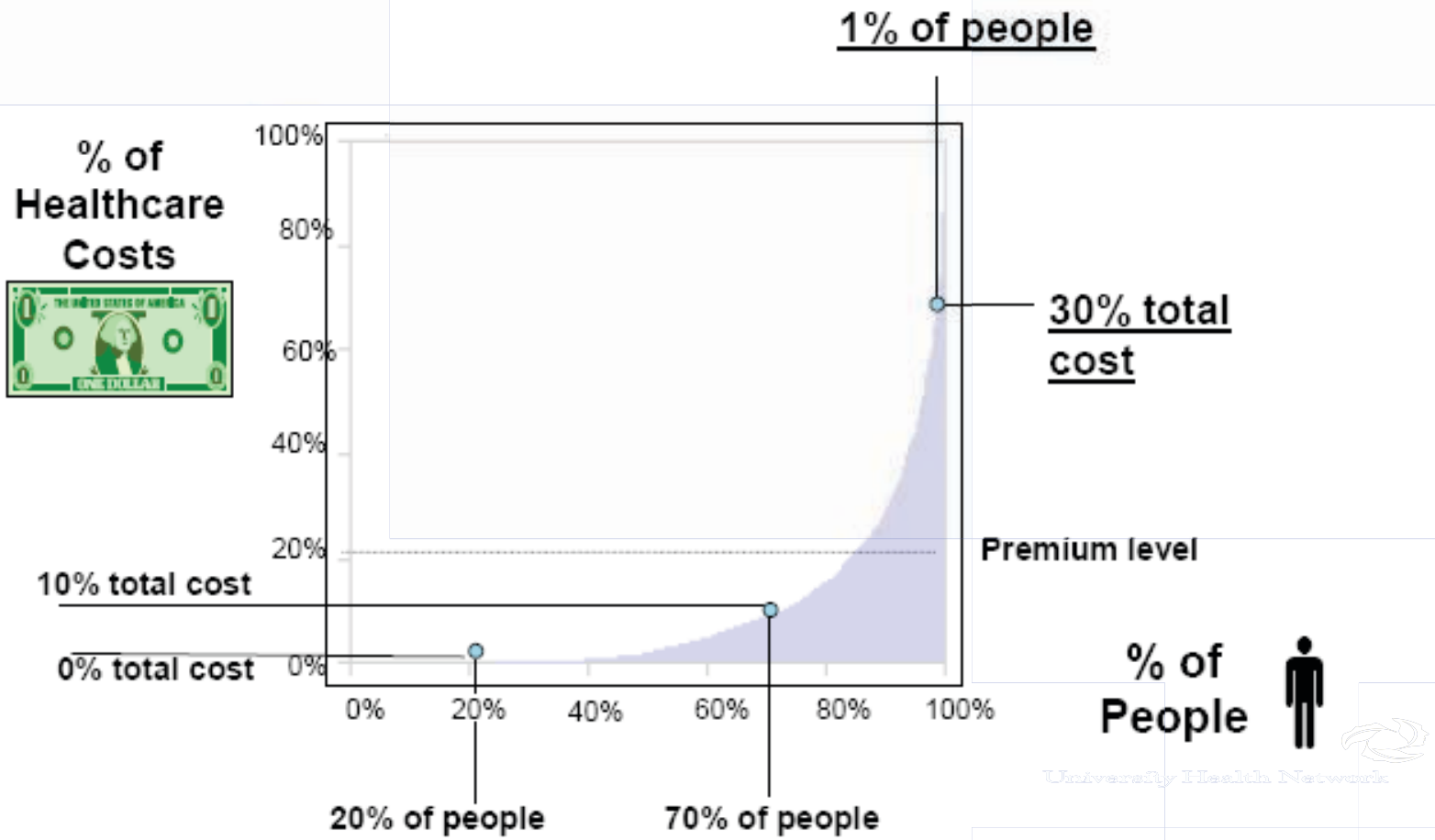
Cost Distribution

KAISER PERMANENTE® thrive



Source: Milliman USA Health Cost Guidelines – 2001 Claim Probability Distribution

Value for Money and Getting More Valuable

- Hospitals in Toronto & Ontario are the most efficient in Canada
- 80% of Canada's life science research is done in hospitals with more than half done in three Toronto hospitals
- Increased emphasis on commercialization of knowledge and development of evidence that changes healthcare policies

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