Toronto's Discovery District

- Research Institute's Firsts and Breakthroughs -

Innovation – Technology - Business

1914 John Gerald Fitzgerald of the Faculty of Medicine establishes the anti – toxin laboratories, which subsequently become the Connaught Laboratories

1921 Working in a University laboratory, Frederick Banting, Charles Best, J.J.R. Macleod and J.B. Collip are the first to obtain **insulin in a form consistently effective for treating diabetes mellitus**. In 1923, Banting and Macleod would receive the Nobel Prize.

1929 Davidson Black, a medical graduate, **discovers the skull of "Peking Man", an important clue to the nature of humanity's ancestors**

1930 Frederick Tisdall, Theodore Drake and Alan Brown of the Faculty of Medicine announce the **creation of the infant cereal, "Pablum"**

1933 Under the direction of Charles Best, a university – based research team begins work on heparin, an anti – coagulant, which would open the fields of vascular surgery and renal dialysis

1936 Medical graduate Norman Bethune, later a hero of the People's Republic of China, organizes the **world's first mobile blood transfusion unit** in Spain

1942 Wilbur Franks, a medical graduate, develops the **"anti-black-out" suit**. Credited with saving thousands of Allied fighter pilots during WW II, his invention would be **worn by every air force pilot in the world and eventually be developed into the space suit worn by astronauts**

1945 Raymond Parker of the university's Connaught Medical Research Laboratories discovers a **defined chemical nutrient medium in which cells can grow and replicate**. His discovery helps Jonas Salk to develop the polio vaccine

1948 W.G. Bigelow begins studies of hypothermia as a means of performing open-heart surgery. Later, he would be part of the team that designs the **first electrical cardiac pacemaker**.

1961 James E. Till and Ernest A. McCulloch discover the hemopoietic stem cell. This is the basis for **bone marrow transplantation**, which is a highly successful clinical story today.

1962 Dr. Harold E. John establishes Canada's first Department of Medical Biophysics and develops cobalt therapy units which **revolutionise radiation treatment of cancer** around the world.

1963 W.T. Mustard perfects his surgical method for **correcting "blue baby" syndrome**.

1978 Dr. Cecil Yip identifies the **insulin receptor**.

1981 Drs. Griffith Pearson and Joel Cooper perform the world's **first single lung transplant**.

1984 Geneticist Tak Mak helps identify the **T-cell receptor gene**, a major advance in our understanding of the body's immune system.

1988 Surgeons Alan Hudson and Susan MacKinnon perform the world's **first nerve transplant** on a nine-year-old boy.

1988 Dr. Victor Ling discovers the process which cancer cells use to **resist anti-cancer drugs**.

1989 George Alexander Patterson performs the **first double lung transplant**.

1989 Lap-Chee Tsui and Manuel Buchwald of the Department of Medical Genetics and Jack Riordan of the Department of Biochemistry & Clinical Biochemistry **isolate the gene that causes cystic fibrosis**.

1991 A team led by Tony Pawson of medical genetics and microbiology and Mount Sinai Hospital's Samuel Lunenfeld Research Institute identifies how **cell receptors transmit signals instructing the cell to change**. This discovery will have many benefits, including the development of new cancer drugs.

1991 Dr. Philip Seeman identifies two **new dopamine receptor proteins**, D4 and D5, clearing the way to finding more effective and safer medicines for treating psychosis, schizophrenia and possibly cocaine addiction.

1994 Dr. Endel Tulving, one of three scientists awarded the annual Killam Memorial Prize, proves that different **areas of the brain** are activated when different types of memory are engaged.

1995 A research team led by Peter St. George-Hyslop, Director of the Centre for Research in Neurodegenerative Diseases, discovers two **genes responsible for early-onset Alzheimer's**.

1996 Dr. Bibudhendra Sarkar developed an **effective treatment of Menkes disease** which is a genetic neurological disorder that kills children with the disorder before the age of three. The disease is caused by a defect in the transport of copper, which is required for the activity of many life-sustaining enzymes. The effectiveness of this treatment has been proven in two Canadian patients who are still living at age 20 and 10.

1996 Brenda Gallie and co-workers develop a **new therapy for retinoblastoma**, a cancer of the eye that leads to blindness. It represents the first major change in the management of this disease in 35 years.

1996 Dr. Michael Moran and colleagues discovered that a protein called GRB2 found inside a cell functions as a kind of ON-OFF switch responsible for turning on or off the signalling for cell growth and division elicited by growth factors. This discovery lays the **groundwork for the development of drugs targeting this protein to prevent cancer cells** from responding to growth factors to grow and divide.

1997 Dr. Christopher Feindel developed a **new technique for preserving hearts for transplantation** by using the shed blood from a donor to provide nutrient blood flow to the heart prior to being transplanted into the recipient. The recycling of donor blood can increase the safe preservation of the heart from 4 to 8 hours in a pig transplant model.

1997 Yoshio Masui wins the Albert Lasker prize for his innovative contributions in understanding cell division. Among them are the discovery of maturation promoting factor, a protein that controls cell division in fertilized eggs, and the **discovery of cytostatic factor**, another critical substance in cell division. Dr. Masui's groundbreaking work has important implications for cancer research.

1998 Dr. John Dick, Department of Molecular and Medical Genetics, **identifies a class of human hematopoietic cells** with SCID-repopulating activity. The identification demonstrates complexity of the organization of the human stem-cell compartment and has important implications for clinical applications involving stem-cell transplantation.

1999 The tumour-necrosis-factor-family molecule osteoprotegerin ligand (OPGL; also known as TRANCE, RANKL and ODF) has been identified as a **key regulator of osteoclastogenesis, lymphocyte development and lymph-node organogenesis** by Josef Penninger and Young-Yun Kong.

2000 Dr. Peter St. George-Hyslop, director of the Centre for Research in Neurodegenerative Diseases in U of T's Faculty of Medicine and a neurologist at the University Health Network, announces that a new **vaccine that may help prevent and treat Alzheimer's disease** is ready to be tested on human subjects.

2000 Dr. John Davis of the Institute for Biomaterials and BioMedical Engineering develops new **three-dimensional (3D) scaffolds for bone tissue engineering** throughout which bone cells grow, differentiate, and produce mineralized matrix.

2002 Dr. Stanley Zlotkin of paediatrics and nutritional sciences wins a CIDA Nutritional Information Project award worth $1.9 million for his groundbreaking work on Supplefer Sprinkles. A tasteless, inexpensive powder that can be added to any food, the iron supplement helps **eliminate childhood anemia** in developing countries.

2002 Josef Penninger and Peter Backx make a decisive discovery finding that angiotensin-converting enzyme 2 is an essential **regulator of heart function** and disruption of this enzyme results in a severe defect of heart morphogenesis. Dr. Penninger's and Dr. Backx's groundbreaking work has important implications for cardiovascular diseases.

2003 Dr. Tom Wolever of the Division of Endocrinology and Metabolism discovers that Acarbose **improves the glycemic profile and insulin sensitivity in elderly patients** with type 2 diabetes who are inadequately controlled on diet alone.

1922 Clinical use of insulin for diabetes – Dr. Frederick Banting and Dr. Charles Best

1935 Clinical use of Heparin as a blood thinner – Dr. Gordon Murray

1946 Design and use of North America's first artificial kidney – Dr. Gordan Murray

1950 Use of first regulated cardiac pacemaker – Dr. Bill Bigelow

1950 Use of total body cooling as a method of making heart surgery safer – Dr. Bill Bigelow

1950s Introduction of lumpectomy for breast cancer – Dr. Vera Peters

1950s Use of radiation to cure Hodgkin's disease – Dr. Vera Peters

1951 Use of cobalt radiotherapy units for cancer – Dr. Harold Johns

1955 Human heart valve transplant – Dr. Gordan Murray

1960s Coronary Care Unit – Dr. Robert MacMillan and Dr. Ken Brown

1961 Discovery of blood forming stem cells enabling bone marrow transplants – Dr. Ernest McCulloch and Dr James Till

1965 Developed prototype aneurysm clip – Dr. William Lougheed

1973 Use of pulmonary testing called flow volume loop to diagnose small airway disease (e.g., asthma and COPD) – Dr. Noe Zamel

1975 Development of software used worldwide for 20 years to control radiation therapy – Dr. Jack Cunningham

1976 Identification of P-glycoprotein as a major cause of cancer drug resistance – Dr. Victor Ling

1977 Developed a technique for Peritoneal Dialysis that made it possible on a large scale – Dr. Dimitri Oreopoulos

1978 Discovery of reversibility of brain damage from alcohol with abstinence – Dr. Peter Carlen

1983 Successful single lung transplant – Dr. Joel Cooper

1984 First cloning of the T-cell receptor genes, significant in the field of immunology - Dr. Tak Mak

1985 Reconstruction of the mitral annulus (the supporting structure for cardiac valves) – Dr. Tirone David

1986 Successful double lung transplant – Dr. Joel Cooper

1986 Use of a patch technique to repair ruptures of the heart wall following a heart attack – Dr. Tirone David

1987 Development of a new pig valve to replace the diseased aortic valve – Dr. Tirone David & Dr. Chris Feindel

1988 Mapping and surgical correction of cardiac rhythm disorders – Dr. Lynda Mickleborough and Dr. Eugene Downar

1988 Operation to spare the aortic valve in patients with aortic aneurysm – Dr. Tirone David and Dr. Chris Feindel

1989 Treatment of sleep apnea in patients with heart failure by mechanical assist device (CPAP) reduces morbidity and mortality – Dr. Doug Bradley and Dr. John Floras

1990s Identification of genes responsible for hereditary blindness, Alzheimer's, Lou Gehrig's and Huntington's disease – Dr. Peter St. George Hyslop

1991 Reconstruction of the inflow and outflow tracts of the heart using two conduits – Dr. Tirone David

1992 Developed a novel experimental technique that employs chemical substances to prevent or treat brain damage from stroke or trauma by regulating cell calcium levels – Dr. Chris Wallace

1994 Showing genetic predisposition to developing Reflex Sympathetic Dystrophy – Dr. Angela Mailis

1996 Awake craniotomy with same day discharge for brain tumour removal using image guided approach - Dr. Mark Bernstein

1996 Chemotherapy treatment for hormone-resistant prostate cancer – Dr. Ian Tannock and Dr. Malcom Moore

1996 Description of a substance that causes intestines to regrow (GLP-2) – Dr. Dan Drucker

1996 Transplantation of heart cells into damaged and scarred heart muscel to improve heart function – Dr. Ren-Ke Li and Dr. Richard Weisel

1999 Identifying the individual brain cells that control pain – Dr. Karen Davis and Dr. Andres Lozano

2000 Identification of novel T regulatory cells to induce tolerance in transplant patients – Dr. Li Zhang

2000 Identification of the novel immune molecule CD 200 to modify host immune response in transplantation – Dr. Reg Gorczynski

2001 Determining the utility of 2 hour post dose cyclosporine levels to improve clinical outcomes in transplantation – Dr. Gary Levy and Dr. Ed Cole

2001 Development of new pig valve and aorta to replace the diseased aortic root – Dr. Tirone David

2001 Development of the "Marshall Score" for classifying Multiple Organ Dysfunction Syndrome – Dr. John Marshall

2001 Discovery that a protein called Interleukin 13 fuels the growth of Hodgkin's lymphoma – Dr. Tak Mak

2002 Deduction of the structure of a molecular complex in the brain involved in many functions including memory and learning – Dr. Mitsu Ikura

2002 Demonstrating that dense breast tissue, a major risk factor in breast cancer, is mainly determined by genetic factors - Dr. Norman Boyd.

2002 Description of the role of IRAK-4, an immune molecule, critical for first-line defense against infections – Dr. Wen-Chen Yeh, Dr. Tak Mak and Dr. Pam Ohashi

2002 Discovery that fragile X syndrome (most common inherited cause of mental retardation) is related to glutamate in the brain – Dr. Peter Carlen

2002 Identification of protein that triggers autoimmune response in Sjögren's syndrome, as well as a vaccine to treat the condition – Dr. Arthur Bookman

2002 Identifying gene clusters using microarray technology that are involved in lung cancer – Drs. Denis Wigle, Igor Jurisica, Jim Woodgett, Shaf Keshavjee, Gail Darling, Frances Shepherd and Ming Tsao

2002 Proof of efficacy of new treatment for HIV infection – Dr. Sharon Walmsley

2003 Developing method for detecting gene mutations that enhance care for families with retinoblastoma – Dr. Brenda Gallie

1991 Stuart Foster and his team invent and license the world's first high **frequency ultrasound micro-imaging scanner** for preclinical imaging. This scanner is now used around the world for research applications and clinical imaging of the eye to detect glaucoma and anterior segment tumours.

1993 The International Digital Mammography Development Group, led by scientists at SWRI, is formed. This collaboration of leaders in **breast imaging** has made dramatic breakthroughs in developing new technologies to detect breast cancer.

1994 Martin Yaffe of SWRI and Norman Boyd of Princess Margaret Hospital (University Health Network) show a correlation between breast density and increased **risk of breast cancer**.

1998 Heart and circulation scientists first analyze the dramatic fall and rise in the rates of carotid endarterectomy, a **surgical procedure to prevent strokes**, in the United States and Canada related to the publication of first unfavourable and then favourable clinical studies.

1999 Imaging scientists led by Peter Burns develop the world's first method to **image blood flow** in the microscopic vessels in the muscle of the heart in real-time, a technique now used internationally. An accurate view of cardiac microscopic vessels is critical to improving diagnosis of and treatment for heart attacks.

2000 Robert Kerbel and his team show that much lower doses of **chemotherapy in combination with antiangiogenic drugs** (drugs that stop the development of blood vessels in tumours) will significantly delay tumour progression in animal models. Clinical trials are underway to validate these results in Ontario and around the world. If successful, this treatment would have less severe side effects than conventional treatments, and it could help to prevent drug resistance.

2000 In an international trial on **breech delivery**, scientists led by Mary Hannah find substantially lower rates of death or serious complications for breech babies delivered by planned caesarean section compared with those delivered by vaginal delivery.

2001 Michael Julius at SWRI and his collaborators at the University Health Network and Osaka University in Japan **discover a protein in human breast milk** that stimulates the immune system of newborns. This discovery underlines the importance of breast feeding. It also offers the opportunity to supplement baby formula to provide immune system benefits similar to those of breast milk.

2002 Steven Narod finds that there is a slightly higher **risk of breast cancer** for women who are BRCA gene carriers who take oral contraceptives before age 25 and for longer than five years. This finding has implications for the BRCA gene carriers aged over 25, as Narod's previous research showed that taking the pill should lead to a 60% reduction in risk of ovarian cancer without any increase in risk of breast cancer.

2002 Thomas Schmitt and Juan Carlos Zúñiga-Pflücker create a simple system to **generate T-cells** in a Petri dish. T-cells are a vital component of the immune system that orchestrate, regulate and coordinate the overall immune response. This discovery provides a method to create model systems to study the genetics and molecular biology of T cell development and points to future clinical therapies for people whose immune systems have been destroyed, for example, by HIV or toxic cancer therapies.

2002 Immunology scientists Philippe Poussier and Michael Julius show that a cell population of unknown function but present in the gut of normal people plays a key role in preventing ulcerative colitis from developing.

2003 Imaging scientists led by Martin Yaffe publish the first results to use **digital mammography with a contrast agent** (dye) to show tumours that cannot be viewed with current clinical mammography.

2003 Jorge Filmus discovers **a molecular marker to diagnose hepatocellular carcinoma** (HCC), the most common type of liver cancer. HCC is usually asymptomatic at early stages, and has great propensity for invasion, making it difficult to treat. Filmus developed a test for the early diagnosis of HCC, which could also be useful for the screening of individuals that are at high risk of developing this disease, such as people chronically infected with Hepatitis B and C.

2003 Yaacov Ben-David and Robert Kerbel discover that TRP-2, a gene involved in melanin synthesis, is responsible for **intrinsic drug and irradiation resistance** in human melanoma.

2003 Neil Cashman at SWRI and researchers at Caprion Pharmaceuticals discover a way to make the immune system specifically recognize infectious prions, proteins that cause brain-wasting diseases like mad cow disease and Creutzfeldt-Jakob Disease, its human equivalent. This discovery paves the way for the development of diagnostic tools, immunotherapy and a vaccine.

2004:

Neuroscientists use wireless handheld technology to collect data from patients with bipolar disorder -- more than 40,000 responses -- and thereby build the largest database of its kind in Canada. This allows the analysis of mood dynamics with unprecedented detail.

Radiation oncologists at Toronto Sunnybrook Regional Cancer Centre are the world's first to use beads of palladium, a low-dose radioactive material, to treat women with breast cancer as outpatients. This therapy holds the promise to eliminate anguishing side effects and enhance the quality of life of women considerably.

A research team led by Ellen Warner finds magnetic resonance imaging detects more breast cancer tumours, earlier, compared with mammography, ultrasound or clinical examination in women with the BRCA1 and BRCA2 genes. This finding offers hope for genetically at-risk women, for whom removal of both breasts is the only other option.

In the first large, multi-centre clinical trial of its kind, researchers provide compelling evidence to suggest that artery grafts from the forearm should be used in place of vein grafts from the leg in heart bypass surgery, because radial arteries have significantly higher graft patency over one year. Graft patency, a measure of whether the bypass remains open enough to permit efficient blood flow, is critical to achieving a good outcome after surgery.

2005:

Robert Kerbel and colleagues publish findings suggesting that measuring the peripheral blood cells that circulate in the blood and contribute to tumour growth may provide a way to measure and monitor the effectiveness of antiangiogenic therapies that work by stopping the formation of blood vessels. Right now, determining the optimal dose of antiangiogenic drugs is difficult and thus a limiting factor in their clinical development.

By expressing too much of a certain receptor, Dan Dumont’s laboratory creates the first mouse model that reflects many of the main features of the human disease psoriasis and responds to cyclosporine A, a classic treatment for the immune system disease. This finding could lead to the development and testing of therapies for psoriasis that target the implicated receptor.

Georg Bjarnason’s research team finds that patients treated with high-dose radiation for head and neck cancer in the morning have a lower risk of developing a kind of side effect that damages the mouth and throat than do patients who are treated in the late afternoon. It is the first study to show a link between circadian rhythms and the development of mucositis due to radiotherapy.

Scientists led by Yaacov Ben-David produce the first results showing that early surgical removal of the spleen in combination with antiangiogenic therapy that stops the formation of blood vessels that feed tumour growth leads to prolonged survival in a mouse model of leukemia.

In the first trial of its kind in the world, radiation oncologists at Toronto Sunnybrook Regional Cancer Centre begin treating prostate cancer patients using a 3-D image-guided radiation therapy device that oncologists expect will improve the delivery of radiation treatment. This revolutionary, non-surgical technique allows the oncologist to visualize the exact position of the target and deliver precise external beam radiation therapy.

1918 First **research lab** set up at HSC.

1930 Nutritional research by Drs. Alan Brown, Fred Tisdall and Theo Drake leads to the development of a **new cereal food** that later becomes famous the world over as Pablum.

1934 Doctors Fred Tisdall and Theo Drake, working with the National Dairy Council demonstrate the value of **enriching milk with vitamin D**.

1935 Dr. John Ross studies lead poisoning in children, resulting in the **prohibition of lead pigments in paints** on children's toys and furniture.

1951 A **heart-lung machine** is developed by HSC physicians Lawrence Chute, William Mustard and John Keith along with Campbell Cowan, Banting Institute.

1954 The **Research Institute** is formally established as a division within the Hospital.

1963 Dr. William Mustard pioneers to **correct the birth defect of "blue babies"** (transposition of the great arteries of the heart).

1965 Researchers develop a **lab procedure** that cuts the time required to diagnose whooping cough from five days to 30 minutes.

1971 Canada's first successful **surgical separation of conjoined twins** takes place at HSC. Dr. B. Shandling led the team. There have been five surgical separations since then.

1973 Canada's first transplant operation where a **kidney from a living donor** was given to a child took place at HSC.

1979 Dr. Robert Salter develops continuous passive motion, an **improved method of treating patients with damaged cartilage**.

1987 Gene responsible for **Duchenne Muscular Dystrophy** identified.

1988 Gene defect that causes **Tay-Sachs disease** identified.

1990 HSC's first **heart transplant** was performed. Sick Kids now performs approximately 15 heart transplants each year - about 80 per cent of Canada's paediatric heart transplants.

1994 The first biological proof that **second-hand cigarette smoke** can affect a fetus is provided.

1996 Sick Kids researchers discovered a gene implicated in the **development of colon cancer**, bringing cancer researchers a step closer to understanding what causes cells to multiply uncontrollably - an activity that leads to the development of malignancies.

1996 The **Telemedicine Clinic** opens (now known as Telehealth), providing an interactive video link between HSC and Health Sciences North in Thunder Bay. A physician at Sick Kids can now direct an examination, make a diagnosis, and provide follow-up care. The clinic is used to see children requiring any type of pre-operative, post-operative and follow-up treatment.

1997 An HSC geneticist leads an international team of researchers that **identifies a human blood cell** that regrows the entire blood system. The discovery provides greater understanding of how the blood system functions and enables development of new for blood diseases such as leukemia, thalassemia and sickle cell anemia.

1998 The Hospital for Sick Children (HSC) has created a research facility that will help ensure Canada maintains its prominent international role in **genetic research**.

1999 Canada's first basic science **brain tumour research centre** was opened at Sick Kids this year with a $5-million donation from Arthur and Sonia Labatt. The Arthur and Sonia Labatt Brain Tumour Research Centre brings together clinicians and scientists from Sick Kids, Toronto Western Hospital, and the University of Toronto to form a leading-edge collaborative laboratory focused on basic science research of human brain tumours, both in adults and children.

2000 **Inhaled steroids** are found to be safe and effective for children with asthma.

2000 Researchers **reverse fatal pulmonary hypertension**.

2001 A team of researchers led by The Hospital for Sick Children senior scientist has determined that **multiple sclerosis** and type I (Juvenile) **diabetes** mellitus are far more closely linked than previously thought, including the role cow milk protein plays as a risk factor in the development of both diseases for people who are genetically susceptible.

2002 Researchers find relationship between environmental **tobacco smoke and the risk of SIDS.**

2003 Researchers find chemotherapy is an effective **alternative to bone marrow transplant** in acute myeloid leukemia patients with good prognosis.

2003 **SARS** found to affect children less severly than it does adults.

2004 SickKids researchers show an association between paediatric **multiple sclerosis** (MS) and the **Epstein-Barr virus**, indicating that exposure to the virus at a certain time in childhood may be an important environmental trigger for the development of MS.

2004 Scientists at SickKids confirm that childhood and **adult brain tumours originate from cancer stem cells** and that these **stem cells fuel and maintain tumour growth**. This discovery has led to development of a mouse model for human brain tumours and opens the door for new therapeutic targets for the treatment of brain tumours.

Achievements

- The discovery of the SH2 domain, a vital cell signaling ingredient within a cell. This domain has been found to be altered during the process of a normal cell turning into a cancerous cell.

- The identification of a molecular genetic marker that is a predictor of prognosis for women with node-negative (cancer that has not spread to lymph nodes) breast cancer. Working with colleagues at the Robarts Institute in London, Ontario the identification of the gene responsible for the high incidence of diabetes in the First Nations Band at Sandy Lake.

- The discovery of a genetic maker for Wiskott-Aldrich syndrome (a fatal immune deficiency disorder) that resulted in genetic counselors from across North America contacting MSH for help inn prenatal diagnosis.

- The identification of a mutation in the colon cancer gene (the APC gene) that is present at a high incidence in Jews of Ashkenazi descent.

- A study finding that blood insulin levels appear to be a reliable predictor of whether a woman with breast cancer will survive long term, which women with breast cancer will respond well to treatment, and which are at high risk of losing their fights against this cancer.