

Comprehensive Childhood Marrow Failure & Myelodysplasia Program

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Marrow Failure and Myelodysplasia Program

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Cell Biology Program, Research Institute

The Hospital for Sick Children

and The University of Toronto

SickKids

U_{of}T

Comprehensive Care for Rare Blood Disorders Conference
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Topics for Discussion

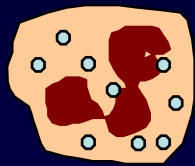
- **Introduction**
- **Missions and Objectives of a Comprehensive Childhood Marrow Failure and Myelodysplasia Program (CCMFMP)**
- **Current Status of the Marrow Failure and Myelodysplasia Program at SickKids**
- **Gaps towards a comprehensive Program**

**Bone Marrow Failure
Syndromes and
Myelodysplastic Syndromes
(Pre-Leukemia)**

Bone Marrow Failure Syndromes

- a large number of **inherited and acquired** conditions
- **low blood counts** due to reduced production of cells in the bone marrow
- **Extra-hematological** complications
- In many disorders there is a high risk of **cancer**
- **Treatment** includes
 - Supportive care (transfusions, antibiotics etc)
 - Immunosuppressive therapy
 - BM stimulants (steroids, growth factors, others)
 - Hematopoietic stem cell transplantation (HSCT)
- **Life expectancy** is reduced for most syndromes due to the disease-related or treatment-related mortality

BMFSs - General Classification



White blood cells (neutropenia)

Severe cong. N
Cyclic N
Myelokathexis
Barth
GSD Ib
Acquired

Fanconi

Aplastic anemia

Shwachman-D
CAMT

Acquired

Dyskeratosis
Cong.

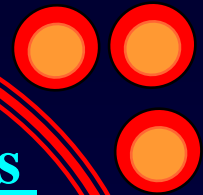
Red blood cells (anemia)

Diamond-Blackfan
Cong. Dyseryth
Sideroblastic
Acquired

Platelets

(Thrombocytopenia)

TAR Acquired
MYH9-related
MASTL-related
Grey Platelets
FT/AML



What are Myelodysplastic Syndromes (Pre-Leukemia)?

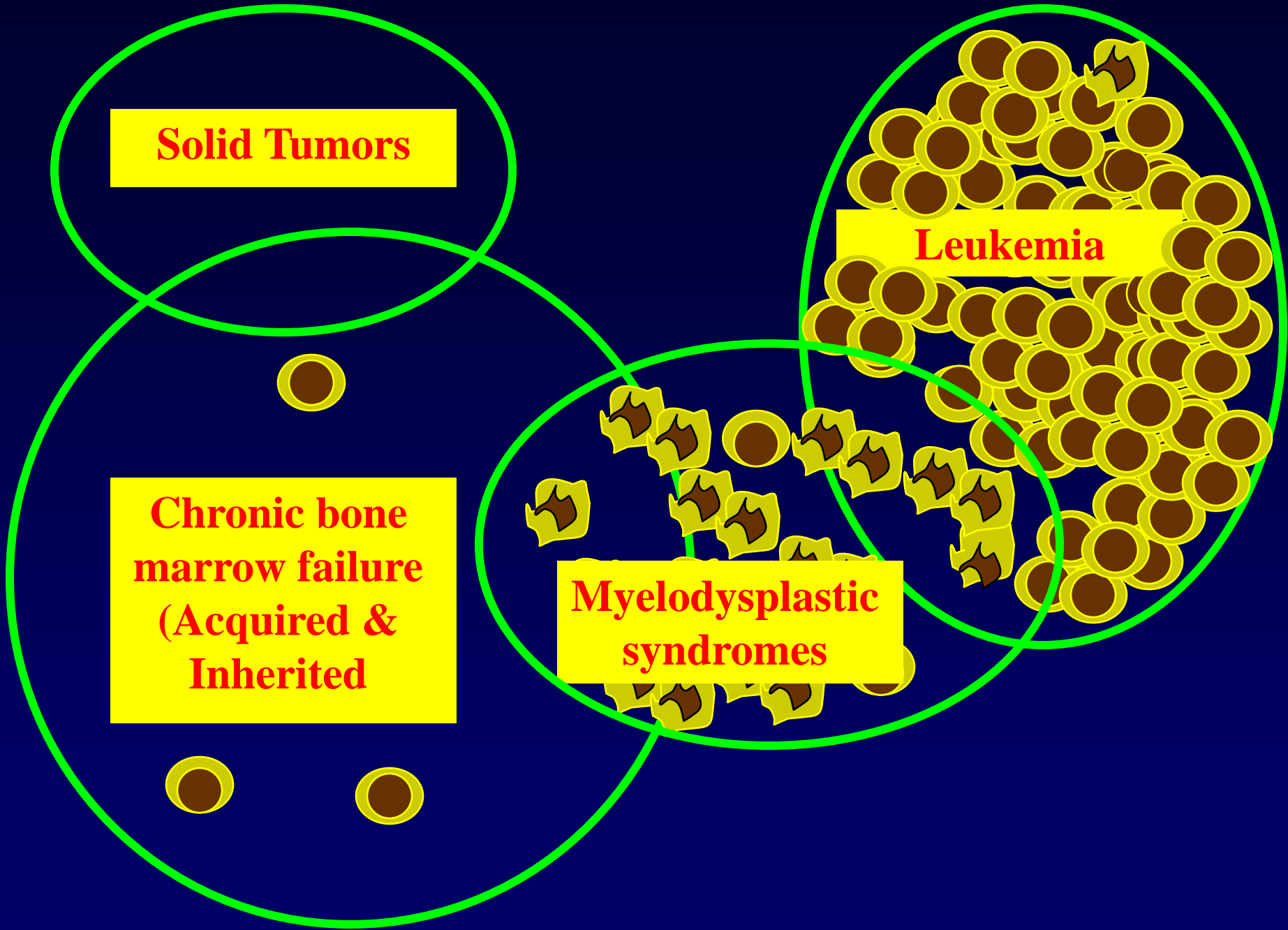
- Disorders of the **hematopoietic stem cell**
 - **Ineffective production** of blood cells in the bone marrow (early cell death)
 - **Low blood counts**
 - **High rate of conversion to leukemia**
-
- **Treatment** in children is mainly HSCT
 - **Overall survival** is about 50%

Solid Tumors

Leukemia

**Chronic bone
marrow failure
(Acquired &
Inherited)**

**Myelodysplastic
syndromes**



Rationale of CCMFMP

- **Rare, unique and complex group** of disorders with major needs
 - Hematological
 - Non-hematological manifestations
 - Cancer
 - Complex genetic background
- **Require high level of expertise** of health care professionals
- **Significant number of patients** at large institutions such as SickKids
- **A dedicated program** will promote standard of care
- **Opportunity for advancing the field by research**
- **Opportunity for education**

**Mission and Objectives of a
Comprehensive Childhood
Marrow Failure and
Myelodysplasia Program
(CCMFMP)**

Mission & Objectives of CCMFMP

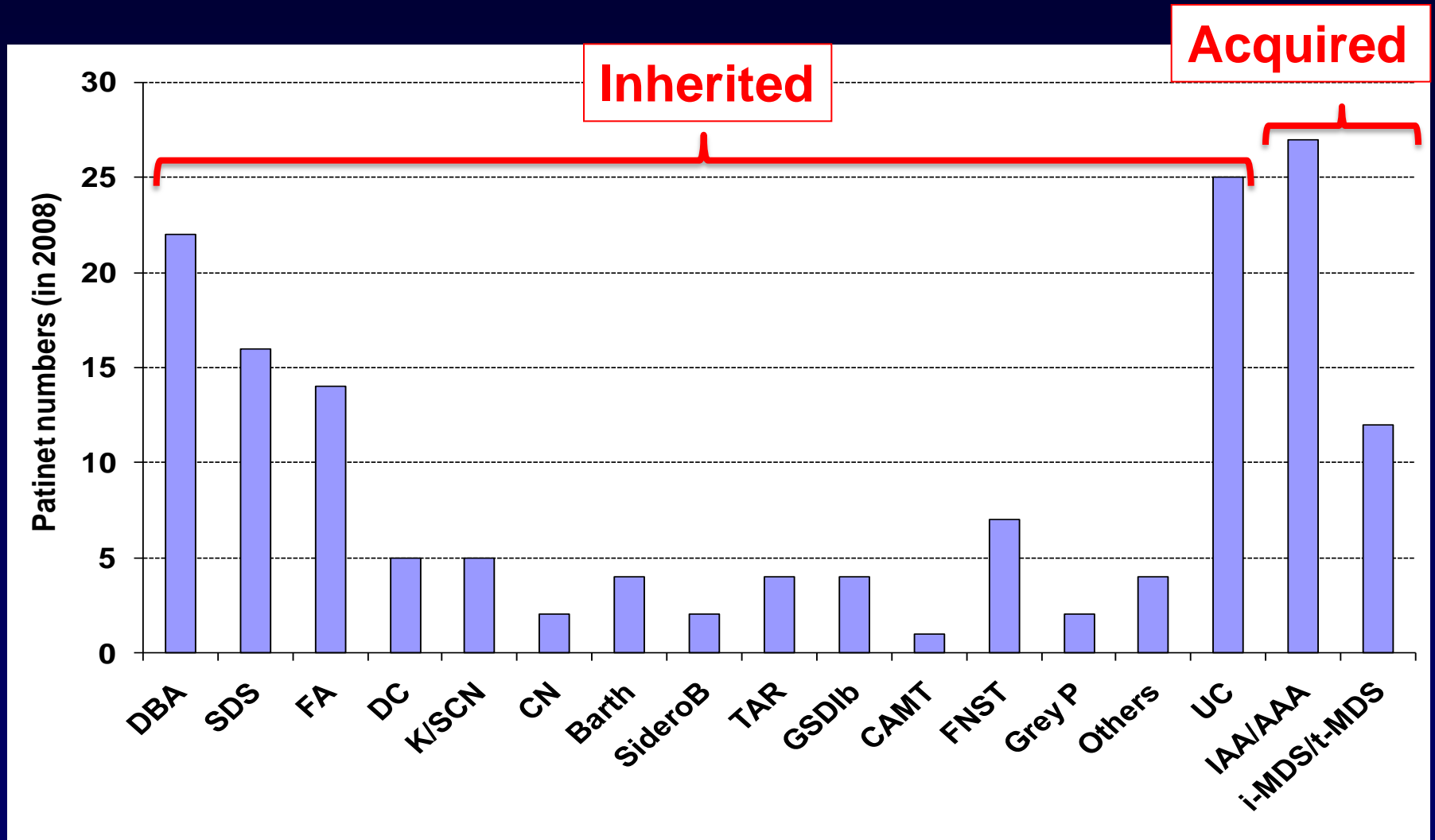
1. To be regionally, nationally and internationally recognized as a **center of excellence**
2. To promote **clinical, research and education**
3. **To collaborate** with other health care professionals at the regional, national and international levels
4. **To advocate** for the disorders at the local, provincial, national and international levels
5. To partner with **disease associations** to set priorities and address general patient and family-related challenges

**Current Marrow Failure
and Myelodysplasia
Program at SickKids
(MFMP)**

Current Marrow Failure & MDS Program

- **Established** in 2001
- The **only pediatric MFM program in Canada** and one of the largest in the world
- **Provides infrastructure** for clinical care, research and education
- About **170 patients** with acquired and inherited marrow failure syndromes and/or MDS
- Since 2002, the program has been recognized as a **Centre of Excellence** in research and clinical care in pediatric MDS by the International MDS Foundation
- **Research** at laboratory, translational and clinical levels
- The program coordinates the Patient Sample **Repository and Database** of the Canadian Inherited Marrow Failure Registry (15 academic pediatric hematology programs in Canada; > 270 enrolled patients)

Prevalence of the Chronic Bone Marrow Failure Syndromes (SickKids, Toronto)



Core Team

Clinical Team

M.D.

Yigal Dror

Isaac Odame

Nursing

Pat Canning

Social Worker

Diana Cottingham

Pharmacist

Elyse Zylunka

Dietician

Mary Baron

Research Laboratory

Lab coordinator: Sally-Lin Adams

Lab technician: Hanming Wang

Clinical research coordinator:

Chris Allen

Students/trainees: Santhosh

Dhanraj, Elena Tsangaris, ChiLan

Nghan, David Choi, Catherine

Segbefia, Rabah Almahmoud,

Machiel Van Der Akker

Multi-Disciplinary Approach

Dietician
Mary Baron

Nurse
Pat Canning

M.D.
Yigal Dror
Isaac Odame

Pharmacist
Elyse Zylunka

Social Worker
Diana Cottingham

Additional Care Givers
BMT, Oncology

Consultants
Genetics, Endocrinology, Gastroenterology,
Orthopedics, Cardiology, Otolaryngology,
Ophthalmology, Neurology, Nephrology,
Urology, Psychiatry

List of Research Studies (Nov 2009)

1. Lab

- Mechanism of bone marrow failure in Shwachman-Diamond syndrome and the functions of the **SBDS protein**
- **Genetic basis** of inherited marrow failure syndromes
- **Molecular mechanism of MDS/leukemia** in inherited marrow failure syndromes

2. Canadian Inherited Marrow Failure Registry (CIMFR)

- **The genetic basis** of inherited bone marrow failure syndromes
- **Misdiagnosis and mistreatment** of inherited bone marrow failure syndromes
- Clinical and laboratory characteristics of **MDS secondary** to inherited bone marrow failure syndromes
- Genetic and clinical characteristic of **Diamond blackfan anemia** in Canada

3. Retrospective analyses

- Clinical and laboratory characteristics of **idiopathic MDS**

MFMP Research Collaborators

SickKids

- Chet Taylor, Joseph Beyene, Steve Scherer, Mary Shago

National

- 17 researchers across Canada who participate in the Canadian Inherited Marrow Failure Study

University of Toronto

- Michael Glauguer, Aaron Schimmer, Jeffrey Lipton

International

- SCNIR Members

Canadian Inherited Marrow Failure Registry (CIMFR) Co-IPs

Jardine

Klaassan

Ali

Brossard

Dower

Samson

Steele

Hand

Fernandez

Scherek

Yanofsky

Athale

Dror

Silva

Abish

Champaigne

Lipton



Transition to Adulthood

- **Inherited Bone Marrow Failure Clinic**
 - **Dr. Jeffrey Lipton**
 - **Judi Killoram (RN) & Nancy Pringle**
- **Acquired Bone Marrow Failure Clinic**
 - **Dr. Vikas Gupta**
 - **Judi Killoram (RN)**

Status & Gaps

Clinical Care at SickKids MFMP

Current Status

- **Reference center** for marrow failure and MDS in children: +
 - treat all/most patients from TGA
 - consultation for complex cases
- **Comprehensive care:** inpatient service, outpatient service and self/family administration of therapeutics +
- **Multi-disciplinary care:** physicians, nurse, social worker, dietician, pharmacist and genetic counselor +

Clinical Care at SickKids MFMP

Current Status

- **Standard-of-care** guidelines for pediatric marrow failure syndromes and MDS +
- **Strong pharmacy and blood bank** +
- **Person-power**
 - CNS/Nurse practitioner -
 - Meeting **nursing and social** needs and in timely fashion -
 - Core genetic counselor -

Clinical Care at SickKids MFMP

Current Status

- **Consultants** with expertise in the field +
 - Endocrinology, Gastroenterology, Orthopedics, Cardiology, Otolaryngology, Ophthalmology, Neurology, Nephrology, Urology, Child Development, Genetics, Psychiatry
- **Diagnostic facilities**
 - imaging +
 - Hematopathology +
 - Cytogenetics, telomere length measurement +/-
 - Protein assays: erythrocyte adenosine deaminase levels, FANCD2 -
 - Molecular genetics -/+

Clinical Care at SickKids MFMP

Current Status

- **Collaborative work with regional centers** in the Toronto Greater Area and outreach programs to decentralize care whenever possible
 - laboratory tests +
 - transfusions -/+
 - systematic treatment plan and interim check-ups by local general pediatricians -

Research at SickKids MFMP

Current Status

- **Basic (lab)**

- genetic, biology and mechanism of disease

+

- **Translational (clinic-lab-clinic)**

- disease mechanism

+

- drug discovery

-

- gene therapy

-

Research at SickKids MFMP (Cont'd)

Current Status

- **Clinical (Clinic)**

- Registry (Need funding for IAA and I-MDS)

+

+

- Disease characteristics, disease course, risk evaluation

-

- clinical trials (e.g. in HSCT, novel drugs)

- **Secured funding** for research infrastructure: registry, sample repository, a clinical research coordinator and a research fellowship program.

-

Education at SickKids MFMP

Current Status

- **Research lab training** +
- **MFEM Fellowship Program** -
- **Nursing training** -
- **Programs for education of patients, families**
 - **biennial conference** +
 - **reading material** +/-

Collaboration with Consumers, Other Medical Centers and Accreditation

Current Status

- **Collaboration with patients/families/disease associations** who advise about priorities, directions and strategies **+/-**
- **National collaboration with health care professionals** **+**
- **Evaluation process and accreditation processes** **-**

Acknowledgement

MFM Program Clinical Team

- Pat Caning
- Isaac Odame
- Diana Cottingham
- Elyse Zylunska
- Carol Snushal

Dror Lab

- Chris Allen
- Sally-Lin Adams
- Hanming Wang

CIMFR Co-IP's

- 16 Canadian Centers

Patients and families with bone marrow failure/ MDS

Research Funding Support

- FA Canada
- SDS Canada
- C17 Research Network
- CIHR