

# Comprehensive Childhood Marrow Failure & Myelodysplasia Program

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**The Hospital for Sick Children**

**and The University of Toronto**

**SickKids**

**U<sub>of</sub>T**

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# Topics for Discussion

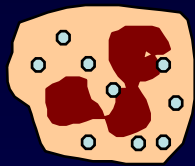
- **Introduction**
- **Missions and Objectives of a Comprehensive Childhood Marrow Failure and Myelodysplasia Program (CCMFMP)**
- **Current Status of the Marrow Failure and Myelodysplasia Program at SickKids**
- **Gaps towards a comprehensive Program**

**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.

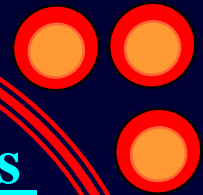
## Red blood cells (anemia)

Diamond-Blackfan  
Cong. Dyseryth  
Sideroblastic  
Acquired

## Platelets

## (Thrombocytopenia)

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



# What are Myelodysplastic Syndromes (Pre-Leukemia)?

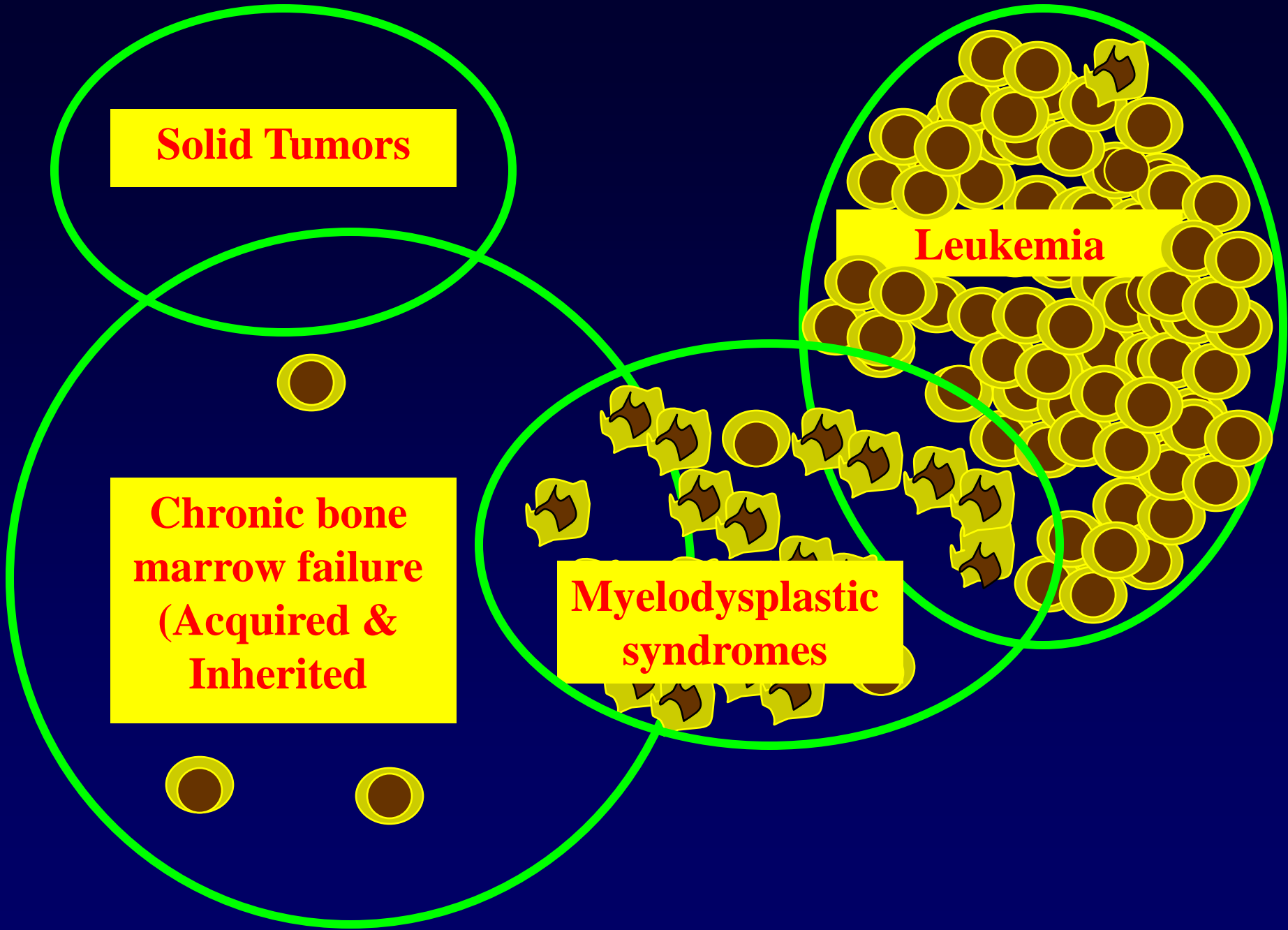
- Disorders of the **hematopoietic stem cell**
  - **Ineffective production** of blood cells in the bone marrow (early cell death)
  - **Low blood counts**
  - **High rate of conversion to leukemia**
- 
- **Treatment** in children is mainly HSCT
  - **Overall survival** is about 50%

**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

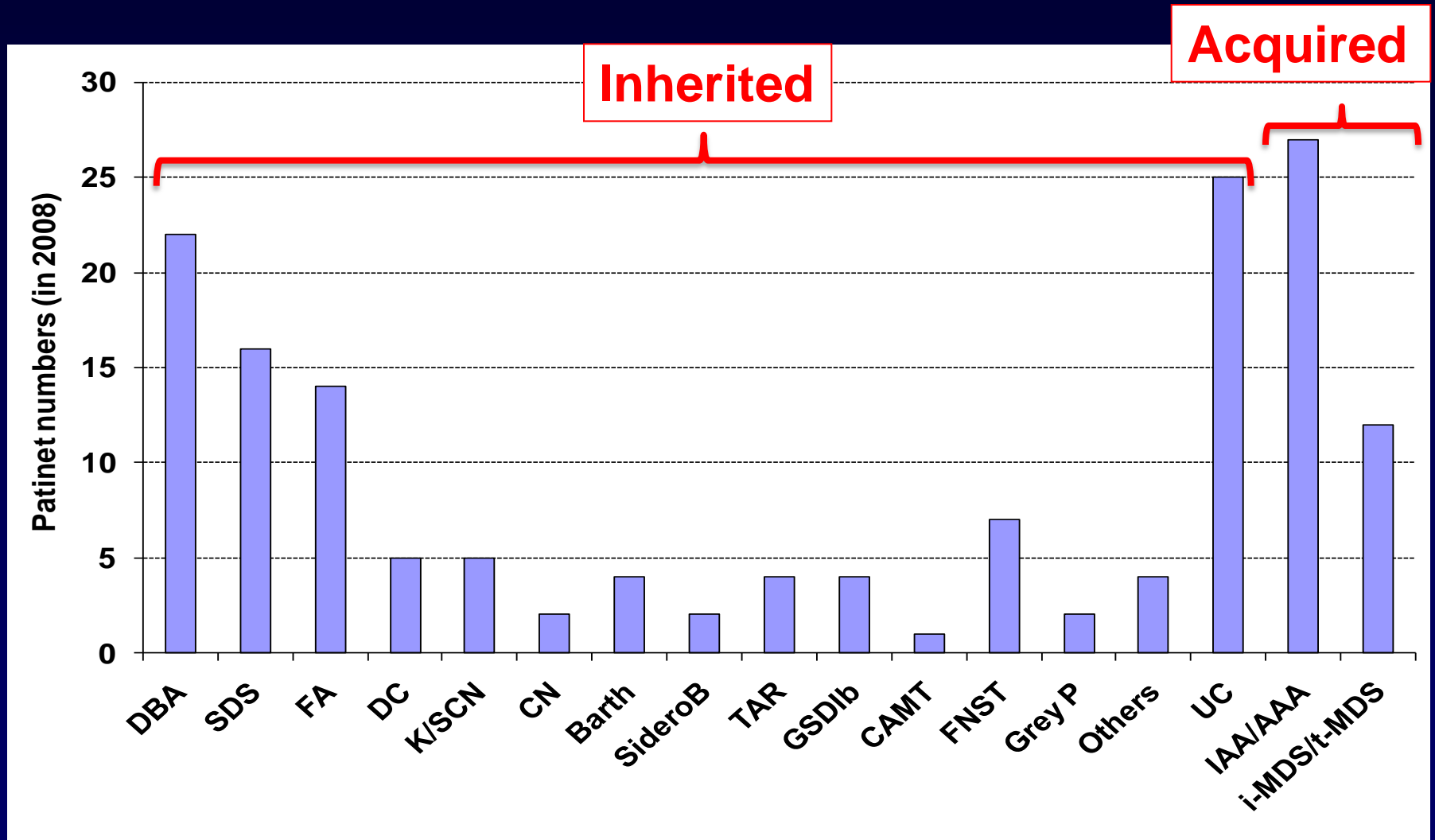
1. To be regionally, nationally and internationally recognized as a **center of excellence**
2. To promote **clinical, research and education**
3. **To collaborate** with other health care professionals at the regional, national and international levels
4. **To advocate** for the disorders at the local, 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