

The Childhood Leukemia International Consortium (CLIC)

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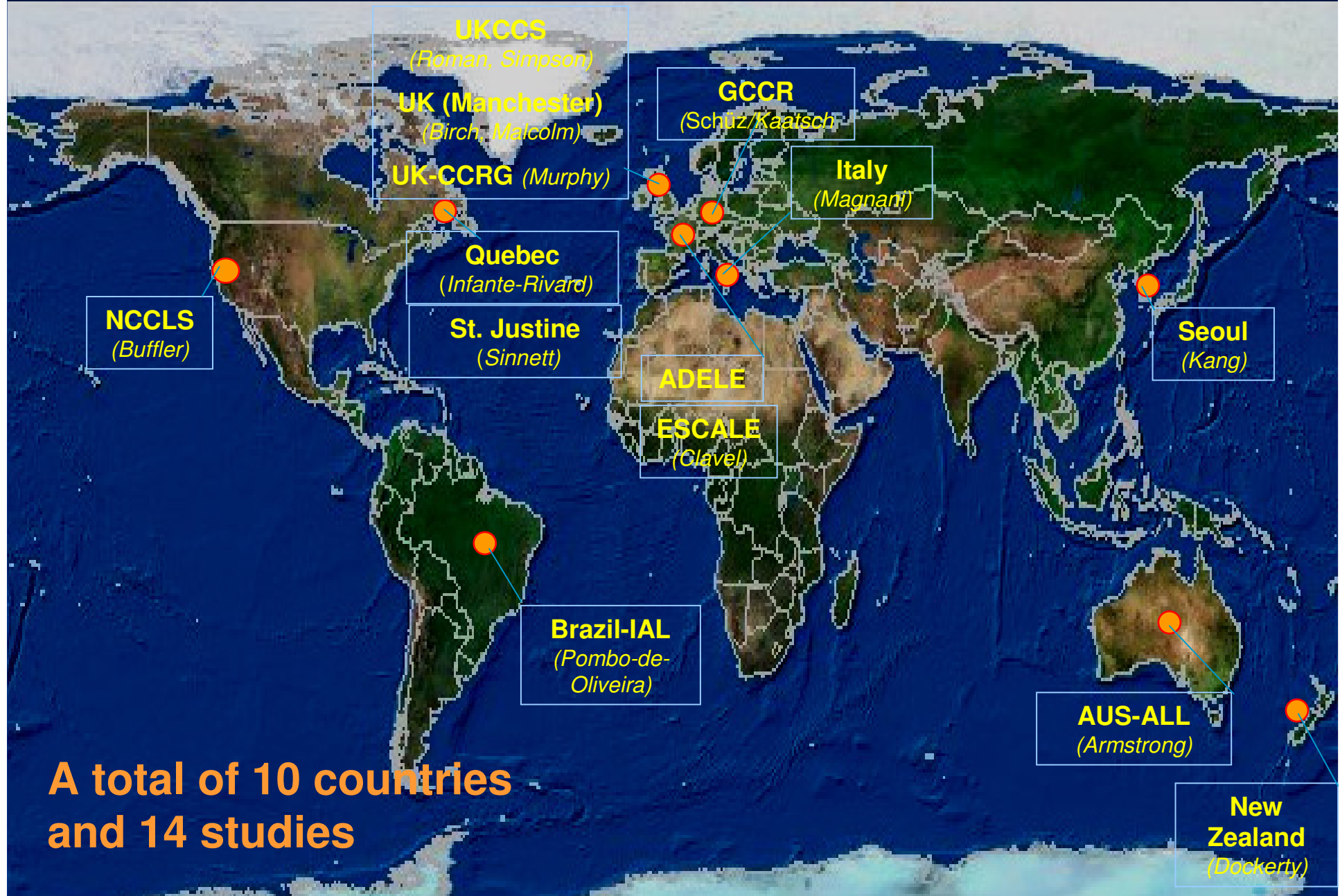
CLIC History

- Recently established in collaboration with **UC Berkeley and the International Agency for Research on Cancer (IARC)** to overcome limitation of childhood leukemia studies with limited sample size, especially for rare subtypes
- 1st informal meeting in Washington DC in **2006** with Australian, Canadian, and French research groups
- 1st formal meeting in LA, in April, **2007** with additional groups from Brazil, Italy, Korea, New Zealand
- 2nd meeting, November **2007**, Sausalito
- 3rd meeting, April **2008**, San Diego

Objectives

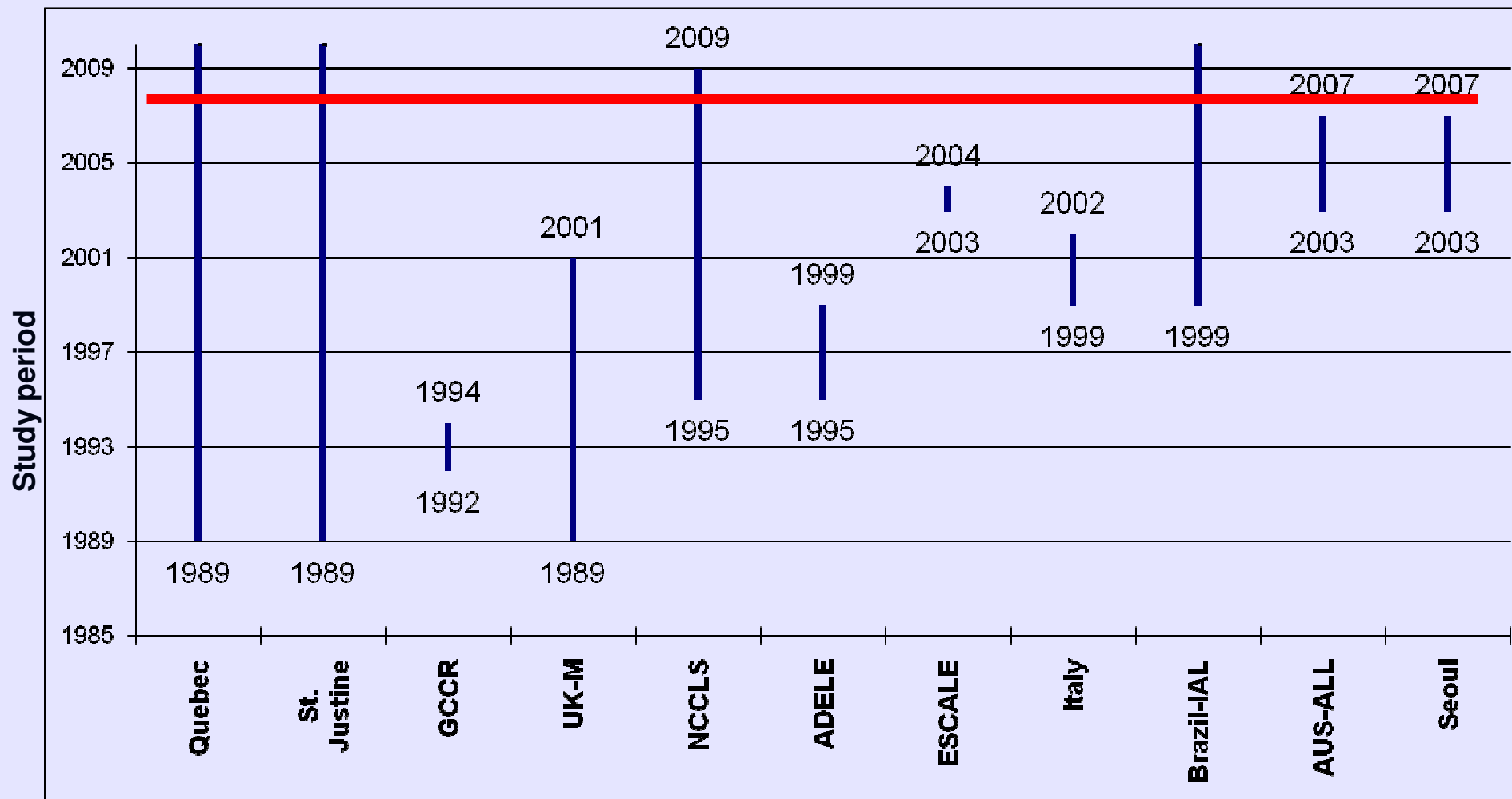
- ❑ Combine existing data from several comparable case-control studies conducted in Europe, Northern and Southern America, and Asia leading to expected numbers of ~ 8,000 childhood leukemia cases and 13,000 controls
- ❑ Foster collaboration with other research teams that are in the planning phase for future studies childhood leukemia.

CLIC Research Groups and Study Areas in the World as of April 2008



**A total of 10 countries
and 14 studies**

Time Period of the Recruitment



Sample Size

Study Name (Study location)	Case-control				Trio	
	Case		Control		Current	Target
	Current	Target	Current	Target		
AUS-ALL (All states in Australia)	327	350	863	700	316	350
Brazil-IAL (Brazil)	230	400	480	600	0	0
ESCALE/ADELE (France national)	956	956	1009	1009	697	697
GCCR (Germany)	1184	1184	2588	2588	0	0
Italy (Italy 15 regions)	685	1000	1063	1063	0	0
NCCLS (35 counties in N/C California)	997	1000	1226	1013	0	750
NZ (New Zealand)	121	121	303	303	0	0
Quebec (Province of Québec, Canada)	790	790	790	790	546	790
Seoul (Seoul, Korea)	250	350	350	450	0	0
St. Justine (St. Justin Hospital)	520	468	629	629	222	222
UKCCS (York)	1735	1735	3450	3450	850	850
Total	7795	8354	12751	12595	2631	3659

DNA Specimen

- Available in about 50% of cases and controls

Levels of Collaborations

- ❑ Short term
 - Pooled analysis

- ❑ Medium term
 - Replications of novel findings
 - Coordinated genotyping

- ❑ Long term
 - Design a new study to address the novel hypothesis based on the network

Organization of CLIC

Coordination Group

Principal Investigators and/or designates of each participating study in CLIC

Management Group

Day to day maintenance,
Overall coordination,
Communication,
General assistance

4 Core Logistic Groups

Responsible for advising and facilitating cross-cutting logistic issues

Interest Groups

Promote collaborative projects in specific areas of childhood leukemia research

Working Groups

Pursue proposed research

Coordination Group

Study Name (Study location)	Principal Investigator & co-PI
AUS-ALL (All states in Australia)	Bruce Armstrong & Elizabeth Milne
Brazil-IAL (Brazil)	Maria S. Pombo-de-Oliveira & Sergio Koifman
ESCALE/ADELE (France national)	Jacqueline Clavel
GCCR (Germany)	Peter Kaatsch & Joachim Shüz
Italy (Italy 15 regions)	Corrado Magnani
NCCLS (35 counties in N/C California)	Patricia A. Buffler & Catherine Metayer
NZ (New Zealand)	John Dockerty
Quebec (Province of Québec, Canada)	Claire Infante-Rivard
Seoul (Seoul, Korea)	Daehee Kang
St. Justine (St. Justin Hospital)	Daniel Sinnett
UK (Manchester)	Jill Birch & Malcolm Taylor
UK CCRG	Michael Murphy
UKCCS (York)	Eve Roman & Jill Simpson

The responsibilities of the Coordination Group are as follows:

- Elect the Management Group members;
- Oversee scientific agenda/priorities;
- Approve new membership (studies and individuals);
- Review and approve proposed CLIC pooled analyses;
- Develop policies/guidelines related to governance of CLIC (i.e. data pooling, authorship);
- Be a point of reference for conflict resolution; and
- Attend the annual meeting or send a representative if the principal investigator cannot attend.

Core Logistics Groups

- Responsible for advising and facilitating cross-cutting logistic issues. There are currently four Core Logistics Groups:
 - Biospecimens/Biorepository
 - Data Management/Inventory
 - Disease Classification/Pathology
 - Timing for Data Sharing/Pooling

Interest Groups as of 2008 Meeting

- ❑ **AML (including APL)**
- ❑ **Birth characteristics**
- ❑ **Environmental exposures**
- ❑ **Family history**
- ❑ **Genetic studies**
- ❑ **Immunity and infection**
- ❑ **Infant leukemia**
- ❑ **Occupational exposures**
- ❑ **Pathology (ALL and MLL)**

Working Groups: Prototypes for Pooled Analyses in CLIC

- Effect of maternal folate intake and *MTHFR* gene polymorphism in childhood ALL (1 R03 CA132172-01)
 - Participating studies in US, UK, France, Canada, and Australia
- Birth characteristics research grant proposal submitted to the Children with Leukaemia Foundation in September 2008
 - Entitled: “Investigating the genetic and environmental causes of childhood ALL using data from the Australian Study of Causes of ALL in Children (AUS-ALL) and the Childhood Leukaemia International Consortium (CLIC)”

Management Group

- Responsible for day to day maintenance, overall coordination, communication, general assistance
 - Members:
 - Bruce Armstrong, University of Sydney, Australia
 - Patricia Buffler, University of California, Berkeley
 - Jacqueline Clavel, INSERM, France
 - Claire Infante-Rivard, McGill University, Canada
 - Elizabeth Milne, University of Western Australia
 - Catherine Metayer, University of California, Berkeley
 - Alice Kang, University of California, Berkeley

Strength of CLIC

- Childhood leukemia is a heterogeneous disease that encompasses several molecular and cytogenetic subtypes
- Subgroups of childhood leukemia may have specific causes related to environmental chemical exposures
 - Commitment to work together to achieve adequate sample sizes

Approximate Sample Sizes to Date for ALL Cytogenetic Subtypes

Location	t(12;21)	t(1;19)	t(9;22)	11q23 /MLL	del 9p	del 12p	del 6q	High HD* (51-67 chr)	Low HD* (47-50 chr)	Hypo (< 46 chr)
Australia	55	6	5	5	10	10	10	70	27	10
Northern California	74	16	9	26	13	14	18	133	82	33
New Zealand								23*	14*	6*
Brazil		3		98				35		
UK, York	146	28	35	69				337	101	
Quebec, Canada (St. Justine)	44	2	5	3				22	2	8
Total	319	54	54	201	23	24	38	674	258	70

*HD = Hyperdiploidy

Approximate Sample Sizes to Date for AML Cytogenetic Subtypes

Location	inv(16)	t(8;21)	t(15;17)	11q23/MLL	tri 8
Australia				5	
Brazil	2	4	4	98	?
France	1	0	1		?
Northern California	4	16	9	26	42
Quebec, Canada (St. Justine)				3	
UK, York	11	17	16	69	?
Total	18	37	30	201	42

CLIC Website

□ <http://clic.berkeley.edu>



Thank You



Acknowledgements

Participating Children and their Families
National Cancer Institute, US (1 R03 CA132172-01)
Children with Leukaemia Foundation, UK