

**UNIVERSITA' DEGLI STUDI DI PADOVA**

**Dipartimento di Pediatria**



Dottorato di ricerca in Medicina dello Sviluppo e Scienze della Programmazione  
Indirizzo Ematonecologia e Immunologia – Ciclo XX

**Zebrafish model of *MLL* leukemogenesis:  
implication for fish favorable model of *MLL*-  
related leukemia development**

**Direttore della Scuola:** Ch.mo Prof. Giuseppe Basso

**Supervisore:** Ch.mo Prof. Giuseppe Basso

**Dottorando:** Giuseppe Germano

**31 Gennaio 2008**

*a Toni*



## *Table of contents*

Introduzione	1
Introduction	3
CHAPTER 1	
<i>MLL</i> an unusual promiscuous oncogene	
1.1 Clinical features of leukemias with <i>MLL</i> translocations	7
1.2 <i>MLL</i> , <i>MLL</i> fusion proteins and leukemogenesis	9
1.3 Two consecutive immunophenotypic switches in a child with <i>MLL</i> rearranged acute lymphoblastic leukemia	13
<i>General references</i>	19
CHAPTER 2	
Panhandle PCR approaches and the <i>ARMC3</i> gene	
2.1 Panhandle PCR approaches	28
2.2 Characterization of genomic breakpoints in secondary leukemias by panhandle PCR approaches	33
2.3 Cryptic, complex <i>MLL</i> , <i>AF10</i> , <i>ARMC3</i> rearrangement in secondary AML disrupts mammalian armadillo homologue	44
<i>General references</i>	59
CHAPTER 3	
Zebrafish and <i>MLL</i> leukemogenesis	
3.1 Zebrafish as a model system for hematopoiesis and leukemia	62
3.2 Cloning and characterization of the zebrafish <i>mll</i> ortholog	64
<i>General references</i>	79
PUBBLICATIONS	
<i>Credits</i>	

**-THANKS-**

*I would like to thank Giuseppe Basso, Martina Pigazzi, Francesco Argenton, Natascia Tiso @ UNIVERSITY OF PADUA, Carolyn Felix, Blaine Robinson, Anna Sechser Perl, Christos Kolaris, Alena Zhang, Christian Freguia, Paola Picozzi, Stefano Baila @ CHOP, Rita-Balice Gordon, Yuanquan Song @ UPENN UNIVERSITY, and FONDAZIONE CITTA' DELLA SPERANZA and everyone that I have forgotten.*