1) Genesis and progression of human cancer are accompanied by complex changes in the expression patterns of genes involved in multiple stages of tumorigenesis and metastasis including oncogenes, tumor suppressor genes, genes encoding growth factors and their receptors, and angiogenesis factors. To capture a more complete picture of the molecular state of cancer the technology has turned to cDNA arrays that can be used to survey patterns of expression for thousands of genes simultaneously. These studies are very important to improve the accuracy of prognosis in cancer and to predict any possible evolution. Not only: gene expression profiling, particularly of bone and soft tissues can be used to identify the genes and pathways that really matter for the tumorigenic process, thereby revealing new targets for therapy

- The researchers of Pediatric Oncohaemathology, Az.Meyer, Florence are now conducting microarrays studies on molecular biology of some pediatric tumors (neuroblastoma, CNS tumors, bone tumors) that relapse in spite of conventional or high dose treatments. The purpose is a more specific molecular characterization that can identify the target for a different and more appropriated therapy. Very interesting are the results concerning medulloblastoma and Ewing sarcoma.

2) Very interesting are also the research on loss of heterozygosity and p53 polymorphism Pro72Arg in medulloblastoma in collaboration with Genetic Unit published on Oncol. Rep. 10, 773-775, 2003 (I.F. 1.224)

3) Another very important research concerns detection of minimal residual disease in acute lymphoblastic leukaemia in childhood in collaboration with other national and international institutes. Preliminary results are been published on Hemathologica 88, 1245-1252, 2003 (I.F.: 3.216) and on Leukemia, Advance online publication, 11 November 2004 (I.F. 5.116)

4) Finally particular attention is directed to acute and chronic side effects of antitumoral therapy. So a retrospective study has been took up on pharmacogenetics of methotrexate (MTX) in order to determine a correlation between toxicity reponse and mutated gene traits analysed in these patient in collaboration with Metabolic Deseases Research Service, Dept. of Pediatrics, University of Florence (researcher A. Morrone). The research has opened to other Italian Insitutions. The aim is to confirm and/or demonstrate that chemotherapeutic treatment sensitivity to MTX vary with genetic variability in folate metabolising enzymes and it would become a useful indicator in determining the appropriate dose patients undergoing to chemotherapeutic treatment.

The title is: On the role of polymorphism of genes involved into folic acid metabolism in a select group of pediatric patients

5) Another very interesting study is on acute and chronic Cardiotoxicity following antracyclines therapy toghether with pediatric Cardiology Service of Azienda O.U.A. Meyer, Florence

6) New molecular targets for therapeutic strategies in paediatric ALL: The human eag-related gene (h-erg) appears to be expressed at low levels in normal (i.e. unstimulated) mature peripheral blood lymphocytes (PBL) and dramatic upregulated in primary B-cell chronic lymphocytic leukemia and in the pro-B-cell acute lymphoblastic leukemia, CEM. Moreover has been demonstrated that h-erg was not up-regulated in proliferating noncancerous lymphocytes (activated tonsillar cells, EBV-transformed cells, cells from Sjögren's Syndrome patients), indicating that it is not a marker of proliferation but is selectively up-regulated in leukemic cells (Smith GAM, 2002). It has been also reported that the hERG1 channel activity is necessary for the progression of myeloid and lymphoid leukemic cells beyond the G1/S boundary (Pillozzi S, 2002; Smith GAM, 2002), and hence the clonogenic potential of AML circulating blasts is reduced by hERG1-specific blockers (Pillozzi S, 2002).

In the present study we evaluated the expression of the two alternative herg1 transcripts, herg1a and herg1b, by quantitative RT-PCR, in order to assess the possible relationship between herg1a and herg1b expression and clinical features at diagnosis and treatment outcome.

The study, open in 2004 by Molecular Oncology Dpt, University of Florence is in progress toghether with Paediatric Haemathology Oncology Depts of Florence and Padua Universities