(95% CI) = 0.51–0.89, $P = 0.006$). The *TGFBR2–875G>A* polymorphism frequencies for homozygous GG and GA/AA were 63% and 37% in PC group and 62% and 38% in the control group, respectively. We found lack of statistical significant association of *TGFBR2* genetic variants with PC risk (aOR = 1.05, 95% CI = 0.80–1.38, $P = 0.731$).

Conclusions: Our results show a protective effect associated with C allele (*TGFB1+869T>C*) for PC development. Functional polymorphisms that influence cellular microenvironment may help determine individual higher risk genetic profiles, which can impact PC diagnosis and chemoprevention strategies.

90 NQO1 polymorphism, maternal exposure and the risk of infant leukemia

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Introduction: Chromosomal abnormalities associated with infant leukemias (IL) originate during fetal life and often involve rearrangements of the *MLL* gene. The finding that similar abnormalities develop in children and adults treated with inhibitors of topoisomerase II (topo II) has led to the hypothesis that maternal exposure to topo II inhibitors, such as pesticides and benzene metabolites, during pregnancy might induce infant leukemias. NAD(P)H:quinone oxidoreductase 1 (NQO1) protects cells against oxidative stress and toxic quinones. A C609T polymorphism in the *NQO1* gene destabilizes and inactivates the enzyme and it has been reported as a susceptibility factor to IL. Taken together, infant and maternal genotypes of *NQO1*, in combination with exposure, could be important in etiology of IL. The aim of this study was to explore *NQO1* polymorphism in IAL with *MLL* translocation and, also evaluate mothers' genotypes in relation to different exposures during pregnancy.

Materials and Methods: The study population comprised 332 children (ages, 0−24 months-old), being 143 IL and 189 aged-matched controls. Samples from 177 mothers, who answered an epidemiological questionnaire, were also genotyped. Cases were diagnosed according to standard classifications. *MLL* characterization was done by reverse transcription-PCR and/or by fluorescence *in situ* hybridization. The *NQO1* C609T polymorphism was evaluated by PCR-RFLP. Statistical analyses were done using the SPSS 15.0 software. The differences in the genotype distribution between patients and controls, and across mothers of cases and controls were tested by logistic regression analysis to calculate ORs and 95% confidence intervals (CIs).

Results: Fifty eight percent of infants were positive for *MLL* rearrangements. We found the following CT + TT genotypes frequencies: 48.1% for controls and 45.4% for cases, whereas 47.8% for cases' mothers and 45.9% for controls' mothers. There was no difference across cases and controls in relation to *NQO1* genotypes frequencies [OR = 1.28; CI 95%, 0.82–1.99], nor even for mothers [OR = 1.93; CI 95%, 0.61–6.11]. Children with CT or TT genotypes didn't appear to be more prone to have *MLL* translocations [OR = 0.90; CI 95%, 0.43–1.86].

Conclusion: These preliminary results didn't show any association between *NQO1* polymorphism and *MLL* rearrangements. We noticed a higher CT + TT genotype frequency in cases' mothers but it is not statistically significant. Also, we observed that mothers who are exposed to hormones and pesticides during pregnancy have a higher risk to give birth to children who later developed leukemia. We believe that further analyses increasing the sample size may be able to demonstrate an association across mother's genotypes.

91 Analysis of BRIP1 in italian male breast cancer patients

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Background: Male breast cancer (MBC) is a rare disease compared to female breast cancer (FBC). MBC shares many similarities with FBC, including genetic predisposition factors such as *BRCA1/2* mutations. The frequency of *BRCA1/2* mutations ranges between 4 and 40% for *BRCA2* and up to 10% for *BRCA1* in different MBC series, thus suggesting the contribution of additional susceptibility genes.

Several studies identify *BRIP1* (BRCA1-interacting protein 1, also known as BACH1 and FANCJ) as a moderate-penetrance breast cancer (BC) susceptibility gene, accounting for about 1% of *BRCA1/2* negative familial/early-onset BCs. *BRIP1* encodes a DEAH helicase which interacts with the BRCT domain of BRCA1 and has BRCA1-dependent DNA repair and checkpoint functions. Interestingly, there are evidences that *BRIP1* might also play a role in susceptibility of prostate cancer, a tumour which may share risk factors with MBC. However, the role of *BRIP1* in MBC susceptibility is still unknown. In this study, we aimed to assess whether *BRIP1* alterations may contribute to MBC risk in Italy.

Material and Methods: We performed a mutational screening in 70 Italian MBC cases, negative for *BRCA1/2* mutations, selected from a population-based series of 123 MBCs. The complete coding region and intron-exon boundaries of *BRIP1* were analyzed by using SSCP (Single Strand Conformation Polymorphism). Cases displaying abnormal SSCP patterns were evaluated by direct sequencing. Statistical analysis was performed using the chi-square test.

Results: No truncating mutations were found. Two previously reported variants in the BRCT binding domain (E879E and P919S), and a neutral intronic variant (IVS4−28G>A) were identified. In order to evaluate the putative influence of the *BRIP1* P919S variant on MBC risk, we carried out a population-based case-control study based on a total of 97 MBC cases and 130 healthy adult male population controls from the same area. The frequency of the rare allele in cases was 36.2%, compared to 33.5% in population controls. No statistically significant difference in the distribution of the three specific *BRIP1* P919S genotypes was observed between MBC cases and controls ($p = 0.7$).

Conclusions: Overall, our results suggest that *BRIP1* do not play a major role in MBC susceptibility in Italy. However, larger studies are needed to explore its potential role as low risk gene.

92 Role of EGFR, HER2 and PIK3CA alterations in male breast cancer

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Background: EGFR and HER2 are tyrosine kinase receptors that activate different pathways, including PIK3-Akt, involved in cell proliferation, migration and survival. Thus EGFR, HER2 and PIK3 can play a relevant role in tumourigenesis, by mediating processes involved in neoplastic progression. *EGFR, HER2* and *PIK3* are frequently alterated in breast cancer (BC). EGFR and HER2 are amplified or over-expressed in about 20−40% of BC and mutations at their kinase domains are observed in about 2−4% of BC. Mutations at helical and kinase domains of *PIK3CA* gene, coding the catalitical subunity of PIK3, are reported in 8−40% of BC.

Male BC (MBC) is a rare and less investigated disease compared with female BC (FBC). Current knowledge on MBC biology is mainly derived from FBC. MBC shares many similarities with FBC, including genetic predisposition factors.

To date, the role of *EGFR*, *HER2* and *PIK3CA* alterations in MBC is very limited. Taking into account that EGFR, HER2 and PIK3CA have both prognostic and predictive value in BC, studies on the role of these genes could have important implications in the elucidation of pathogenetic mechanisms of MBC and in the clinical management of MBC patients.

Material and Methods: This study was performed on a series of 102 MBC cases characterized for clinicopathological features and *BRCA1*/*BRCA2* germ-line mutations. We have analyzed the presence of somatic mutations, amplification and expression of *EGFR*, *HER2* and *PIK3CA* by SSCP and automatic sequencing, qRT-PCR and IHC respectively.

Results: A mutation frequency of 4% was observed for *PIK3CA.* In our series *PIK3CA* common mutation (E545K) was identified in three different cases and a novel mutation (S553X) in one case. Interestingly, all tumours harboring *PIK3CA* mutations were ER+/PR+, in agreement with data obtained in FBC. Moreover *PIK3CA* resulted amplified with a frequency of 16%. No pathogenetic mutations were identified in *EGFR* and *HER2* genes but *EGFR* resulted amplified in 17% and HER2 over-expressed in 27.8% of cases and a statistical significant association emerged between HER2 over-expression and PR− ($p = 0.022$), MIB+ ($p = 0.028$), G3 ($p = 0.001$).

Conclusions: Our data indicate that alterations of *EGFR*, *HER2* e *PIK3CA* are involved in the pathogenesis of MBC at a comparable level as in FBC. Over-expression of HER2 allows the identification of a subgroup of MBC cases with specific pathological and biological characteristics indicative of aggressive clinical behavior.

93 Are variations in Helicobacter pylori cag pathogenicity island-genes associated with neoplastic progression in gastric cancer?

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Background: Helicobacter pylori is a bacterium that colonizes the human stomach and can establish a long-term infection of the gastric mucosa. Hp infection affects over 50% of the worldwide population, with a prevalence ranging from 20% in developed countries to over 90% in developing countries. Persistent Hp infection often induces gastritis and is associated