

# EMMA™ TECHNOLOGY

## EPIDEMIOLOGY

### ATM germline mutations in women with familial breast cancer and a relative with haematological malignancy

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**Abstract** Biallelic inactivation of the ATM gene causes ataxia—telangiectasia (A—T), a complex neurological disease associated with a high risk of leukaemias and lymphomas. Mothers of A—T children, obligate ATM hetero-zygote mutation carriers, have a breast cancer (BC) relative risk of about 3. The frequency of ATM carriers in BC women with a BC family history has been estimated to be 2.70%. To further our clinical understanding of familial BC and examine whether haematological malignancies are predictive of ATM germline mutation, we estimated the frequency of heterozygote mutation carriers in a series of 122 BC women with a family history of both BC and haematological malignancy and without BRCA1/2 mutation. The gene screening was performed with a new high throughput method, EMMA (enhanced mismatch mutation analysis).

Amongst 28 different ATM variants, eight mutations have been identified in eight patients: two mutations leading to a putative truncated protein and six being likely deleterious mutations. One of the truncating mutations was initially interpreted as a missense mutation, p.Asp2597Tyr, but is actually a splice mutation (c.7789G > T/p.Asp2597\_Lys 264>LysfsX3). The estimated frequency of ATM hetero-zygote mutation carriers in our series is 6.56% (95% CI: 2.16—10.95), a significantly higher figure than that observed in the general population, estimated to be between 0.3 and 0.6%. Although a trend towards an increased frequency of ATM carriers was observed, it was not different from that observed in a population of familial BC women not selected for haematological malignancy as the frequency of ATM carriers was 2.70%, a value situated in the confidence interval of our study.



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