

## The Brain Tumor Epidemiology Grant

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*Ataxia Telangiectasia (ATM) haplotypes and risk of sporadic and radiation associated meningiomas.*

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### Abstract:

Ionizing radiation is the only confirmed exogenous cause of brain tumors. Yet, only about 1% of individuals who have been exposed to it develop the tumor. This supports the paradigm that genetic factors are involved in the carcinogenic process following the initiating effect of radiation. Experimental and epidemiologic data indicate that heterozygote ATM mutation carriers may represent a radiosensitive subpopulation that is at a higher risk of radiation-induced cancer. The aim of the proposed study is to assess the putative role of ATM polymorphisms and haplotypes in the development of sporadic and radiation induced meningiomas using a 4 group nested case-control study balanced for irradiation. The study will build on the Israeli Tinea Capitis studies that include a long follow-up of several thousands of individuals who were treated by ionizing radiation to the scalp and a matched unexposed group. The study population will include 161 cases of radiation associated meningiomas, 85 cases of sporadic meningiomas, 145 unaffected irradiated controls and 135 unaffected non irradiated controls. Data on possible other risk factors and confounders and DNA were collected from all participants. All DNA samples will be genotyped for SNPs encompassing the entire ATM gene by employing the Sequenom™ technology and haplotypes will be constructed using the GERBIL program. Relationship between a single SNP or a single haplotype and disease in unirradiated individuals and an interaction between a single SNP or haplotype and irradiation in disease risk will be evaluated. Genotype-specific relative risks between the study groups will be estimated as Odds Ratios (OR) with associated 95% confidence intervals (CI), and will be adjusted for age, gender and origin. Based on past experience and considering the availability of biological samples and the data already collected, it is estimated that study setup period will last 2 months, genotypings- 6 months and statistical analysis and final report preparation, 4 months. Identification of individuals genetically susceptible to ionizing radiation, will define subpopulations that might benefit from counseling to lower their exposure to ionizing radiation and target them to early cancer detection schemes.