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Excision repair SNPs may influence the extent of DNA damage from radioiodine therapy in lymphocytes from thyroid cancer patients

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Background:

Thyroid cancer (TC) is the most common endocrine malignancy, with rising incidence. Radioactive iodine (^{131}I) is the standard therapy: ^{131}I is captured by thyrocytes, releases ionizing radiation and inflicts DNA damage, inducing cell death. Prognosis is good. Because ^{131}I may enter other cells, raising secondary malignancy risk, TC management guidelines now recommend cautious ^{131}I use. Since DNA repair counteracts DNA damage, DNA repair SNPs may interfere with ^{131}I-induced damage.

Materials and methods:

We assessed micronuclei (MN) frequency in 26 TC patients undergoing ^{131}I therapy – 15 patients exposed to 70 mCi, 11 to 100 mCi. MN levels were assessed before and after ^{131}I exposure (1, 6 and 24 months for 70 mCi-treated patients; 1 and 3 months for 100 mCi-treated patients). Patients were genotyped for excision repair SNPs by real-time PCR, using TaqMan® Genotyping Assays (Applied Biosystems), or by PCR-RFLP. MN level variation from baseline was compared between genotypes, for each time point, in both dose groups. The study was approved by the Ethics Committees of Instituto Português de Oncologia Francisco Gentil (GIC/357) and Faculdade Ciências Médicas (CE-5/2008). Informed consent was obtained from all participants.

Results:

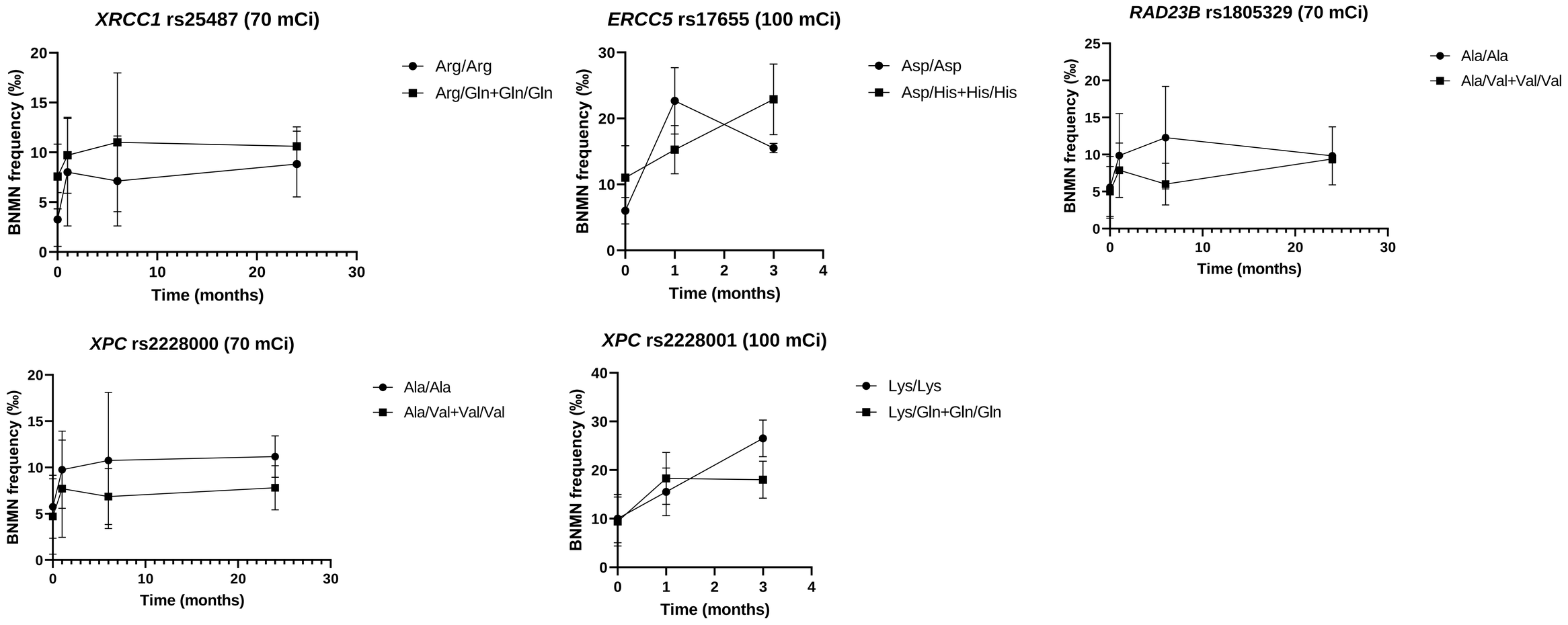

Figure 1. BNMN frequency (‰, mean ± S.D.) in DTC patients before and after (1, 3/6 and 24 months) therapy with ^{131}I, according to genotype and ^{131}I dose group: (a) *XRCC1* rs25487, 70 mCi; (b) *ERCC5* rs17655, 100 mCi; (c) *RAD23B* rs1805329, 70 mCi; (d) *XPC* rs2228000, 70 mCi; (e) *XPC* rs2228001, 100 mCi.

Conclusions:

Excision repair SNPs may influence DNA damage, hence therapeutic outcome in ^{131}I-treated patients. This could modify the risk of developing ^{131}I-induced secondary malignancies and therapeutic efficacy. Further studies are needed to validate these results and to identify additional SNPs contributing to interindividual variability in response to ^{131}I.

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