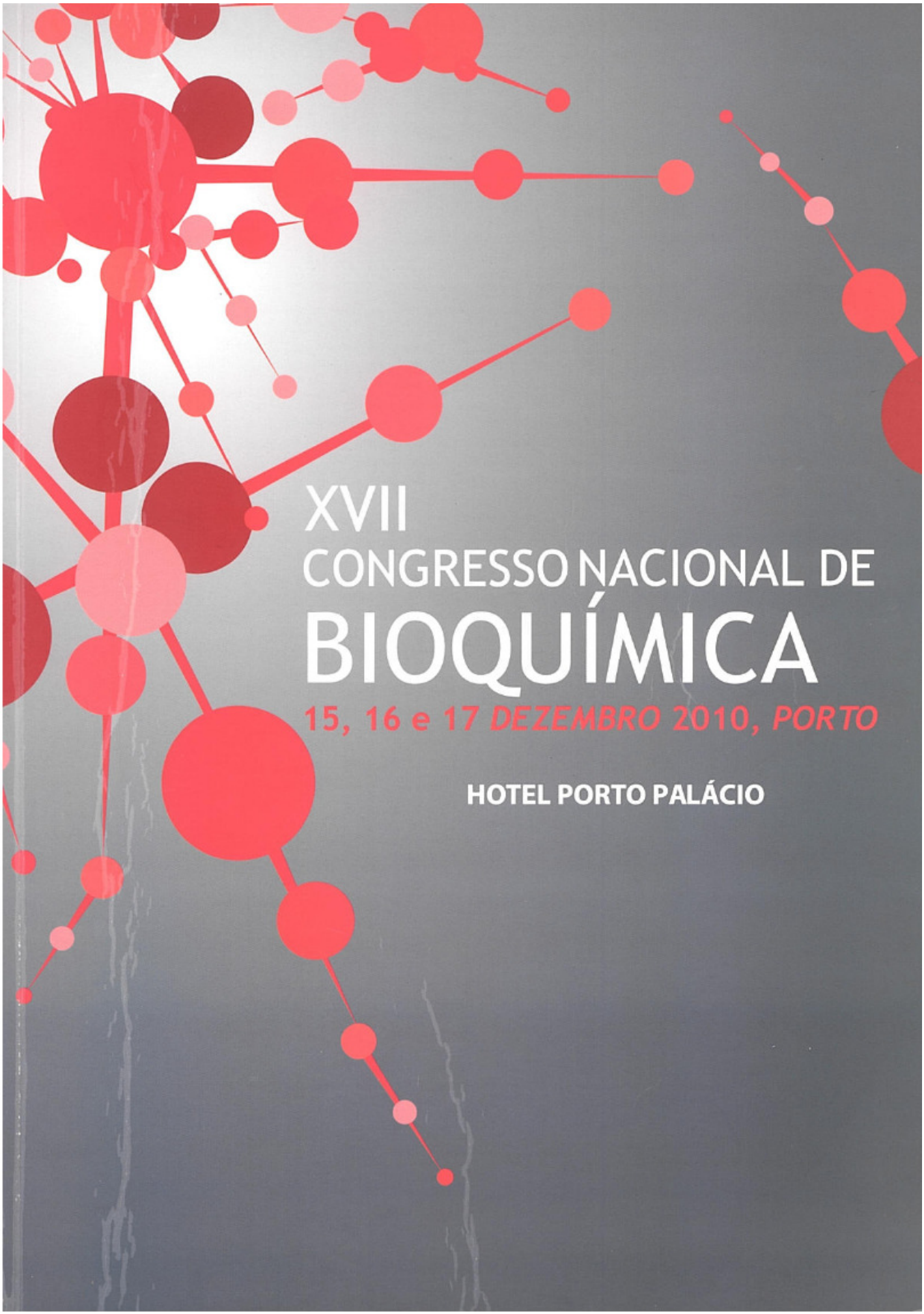
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to elucidate the correlation between evolution of the molecular mechanism of DNA repair and its involvement in regulation of specific gene transcription related to bone development, maintenance and aging. Because zebrafish is a valid alternative model to study these different physiological events, we have chosen to further analyse these aspects using this model system.

In silico, analysis using the available sequences of the *XPD* gene showed a molecular structure similar to other species with 24 coding exons. The coding regions were also found to be largely conserved among all species analysed, suggesting function maintenance throughout evolution. Gene expression analysis in different zebrafish tissues by real time PCR was corroborated by available *in silico* information based on tissue specific EST data, confirming *XPD* expression in brain, heart, kidney and gonads. Next we plan to analyse expression during zebrafish development thus providing a basis for the next series of studies which will focus on the analysis of *in vitro* (using our newly developed zebrafish bone derived cell lines) and *in vivo* (early development) effects of a *XPD* dominant negative.

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POSTER PRESENTATION (P C15)

Fragile X Syndrome: Genetic Backgrouds

Joana Loureiro[1,2]; Isabel Marques[1]; Bárbara Oliveira[1,3]; António Amorim[1]; Rosário Santos[1]; Paula Jorge[1]

[1] Unidade de Genética Molecular, Centro de Genética Medica Dr. Jacinto Magalhães, INSA; [2] Departamento de Biologia Vegetal, Faculdade de Ciências da Universidade de Lisboa; [3] Instituto Politécnico de Saúde do Norte, CESPU; [4] Institute of Molecular Pathology and Immunology of the University of Porto

Fragile X Syndrome (FXS) is the most frequent hereditary form of mental retardation, caused by an expansion of polymorphic CGG repeats in the 5'UTR region of the *FMR1* gene; however, the molecular mechanism of expansion is still unknown. Based on CGG repeat number, three allele classes can be distinguished: normal alleles with 5-50 repeats; pre-mutation alleles with 50-200 repeats and the complete mutation where alleles have expansions of >200 CGG repeats, which are methylated. Previous haplotype analysis of normal and mutant chromosomes among diverse populations had shown linkage disequilibrium between CGG repeats and flanking molecular markers.

In an attempt to contribute to the understanding of the origin and allele instability we studied a cohort of 124 unrelated FXS males and a group of 212 unrelated normal males. Haplotype background in and around *FMR1* locus was constructed using four Short Tandem Repeats (STRs), namely DXS998, DXS548 and FRAXAC1 located upstream the CGG repeat region, and FRAXAC2 located downstream in intron 2.In order to increase the informativity three Single Nucleotide Polymorphisms (SNPs) were also used, specifically rs971000, rs29282 and rs25715, being all in *FMR1* introns 1, 7 e 9 respectively.

For all markers, allele distribution was markedly different between normal and FXS populations. A different haplotype distribution was found among these two populations. Only a few allele profiles were common to both populations yet these shared haplotypes were amongst the rarest. No single founder haplotype was identified. Indeed in the normal population the most represented haplotype (20%) was never found in any FXS individual, whereas in the FXS population a high diversity of haplotypes were found. Several hypotheses are proposed so as to explain this apparent contradiction in the transmission and spreading of the disease and linked markers.