HRAD30A, A GENE ENCODING A CLASS Y LOW-FIDELITY DNA POLYMERASE HAS A LOW COMPLEXITY REGION IN INTRON I ASSOCIATED WITH TISSUE-SPECIFIC ALTERNATIVE SPLICING

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INTRODUCTION. The XP Variant (XPV) is a complementation group of the human disease xeroderma pigmentosum that was recently identified as a caused by mutations in a gene that maps to 6p21, *hRad30A*, that encodes a novel DNA polymerase, pol η [1,2]. Pol η is a member of a large family, class Y, of low-fidelity DNA polymerases. It has the unusual property that although it can replicate UV-induced pyrimidine dimers *in vivo* with the insertion of the correct bases in the daughter strand, *in vitro* it is very error-prone and inserts mutagenic bases at about 1% frequency[3,4]. We recently identified an alternative splice variant of *hRad30A* mRNA in the testis and fetal liver, suggesting that there may be tissue-specific regulation of this gene[5]. This alternative splicing results in the elimination of exon II that contains the ATG start site for transcription and results in a cDNA that does not complement the XPV defect[5].

METHOD. *hRad30A* has 10 coding exons and an unexpressed exon I 5.8 kb upstream from the first coding exon. To investigate the basis for the alternative splicing we subjected the 5' end of

the gene to analysis by a Genome Cryptographer (GC) program[6]. This is an exhaustive genome landscaping mapping that identifies repetitive element density and allows correlation between these elements and functional activity.

RESULTS AND DISCUSSION. GC analysis indicated that many of coding regions of *hRad30A* were regions of low complexity. This was anticipated since these should be informative for gene product synthesis and function. However, the long, 5.8kb intron I also contained at least 1kb of unique sequence with no detectable repetitive DNA, unlike the flanking regions, and a high frequency of CpG islands. This indicates that the intronic region has escaped invasion by repetitive DNA and probably contains important coding or regulatory regions. This region may therefore contain control elements for the tissue-specific splicing we previously observed (5), and will be the subject of further sequence and functional analysis.

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