Loci associated with genomic damage levels in Spanish chronic kidney disease patients

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Chronic kidney disease (CKD) is a multifactorial disorder with an important genetic component, and several studies have demonstrated potential associations with allelic variants. Using different techniques such as the comet and micronucleus (MN) assay, in peripheral blood lymphocytes we have demonstrated that CKD patients present elevated levels of genomic damage. In addition, these patients also showed genomic instability, since the genomic damage induced by *in vitro* irradiation of patient's cells was significantly higher than observed in controls. Furthermore, CKD patients show deficiencies in repair oxidatively damaged DNA. In this scenario, looking for genetic variants explaining the genomic instability of CKD patients seems urgent.

Until now no studies have stablished relationships between DNA damage or genomic instability present in CKD patients and SNPs. To fill in this gap, the potential role of polymorphisms in genes involved in base excision repair (*OGG1*, rs1052133; *MUTYH*, rs3219489; *XRCC1*, rs25487), nucleotide excision repair (*ERCC2/XPD*, rs1799793, rs171140, rs13181; *ERCC4*, rs3136166); phase II metabolism (*GSTP1*, rs749174; *GSTO1*, rs2164624; *GSTO2*, rs156697), and antioxidant enzymes (*SOD1*, rs17880135, rs1041740, rs202446; *SOD2*, rs4880; *CAT*, rs1001179; *GPX1*, rs17080528; *GPX3*, rs870406: *GPX4*, rs713041) were genotyped. In addition, some genes involved in CKD (*AGT*, rs5050; *GLO1*, rs386572987; *SHROOM3*, rs17319721) were also evaluated. Our results showed significant associations with *XRCC1* (rs25487) and *ERCC2/XPD* (rs13181), as genes directly involved in DNA repair pathways. Interestingly the three genes associated to CKD (*AGT*, *GLO1*, and *SHROOM3*) showed positive associations with high levels of DNA damage, oxidatively damaged DNA, and genomic instability.

These results support our hypothesis that genomic instability can be considered a biomarker of CKD status.