GENOMIC INSTABILITY AS AN INDICATOR OF CHRONIC KIDNEY DISEASE PATIENTS

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Chronic kidney disease (CKD) is a multifactorial disease characterized by a decrease of glomerular filtration rate. Cardiovascular disorders in these patients are the main cause of mortality, followed by cancer and infections.

It is known that genomic damage is related to the development of cancer and cardiovascular diseases. In previous studies, and using different techniques such as the comet and micronucleus (MN) assays in peripheral blood lymphocytes, we demonstrated that CKD patients present elevated levels of genomic damage, since the first stages of the disease. We demonstrated that these patients showed intrinsic genomic instability, since genomic damage induced by *in vitro* irradiation of patient's cells was significantly higher than that observed in controls. Furthermore, CKD patients showed deficiencies in repair oxidized damaged DNA. In addition, we identified a positive correlation between the levels of DNA damage and the risk of mortality. Thus, the levels of DNA damage could be used as a biomarker of bad prognosis in patients with CKD. The increase of the genomic damage on CKD patients could be attributed to the increase of the oxidative stress, uremic toxins, deficiency of antioxidants, or to the decrease in the DNA repair capacity. In that sense, our group have demonstrated that the administration of antioxidants to CKD patients submitted to hemodialysis reduce the oxidative DNA damage.

We have also look for genetic variants of genes involved in base excision repair (*OGG1, MUTYH, XRCC1*), nucleotide excision repair (*ERCC2, ERCC4*), phase II metabolism (*GSTP1, GSTO1, GSTO2*) and antioxidant enzymes (*SOD1, SOD2, CAT, GPX1, GPX3, GPX4*) trying to explain the genomic instability of CKD patients. Our results showed significant associations with *XRCC1* (rs25487) and *ERCC2* (rs13181), as genes directly involved in DNA repair pathways. These results support our hypothesis that genomic instability can be considered a biomarker of CKD status.