

## Genomic Damage as a Biomarker of Chronic Kidney Disease Status

Zuray Corredor<sup>1</sup>, Elitsa Stoyanova<sup>1</sup>, Lara Rodríguez-Ribera<sup>1</sup>, Elisabet Coll<sup>2</sup>, Irene Silva<sup>2</sup>, Juan Manuel Diaz<sup>2</sup>, José Ballarin<sup>2</sup>, Ricard Marcos<sup>1,3</sup>, Susana Pastor<sup>1,3</sup>

<sup>1</sup>Grup de Mutagènesi, Departament de Genètica i de Microbiologia, Facultat de Biociències, Universitat Autònoma de Barcelona, Bellaterra, Spain; <sup>2</sup>Fundació Puigvert, 08025 Barcelona, Spain. <sup>3</sup>CIBER Epidemiología y Salud Pública, ISCIII, Spain.

Chronic kidney disease (CKD) is characterized by a progressive loss of kidney function. Thus, CKD patients are defined as those showing either kidney damage or a glomerular filtration rate (GFR) < 60 mL/min per 1.73 m<sup>2</sup> for three or more months. Consequently, a five-stage classification system is used to define the severity of the pathology in adults. As renal disease worsens, from stage 1 to 5, kidney functions deteriorate and at the end-stage of renal failure, kidney replacement or dialysis therapies are required.

It has been reported that patients suffering from CKD exhibit a high incidence of cancer and cardiovascular diseases, as well as high levels of genomic damage. To confirm the association of CKD and genomic damage we have carried out the largest study ever performed using a total of 602 subjects (187 controls, 206 pre-dialysis CKD patients and 209 CKD patients in hemodialysis). We also studied the effect of vitamin E, as antioxidant, in a group of 15 end-stage renal disease patients, submitted to hemodialysis with a membrane with vitamin E during 6 months. Genomic and DNA oxidative damage was measured in all individuals, using the comet assay.

Our results indicate that CKD patients present significantly higher levels of DNA damage, in comparison to controls, but no significant differences were observed between pre-dialysis and dialysis (HD) patients. When oxidative damage was measured, no differences were observed between patients and controls, although HD patients showed significantly high levels of oxidative damage than pre-dialysis patients. No differences neither in the levels of genomic nor oxidative DNA damage were observed after 6 months of hemodialysis with vitamin E (preliminary results). In addition, a good relationship was demonstrated between genomic damage and all-cause mortality.

Our study confirms that the levels of genomic damage can be considered a good indicator measuring the status of CKD patients, and that the presence of high levels of DNA damage may indicate a poor prognosis in HD patients. Individuals with high levels of basal DNA damage have increased risk for chronic renal failure, in addition to other outcomes such as cancer.