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NEWS

European Renal Association – European Dialysis and Transplant Association

Why do CKD patients undergo premature aging?

CDKN2A/p16INK4a is associated with vascular progeria in the uremic milieu

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When chronic kidney disease (CKD) progresses to end-stage renal disease, the risk of cardiovascular mortality increases exponentially and occur at a much younger age. Few other patient groups display such a marked discrepancy between chronological and biological age as patients with CKD. Thus, it has been suggested that CKD could be used as a clinical model to study premature vascular ageing processes. In the uremic milieu several factors promote premature aging, such as increased allostatic load (inflammation and oxidative stress), specific pro-ageing factors (hyperphosphatemia, angiotensin 2 and sodium accumulation) and defective anti-ageing protective mechanisms (such as klotho and vitamin D deficiency and nuclear lamina defects) promote a progeric phenotype.

At the ERA-EDTA Congress in Madrid Professor Stenvinkel, Stockholm, Sweden, gave further details on the impact of senescence on the vascular progeric phenotype in CKD: Proteins derived from the cyclin-dependent kinase inhibitor 2A/B (CDKN2A/B) are functionally involved in maintaining cells in a state of growth arrest. Since cellular senescence increases with age, expression of CDKN2A increases as a function of increasing cellular stress and organismal ageing. It even appears to be superior to telomere length as a biomarker of biological age.

As Stenvinkel explained, calcification and ageing in vascular smooth muscle cells appear to be mediated, at least in part, by p16 protein. A removal of p16INK4a-positive cells in progeric mice led to an attenuation of the ageing phenotype, therefore a functional involvement of p16INK4a in ageing-associated disorders is likely.

Stenvinkel's study group found out that increased arterial expression of CDKN2A/p16INK4a was associated with vascular progeria in the uremic milieu, independently of chronological age [1]. "Thus CDKN2A/p16INK4 is a biomarker of premature vessel aging in CKD patients. Now we need to find out, if it could also be a therapeutic target to address cellular senescence".

[1] Stenvinkel P, Luttrupp L, McGuinness DAging (Albany NY). 2017; 9(2): 494-507



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About ERA-EDTA

With almost 7,000 members, the ERA-EDTA ("European Renal Association – European Dialysis and Transplant Association") is one of the biggest nephrology associations worldwide and one of the most important and prestigious European Medical Associations. It supports basic and clinical research in the fields of clinical nephrology, dialysis, renal transplantation and related subjects. It also supports a number of studies as well as research groups and has founded a special "Fellowship Programme" for young investigators as well as grant programmes. In order to involve young nephrologists in all activities ERA-EDTA has the Young Nephrologists' Platform (YNP), a very active committee whose board includes members who are 40 years old or younger. Besides, it has established various working groups to promote the collaboration of nephrologists with other medical disciplines (e.g. cardiology, immunology). Furthermore, a "European Renal Best Practice" (ERBP) advisory board was established by the ERA-EDTA to draw up and publish guidelines and position statements. Another important goal of the ERA-EDTA is education: several series of CME-courses as well as the annual congress offer an attractive scientific programme to cover the need of continuous medical education for doctors working in the fields of nephrology, dialysis and transplantation. The association's journals, NDT (Nephrology, Dialysis, Transplantation) and ckj (Clinical Kidney Journal), are currently the leading nephrology journals in Europe; furthermore NDT-Educational is the online educational journal, open for free to all uses, of the Society as well as the very important and useful feature of NDT-Educational "Literature Review". The ERA-EDTA Registry is a large epidemiologic database comparing countries by assessing nephrology practice throughout Europe. ENP, the European Nephrology Portal, is the latest new initiative of ERA-EDTA: here all those interested in the activities of the Society can find everything that is done, all in one place! Finally, ERA-EDTA is member of the European Kidney Health Alliance (EKHA), a consortium of patients, nurses, foundations all related to renal issues that actively interacts with the European Parliament. For more information please visit www.era-edta.org