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Histone H3 K79 methyltransferase is a new potential renoprotective factor

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Kidney fibrosis is the hallmark of chronic kidney disease (CKD). Despite aggressive management, CKD often progresses to end-stage renal disease which costs the US >\$40 billion dollars and >90000 deaths annually. The current main therapy targeting the renin-angiotensin-aldosterone system with drugs including Spironolactone often delays but does not stop the progression. Factors modulating the aldosterone global effect from its primary action-site connecting tubule/collecting duct may prove better targets. However, such genetic and epigenetic factors remain virtually unknown, partially because of the intrinsic limitations of the clinical studies. These limitations include lack of kidney biopsies to verify the status of the disease, impossibility of genetic manipulation in patients to establish the causative relationship and impracticability through mutational analyses with blood DNA to identify somatic mutations, which occur at atypical high rate in human kidney. Our published and preliminary data suggest that patients with diabetic nephropathy and CKD may have mutations in histone H3 K79 methyltransferase hDOT1L and abolished H3 dimethylation in their kidney biopsies; Dot1a (encoded by mouse Dot1l) represses ET1 and other aldosterone target genes. Aldosterone relieves Dot1a-mediated repression by multiple mechanisms; connecting tubule/collecting duct-specific ablation of Dot1l in Dot1lAC mice causes abolition of H3 dimethylation, up-regulation of endothelin 1 and development of severe kidney fibrosis throughout the whole kidney under various settings. Our study highlights Dot1l as a potential novel renoprotective player and its somatic inactivation in kidney may cause CKD in mice and humans.

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Increasing primary care physicians' understanding of Agent Orange exposure and diabetes mellitus type-2

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Committee to review the health effects in Vietnam veterans due to exposure to herbicides has found that exposure to Agent Orange is linked to a number of chronic medical conditions including type-2 diabetes mellitus. The American Diabetes Association estimates the average annual medical cost for an individual with type-2 diabetes to be over \$13,000 a year. Fortunately, Vietnam veterans who were exposed to Agent Orange and who have been diagnosed with type-2 diabetes can apply for disability benefits to cover this cost. Unfortunately, we have noted that many Vietnam veterans and primary care physicians outside of the VA medical system are unaware of this. The results of both a literature review of Agent Orange exposure and its correlation to type-2 diabetes, as well as interviews of 15 Vietnam veterans suffering from type-2 diabetes will be presented. As more rural Minnesotan veterans are expected to access care from their local non-VA healthcare providers after the passing of the Veteran Access to Care Act of 2014, it is important to bring primary care physicians up-to-date on healthcare concerns specific to the veteran population, including the association between type-2 diabetes and previous Agent Orange exposure.

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