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**Fan1 deficiency results in DNA interstrand cross-link repair defects, enhanced tissue karyomegaly, and organ dysfunction**

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Xiaoyu Xue, Alma Papusha, Koyi Choi, Jaclyn N. Bonner, Sandeep Kumar, Hengyao Niu, Hardeep Kaur, Xiao-Feng Zheng, Roberto A. Donnianni, Lucy Lu, Michael Lichten, Xiaolan Zhao, Grzegorz Ira, and Patrick Sung  
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*(continued)*
Human FANCD2/FANCI-associated nuclease 1 (FAN1) deficiency results in the chronic kidney disease karyomegalic interstitial nephritis, which is characterized by renal failure and karyomegaly (enlarged and polyploid nuclei) in the kidney, liver, and brain. Shown here is a haematoxylin and eosin-stained section of a renal cortex from a Fan1-deficient mouse. Karyomegalic nuclei (larger blue) are observed in many of the renal tubules but not in the glomerulus. The number of polyploid cells increases with age in multiple tissues and correlates with organ dysfunction in Fan1-deficient mice. (For details, see Thongthip et al., p. 645, and the related paper by Lachaud et al., p. 639.)