Familial juvenile hyperuricemia nephropathy (FJHN), an autosomal dominant disorder, is caused by mutations in the UMOD gene, which encodes uromodulin, a glycosylphosphatidylinositol-anchored protein that is expressed in the thick ascending limb of the loop of Henle and excreted in the urine. Although uromodulin is the most abundant protein secreted in urine, its physiological role remains unclear. FJHN symptoms are characterized by alteration of urinary concentrating ability, tubulo-interstitial fibrosis hyperuricemia and renal cysts at the cortico-medullary junction. We recently reported a patient who carried a novel UMOD mutation of G335A (Cys112Tyr:C112Y), associated with a strong familial history of both gout and renal failure. To study the stability of mutant and its effect on the cellular apoptosis, we examined the function of wild-type and mutant uromodulin in the transfected HEK293 cells. The cytosolic and secreted protein levels of C112Y were significantly decreased in than those of WT with their marked ubiquitination. The half life of C112Y was significantly decreased than that of WT, which was normalized by a proteasome inhibitor associated with increased in Hsp70. The signal of C112Y was significantly decreased in ER and Golgi apparatus with reduced expression at the plasma than WT. The expression of C112Y significantly increased the cellular apoptosis determined by Anexin V staining and flow cytometry. Thus, C112Y mutant showed impaired intracellular maturation and trafficking to induce the cellular apoptosis, which may cause the phenotype of FJHN.