The production trial of high HPRT activity - low XOR activity - Uox knockout mice

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There are three differences between human and mouse in purine metabolism: lacking uricase (Uox); low hypoxanthine phosphoribosyltransferase (HPRT) activity; high xanthine oxidoreductase (XOR) activity. However, Uox knockout (UoxKO) mice have renal impairment due to urinary urate (purine) excretion approximately 25 times that of humans. Thus, the suppression of urinary purine excretion is a challenge for use of UoxKO mice in urate and nucleic acid research. We report the progress of high HPRT activity - low XOR activity UoxKO mice as human urate metabolism model mice.

Xdh knockout (XdhKO) mice were mated with high HPRT activity UoxKO mice to produce high HPRT activity XorKO-UoxKO mice. In collaboration with the National Institute of Genetics, human XDH transgenic (XDHtg) mice were created by introducing a gene fragment linking human XDH cDNA downstream of the human XDH gene promoter. The resulting mice were mated to try to produce HPRT high activity low XOR activity-UoxKO mice.

Although the urinary purine / creatinine (mol / mol) excretion ratio of high HPRT activity UoxKO mice was about 6 -8, that of high HPRT activity XorKO-UoxKO mice was halved to about 3. High HPRT activity XorKO-XORtg-UoxKO mice were obtained and their urinary purine / creatinine excretion ratio was still around 3 and did not decrease. When the normal feed CRF1 was changed to the purified feed AIN93M, the urinary purine / creatinine excretion ratio was further halved to about 1.5. Therefore, excessive urinary purine excretion in mice is thought to be derived from intestinal absorbed purine.