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Abstract

We previously established an experimental model of calcium oxalate crystal deposition in the mouse kidney using C57BL/6 mice [1]. C57BL/6J (B6J) and C57BL/6N (B6N) are two core substrains of C57BL/6 mice. B6J and B6N substrains have approximately the same genomic sequence. However, in whole-genome analyses, substrains have slight genetic differences in some genes [2]. In this study, we used these substrains as kidney crystal formation models and compared their genetic backgrounds to elucidate the pathogenic mechanisms of kidney stone formation. Eight-week-old male B6J and B6N mice (n = 15 in each group) were administered 80 mg/kg glyoxylate for 12 days, and the number of kidney crystal depositions was compared. The expression levels of six genes (*Snap29*, *Fgf14*, *Aplp2*, *Lims1*, *Naaladl2*, and *Nnt*) were investigated by quantitative polymerase chain reaction, and the protein levels were evaluated by western blotting and immunohistochemistry. The number of kidney crystal depositions was significantly higher in B6J mice than in B6N mice on days 6 and 12. The expression of nicotinamide nucleotide transhydrogenase (*Nnt*) gene was significantly lower in B6J mice than in B6N mice. The expression of Nnt protein was observed only in B6N mice, preferential high expression was seen in renal tubular epithelial cells. The results of this study provide compelling evidence that differences in mouse substrains affect kidney crystal deposition and that the absence of Nnt protein could be involved in the crystal formation in B6J mice.

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2. Mekada K, Abe K, Murakami A, Nakamura S, Nakata H, Moriwaki K, Obata Y, Yoshiki A (2009) Genetic differences among C57BL/6 substrains. Exp Anim 58:141-149