Functional analysis of novel mutations associated with Hartnup disorder

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Hartnup disorder is an autosomal recessive inherited disorder, which is characterised by the excretion of large amounts of neutral amino acids in the urine. Clinical symptoms include a photosensitive skin rash, episodes of cerebellar ataxia and other neurological symptoms. Recently, we and others have identified mutations in the neutral amino acid transporter SLC6A19 that cause Hartnup disorder by transporter inactivation (Seow *et al.*, 2004; Kleta *et al.*, 2004). Initial analysis of Australian and American families suggested that Hartnup disorder may be genetically heterogenous, a notion supported by the variability of clinical symptoms. To investigate this question further, we studied an additional ten families and reevaluated families presented in previous studies. Genomic sequencing revealed that in almost all families mutations of SLC6A19 are observed. Functional analysis of mutants was carried out by expression of SLC6A19 cRNA in Xenopus laevis oocytes[*], demonstrating that the transporter is inactivated by all novel mutations detected in these families. This suggests that SLC6A19 is the major gene involved in Hartnup disorder.

Seow HF, Broer S, Broer A, Bailey CG, Potter SJ, Cavanaugh JA & Rasko JE. (2004) Hartnup disorder is caused by mutations in the gene encoding the neutral amino acid transporter SLC6A19. *Nature Genetics*, **36:** 1003-1007.

Kleta R, Romeo E, Ristic Z, Ohura T, Stuart C, Arcos-Burgos M, Dave MH, Wagner CA, Camargo SR, Inoue S & others. (2004) Mutations in SLC6A19, encoding B0AT1, cause Hartnup disorder. *Nature Genetics*, **36:** 999-1002.

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[*]Xenopus laevis oocytes were harvested by surgery of anaesthesized frogs (MS-222, 1.5g/l). The procedure was approved by the Animal Experimentation Ethics Committee of the Australian National University.