Two novel ATP2C1 mutations in patients with Hailey-Hailey disease and a literature review of sequence variants reported in the Chinese population

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ABSTRACT. Hailey-Hailey disease (HHD) is an autosomal dominant disorder in which the ATP2C1 gene has been implicated. Many mutations of this gene have been detected in HHD patients. To analyze such mutations in HHD and summarize all those identified in Chinese patients with this disease, we examined four familial and two sporadic cases and searched for case reports and papers by using the Chinese Biological Medicine Database and PubMed. HHD diagnoses were made based on clinical features and histopathological findings. Polymerase chain reaction and direct sequencing of the ATP2C1 gene were performed using blood samples from HHD patients, unaffected family members, and 120 healthy individuals. Three mutations were identified, including the recurrent mutation c.2126C>T (p.Thr709Met), and two novel missense mutations, c.2235_2236insC (p.Pro745fs*756) and c.689G>A (p.Gly230Asp). Considering our data, 81 different mutations have now
been reported in Chinese patients with HHD. In cases of misannotation or duplication, previously published mutations were renamed according to a complementary DNA reference sequence. These mutations are scattered throughout the \textit{ATP2C1} gene, with no evident hotspots or clustering. It is of note that some reported “novel” mutations were in fact found to be recurrent. Our findings expand the range of known \textit{ATP2C1} sequence variants in this disease.

\textbf{Key words:} Mutation; Hailey-Hailey disease; \textit{ATP2C1}