The Phenotypic and genetic Spectrum of Kabuki Syndrome in Patients of Chinese Descent

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◆**Backgroud** Kabuki syndrome (KS) is a rare dominant disorder of transcriptional regulation with a complex phenotype including cranio-facial dysmorphism, intellectual disability, developmental delay, hypotonia, failure to thrive, short stature and variable cardiac and renal anomalies. Mutations in either KMT2D or KDM6A cause KS. While the phenotype of KS has been reported in many ethnicities, little is known about the phenotypic spectrum of KS in China.

◆**Method** Fourteen Chinese patients with genetically confirmed KS from 2 different hospitals were evaluated in detail in addition to eleven Chinese patients who were identified from the medical literature. The phenotype of these 25 Chinese patients was compared to that of 449 patients with KS from other ethnicities, published in the medical literature. In addition we explored the utility of Face2Gene, a commercially available facial recognition software in recognizing KS as the underlying diagnosis based on facial gestalt.

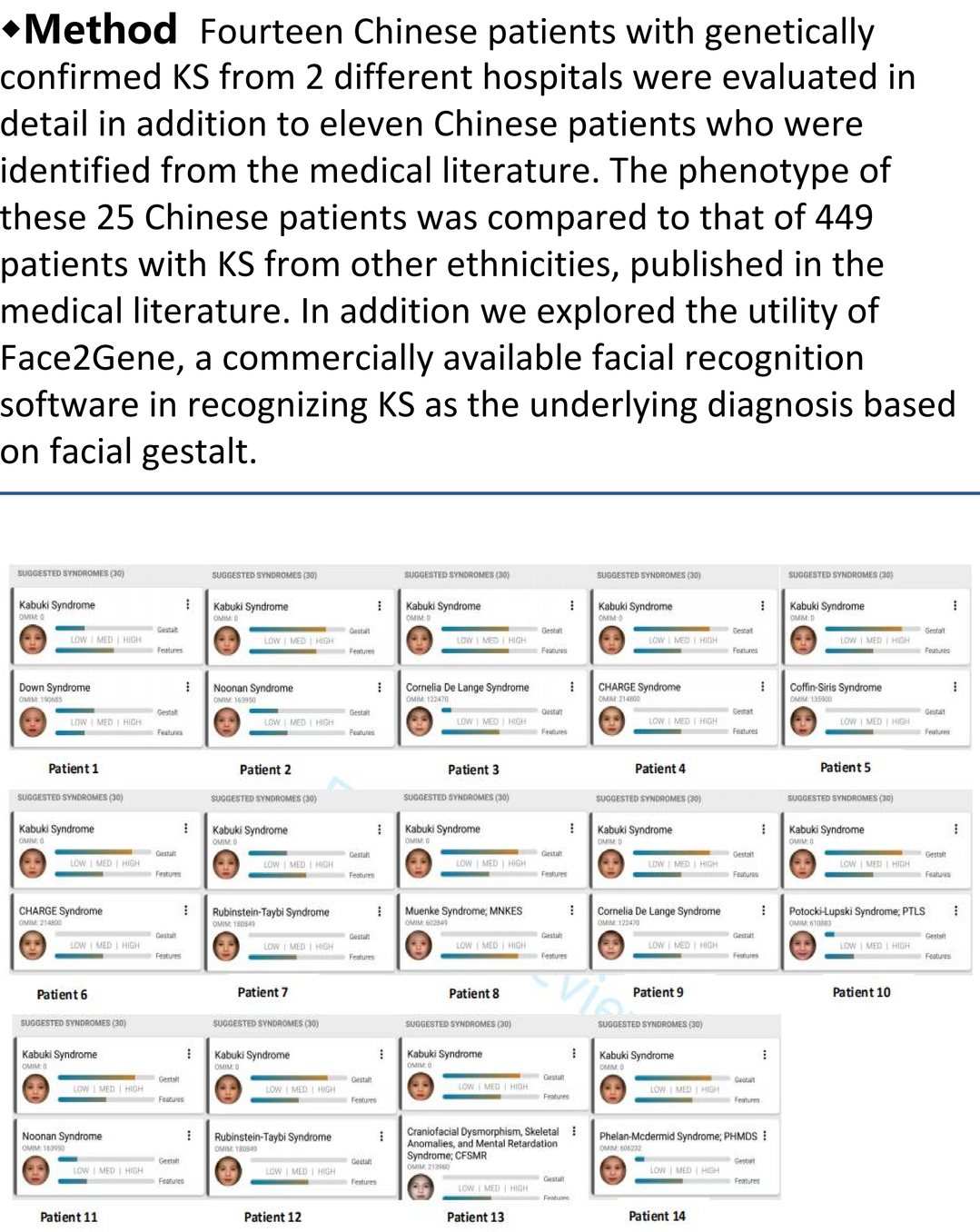
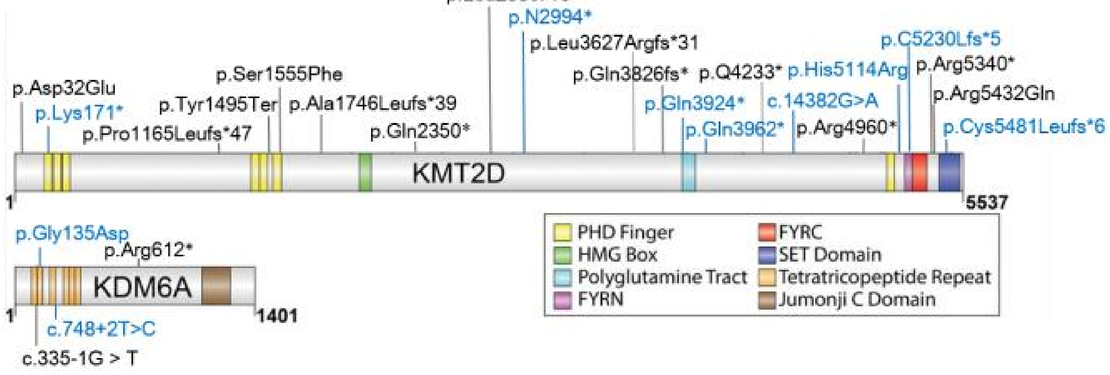
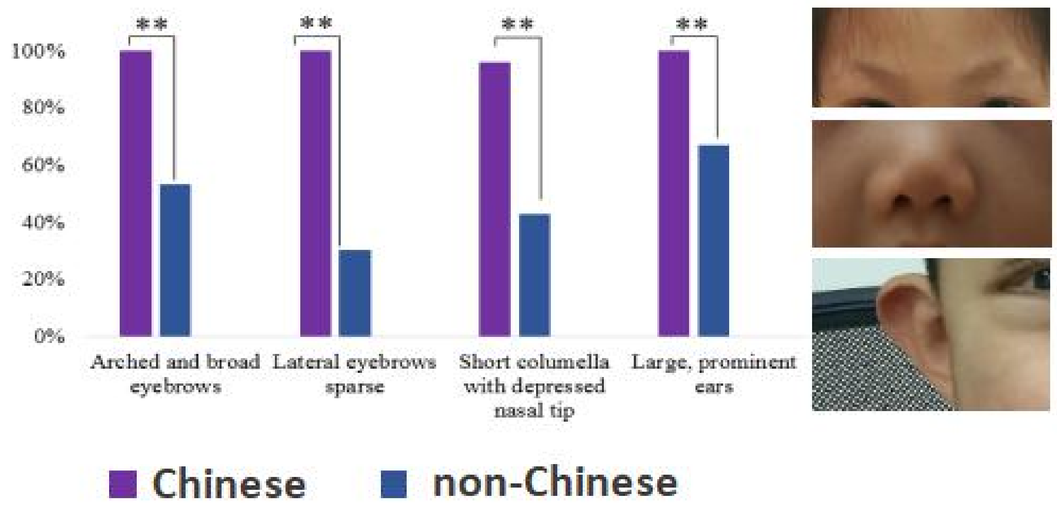


Figure 2 Using patient photographs (Figure 1) including the patient's HPO phenotype, the diagnosis of Kabuki Syndrome reaches a high Gestalt rank in 13 of 14 patients (top row). HPO phenotype only led to a high Gestalt rank in 2 of 14 patients (lower row).

◆**Result** All 25 patients with KS carried de novo, heterozygous likely pathogenic or pathogenic variants in either KMT2D or KDM6A. Three out fourteen patients were female, the mean age of genetic diagnosis was 4 years 1 month (3m-10.7y). Aspects of the facial gestalt including arched and broad eyebrows(25/25 100%), lateral eyebrows sparse or notched at one third of the distal end(18/18100%), short columella with a concave nasal tip (24/25 96%) and large, prominent ears (24/24 100%) were more frequent in Chinese compared to non-Chinese patients (P<0.01). In contrast, the reported frequencies of microcephaly (2/25 8%), cleft lip/palate (2/25 8%) and cardiac defects (10/25 40%) were lower in Chinese compared to non-Chinese patients. All patients in our cohort were recognized by F2G as KS.





◆**Conclusion** As expected, there is marked phenotypic overlap between Chinese and non-Chinese patients with KS, although subtle differences were identified.