Annabelle S. Slingerland[a,b], Andrew Hattersley[a]
[a]*Institute of Biomedical and Clinical Science, Peninsula Medical School, Exeter, United Kingdom;* [b]*Department of Cardiology, Leiden University Medical Center, Leiden, Netherlands*

INTRODUCTION: Recently, interest in "neonatal" diabetes has increased because patients could stop taking insulin and improve glycemic control and associated neurologic features.
OBJECTIVE: Our objective was to determine the anticipated increase in prevalence and incidence of permanent neonatal diabetes in children, adolescents, and adults and investigate the impact of the new definition.
METHODS: We studied 293 (53% male) referrals to the Exeter Laboratory (Devon, United Kingdom) as part of the largest international series to date. The referred patients were diagnosed with diabetes below 6 months of age irrespective of current age, and their conditions had not remitted at the time of study. Data on 27 countries were collected, and age of diagnosis, date of birth, and gender were obtained from standardized forms. All referred patients were tested for *KCNJ11* mutations.
RESULTS: The minimum observed prevalence of the 5 most representative countries was 1.17 (1.01–1.31) per million population, with the estimated true prevalence twice as high. Prevalence was higher for the pediatric versus adult age range (odds ratio: 0.78 [95% confidence interval: 0.54–1.31] vs 0.42 [95% confidence interval: 0–0.50], respectively; $P = .009$). Seventy-five percent of the patients were below 16 years of age with a median (interquartile range) of 5.7 (2.4–10.2) years, which implies underdiagnosis beyond 5 years of age. Age of diagnosis was skewed to a median (interquartile range) of 6 (1–13) weeks, with 62% in the first 8 weeks. During 2000–2004, the minimum observed incidence was 2.95 (0–49.1) per million live births.
CONCLUSIONS: This is the first report to show 2 to 25 times higher prevalence than previous reports from 10 years ago. "Neonatal" should be changed to "diagnosed at <6 months of age irrespective of current age," and awareness should be increased, especially for those who are older than 5 years and present with treatment implications.

Genetics

IDENTIFICATION OF 7 NOVEL TRANSFORMING GROWTH FACTOR β RECEPTOR 2 MUTATIONS IN CHINESE PATIENTS WITH MARFAN SYNDROME

Submitted by Hon Yin Brian Chung

Brian Hon-Yin Chung[a], Susanna Li[b], Stephen Tak-Sum Lam[b], Wanling Yang[b], Kin-Shing Lun[b], Yu-Lung Lau[b]
[a]*Department of Pediatrics and Adolescent Medicine, Queen Mary Hospital and Grantham Hospital, University of Hong Kong, Pokfulam, Hong Kong;* [b]*Second Clinical Genetic Service, Department of Health, Hong Kong Special Administrative Region, People's Republic of China, Hong Kong*

INTRODUCTION: Marfan syndrome (MFS) (Online Mendelian Inheritance in Man [OMIM] No. 154700) is an autosomal-dominant connective tissue disorder that affects multiple systems including the cardiovascular, ocular, and musculoskeletal systems. Fibrillin 1 (FBN1) (OMIM No. 134797) mutations are causative in >90% of the cases, and recent studies have shown that transforming growth factor β receptor 2 (*TGFBR2*) (OMIM No. 190182) mutations could be identified in ~10% of non-*FBN1* probands (Mátyás G, Arnold E, Carrel T, et al. *Hum Mutat*. 2006;27:760–769).
OBJECTIVE: Our objective was to examine the mutation spectrum of *TGFBR2* in non-*FBN1* Chinese patients with MFS and related phenotypes.
METHODS: All Chinese probands who were referred for evaluation of MFS and tested negative for *FBN1* mutations were included. Mutational screening was performed by denaturing high-pressure liquid chromatography (Kosaki K, Udaka T, Okuyama T. *Mol Genet Metab*. 2005;86:117–123). Amplicons with an abnormal elution pattern were selected for direct sequencing.
RESULTS: Seven novel mutations were identified in 7 of 41 probands. All of them had prominent cardioskeletal phenotypes without ocular or dural involvement, which confirmed previous findings (Disabella E, Grasso M, Marziliano N, et al: *Eur J Hum Genet*. 2006;14;34–38). Six mutations were missense (R190H, D247V, T325P, G357R, I510N, and T530I), and 1 was frameshift (P501fsX17). Except for R190H, all were found in the functionally important kinase domain. Bioinformatic analyses showed that (1) all mutations occurred in conserved positions by cross-species comparison between 6 orthologs, and (2) R190H, T325P, T530I, and G357R were also found in conserved positions among 3 paralogs (*TGFBR1* and activin receptors AVR2A and AVR2B) in the TGFBR superfamily. None of the 7 were found in 50 unaffected individuals (100 normal alleles). With the *TGFBR2* mutations, 4 additional probands would fulfill the diagnostic criteria of MFS.
CONCLUSIONS: *TGFBR2* mutation was identified in 17% of our non-*FBN1* probands. It should be considered in the evaluation for MFS after *FBN1* screening, especially if there are compatible clinical features.

MUTATIONAL ANALYSIS OF *PTPN11* AND *KRAS* GENES IN TAIWANESE CHILDREN WITH NOONAN SYNDROME

Submitted by Fu-Sung Lo

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