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INTRODUCTION: Noonan syndrome (NS) is an autosomal-dominant disorder that presents with a characteristic face, short stature, skeletal anomalies, and congenital heart defects. Protein-tyrosine phosphatase nonreceptor-type 11 (*PTPN11*), encoding SHP-2, mutation was the first reported gene involved and accounted for 31% to 60% of cases of NS. The *KRAS* gene was the second reported gene and was recently identified in a small number of patients with NS.
OBJECTIVE: Our goal was to perform mutational analysis of *PTPN11* and *KRAS* genes in children with NS.
METHODS: In this study we screened for mutation of the *PTPN11* and *KRAS* genes in 73 Taiwanese patients with NS. The mutation analysis of the 15 coding exons and exon/intron boundaries was performed by polymerase chain reaction and direct sequencing of the *PTPN11* gene. The mutation analysis of 5 coding exons and exon/intron boundaries was performed by polymerase chain reaction and direct sequencing of the *KRAS* gene. We identified 12 different missense *PTPN11* mutations in 15 (21%) patients with NS and 2 different missense *KRAS* (V14I and I36M) mutations in 2 (3%) patients with NS. These *PTPN11* gene mutations were clustered in exon 3 ($n = 6$) encoding the N-SH2 domain and 13 ($n = 5$) encoding the PTP domain.
CONCLUSIONS: This study provides support that *PTPN11* and *KRAS* mutations are responsible for NS in Taiwanese patients.

SCREENING OF MUTATIONS IN THE *NPHS2* GENE IN GREEK PATIENTS WITH AUTOSOMAL-RECESSIVE STEROID-RESISTANT NEPHROTIC SYNDROME

Submitted by Spyridon Megremis

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INTRODUCTION: Mutations in the *NPHS2* gene, encoding podocin, are a major cause of autosomal-recessive steroid-resistant nephrotic syndrome (SRNS) in childhood and have been observed in 6.4% to 30% of sporadic and 20% to 40% of familial cases.
OBJECTIVE: We investigated mutations in the coding region of the *NPHS2* gene in Greek patients with SRNS and identified a novel A295T mutation.
METHODS: The study included 16 child patients with SRNS (14 families); 11 cases were sporadic, and 5 (from 3 families) were familial. All 8 exons of *NPHS2*, including intron boundaries, were screened for sequence variations by using denaturing gradient gel electrophoresis followed by specific characterization using direct DNA sequencing.
RESULTS: The results revealed 2 pathogenic genotypes in 2 patients with sporadic SRNS (R138Q/R138Q and R229Q/A295T). In addition, 3 previously described *NPHS2* intronic polymorphisms (IVS3–46C→T, IVS3–21C→T, and IVS7+7A→G), 1 thus-far-unreported intronic variant (IVS3–17C→T), and 4 known silent mutations (G34G, S96S, A318A, and L346L) were detected in sporadic and familial cases as well as in healthy controls.
CONCLUSIONS: These findings indicate that *NPHS2* mutations are not a frequent cause of familial SRNS in Greek patients. Among patients with sporadic SRNS, the genotypes R138Q/R138Q and R229Q/A295T account for an allelic frequency of 18.2%. The R138Q mutation is well characterized. The novel mutation, A295T (883G→A), is predicted in silico to cause a structural alteration in the cytoplasmic domain of podocin (see the PolyPhen database at http://genetics.bwh.harvard.edu/pph). This is the first report of *NPHS2* mutations in the Greek population and the first description of the A295T amino acid substitution.

CLINICAL STUDIES AND ANALYSIS OF THE RETT SYNDROME GENE (*MECP2*) IN CHILDREN WITH MENTAL RETARDATION IN THE GREEK POPULATION

Submitted by Stavroula Psoni

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INTRODUCTION: Mutations in the methyl CpG-binding protein 2 (*MECP2*) gene are responsible for 70% to 95% of cases of Rett syndrome (RS), an X-linked dominant neurodevelopmental disorder that mostly affects girls. Classical RS is characterized by normal early development followed by psychomotor regression and gradual onset of microcephaly, although variable atypical forms have also been observed. *MECP2* has also been implicated in a variety of other mental retardation (MR) phenotypes, including X-linked MR, fragile X syndrome–like and Angelman syndrome (AS)–like phenotypes.
OBJECTIVE: Our goals were to evaluate the incidence and spectrum of *MECP2* mutations in children with RS

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