hypogammaglobulinemia. Mother and father were first-degree relatives. In his physical examination, height, weight, and head circumference were 17.4 kg (SDS: -0.12), 96.4 cm (SDS: -2.47), and 54.5 cm (SDS: 2.08), respectively. Pubertal stage was A1P1, testes were 2 + 2 mL palpable. He had edema in the eyelids, face was coarse, and umbilical hernia was found. In the lab exam, Hb was 10.4 g/dL, MCV 88.5 fL, RDW 14.7%, electrolytes, liver and kidney function tests were normal, CK and CK-MB were 396 IU/L (41-277) and 55.3 U/L (0-24), respectively. fT_3 was 5.04 pg/mL (2.3-4.2), fT_4 0.93 ng/dL (0.89-1.76), and TSH was 3.89 µIU/mL (0.35-5.5); bone age was 2 years. Craniography revealed thickness of the scalp. Phenotypically hypothyroid findings and at moderate elevation of fT_3 levels, normochrome normocytic anemia and elevation of CK and CK-MB levels were consistent with primary thyroid hormone resistance. In the mutation analysis, a novel *de novo* p.G291S heterozygous mutation in the *THRA* gene was detected. Na-L thyroxin replacement therapy was initiated.

THRA gene mutation should be considered in patients who are clinically hypothyroid with increased/moderately increased fT_3, decreased/normal fT_4, normal TSH levels, and increased muscle enzymes.

(FC-11)

Analysis of THRB Gene in Turkish Patients and Definition of Three Novel Pathogenic Variants

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We aimed to investigate possible new pathogenic variations in Turkish population by determining thyroid hormone receptor-beta *(THRβ)* variations in patients clinically diagnosed as having thyroid hormone resistance.

The results of eighty-two patients [F: 56 (mean age: 30.6), M: 26 (mean age: 31.1) who have been directed to our center between 08.05.2012-28.11.2016 were included in this study. The gene region of interest was amplified by PCR using the deep intronic primers covering exons 7, 8, 9, and 10 of the *THRβ* gene (ENT00000356447.8 transcript) and the nucleotide sequences were determined by the Sanger Sequence method. ProSeq and BioEdit softwares were used to compare patient and reference genomic nucleotide sequences.

Any variation was found in 18.3% of the patients, whereas 29.3% had single nucleotide polymorphisms. 18.3% of patients were determined to have NM_001252634.1:c.735C > T (p.Phe245 =) variation that has been reported as benign SNP (rs3752874) in ClinVar database but reported as modifier variant (CM099823) for thyroid hormone resistance in Human Gene Mutation Database. In 28% of patients, pathogenic variations reported in ClinVar, HGMD, and COSMIC databases were determined. Three novel variations [NM_000461.4: c.701C > A, (p.Ala234Asp), c.737T > A (Leu246Gln), c.1024A > G (p.Lys342Glu)], which were not reported in ClinVar, HGMD, and COSMIC databases before, have been determined in five patients and *in silico* analysis with Mutation Taster, Polyphen tools scored these variants as pathogenic.

This is the first study in Turkish population investigating *THRβ* gene variations in patients clinically diagnosed as having thyroid hormone resistance. In addition, three novel pathogenic variants have been reported in this study.

(FC-12)

Muscular Type Lipodystrophy Diagnosed with Neonatal Findings: Berardinelli-Seip Congenital Lipodystrophy Type 4 and Comparison Between the Types

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Berardinelli-Seip congenital generalized lipodystrophy (BSCL) is characterized by absence of functional adipocytes, thus, lipid is stored in other tissues, including muscle and liver. Classic findings are reduced adipose tissue, muscle hypertrophy, enlarged hands and feet, enlarged external genitalia, hypertriglyceridemia, insulin resistance, hepatomegaly, hypertrophic cardiomyopathy (HCMP), and arrhythmia. Four types have been described. Type 1 (AGPAT2 mutation) and type2 (*BSCL2* mutation) have

similar clinical features, but type 2 can be associated with mild intellectual disability. Type 3 (CAV1 mutation) is very rare, type 4 is the muscular type with pyloric stenosis, flat and striated muscle involvement, and serious arrhythmia. The index case has been followed until the age of 5.5 years, he had a pyloric stenosis operation and elevated CK as different from our three BSCL type 1 patients (5.5, 7.5, and 12-year-old). Interestingly, a Turkish child with BSCL and achalasia was reported with the same PTRF mutation. All of our patients had hypertriglyceridemia, hepatomegaly, and normal neuromotor development. Acanthosis nigricans, HCMP, enlarged hands and feet, and insulin resistance were present in 2 patients with AGPAT2 mutation.

A male infant, who had pyloric stenosis operation, was referred to our department because of developmental hip dysplasia, HCMP, and hepatomegaly. He had reduced adipose tissue, muscular hypertrophy, elevated CK values (1000 IU/L) and normal EMG results. The diagnosis was BSCL.

The identification of homozygous PTRF mutation verified the diagnosis of BSCL type 4.

Because insulin resistance has been described even in the infantile period, BSCL must come to mind in cases with pyloric stenosis and high CK values.

(FC-13)

Progeroid Syndrome Patients with ZMPSTE24 Deficiency Could Benefit When Treated with Rapamycin and Dimethylsulfoxide

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Patients with progeroid syndromes such as mandibuloacral dysplasia, type B (MADB) and restrictive dermopathy (RD) harbor mutations in zinc metalloproteinase (ZMPSTE24), an enzyme essential for posttranslational proteolysis of prelamin A to form mature lamin A. Dermal fibroblasts from these patients show increased nuclear dysmorphology and reduced proliferation; however, the efficacy of various pharmacological agents in reversing these cellular phenotypes remains unknown.

In this study, fibroblasts from MADB patients exhibited marked nuclear abnormalities and reduced proliferation that improved upon treatment with rapamycin and dimethylsulfoxide but not with other agents, including farnesyl transferase inhibitors.

Surprisingly, fibroblasts from an RD patient with a homozygous null mutation in ZMPSTE24, resulting in exclusive accumulation of prelamin A with no lamin A on immunoblotting of cellular lysate, exhibited few nuclear abnormalities and near-normal cellular proliferation. An unbiased proteomic analysis of the cellular lysate from RD fibroblasts revealed a lack of processing of vimentin, a cytoskeletal protein. Interestingly, the assembly of vimentin microfibrils in MADB fibroblasts improved with rapamycin and dimethylsulfoxide.

We conclude that rapamycin and dimethylsulfoxide are beneficial for improving nuclear morphology and cell proliferation of MADB fibroblasts. Data from RD fibroblasts also suggest that prelamin A accumulation by itself might not be detrimental and requires additional alterations at the cellular level to manifest the phenotype.