Genetic Analysis of Lipodystrophies and Novel Mutations

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Lipodystrophies are a group of disorders characterized by selective loss of body fat and predisposition to insulin resistance. Lipodystrophies are caused by genetic defects or acquired conditions. Severity of the associated metabolic complications is determined by the extend of fat loss. Congenital generalized lipodystrophy (CGL) and familial partial lipodystrophy (FPL) are two subgroups of genetic lipodystrophies. Mutations in the *AGPAT2, BSCL2, CAV1, PTRF* genes cause autosomal recessive CGL and mutations in the *LMNA, PPARG, AKT2, PLIN1* genes cause autosomal dominant FPL. Twenty-three patients from 10 CGL and 4 FPL families were investigated by sequencing for causal mutations in the *AGPAT2, BSCL2, CAV1, PTRF, LMNA, PPARG, AKT2,* and *PLIN1* genes according to clinical findings and family information at Ege University Faculty of Medicine, Department of Medical Genetics. In CGL families, mutations were detected in the *AGPAT2* (6 families), *BSCL2* (3 families), and *PTRF* (1 family) genes. Three novel mutations were detected in the CGL group. Three families had mutations in *LMNA* gene and only one family had mutation in the *PPARG* gene in the FPL group. Three of these mutations were novel. As a result, identifying the genetic background of lipodystrophies will help to prevent metabolic complications and to detect the individuals in advance who have the risk of developing lipodystrophy.

Key words: Lipodystrophies, genetics, mutations

RET Mutation Spectrum in Turkish Cases with Medullary Thyroid Carcinoma: Definition of a Novel K710R Mutation

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Medullary thyroid carcinoma (MTC) is a rare malignant tumor originating from parafollicular cells. In most cases, it occurs sporadically, but a hereditary form is also possible. Hereditary forms show autosomal dominant inheritance pattern. MTC can be either isolated or as a part of MEN2 syndromes. *RET* proto-oncogene mutations are responsible for both MTC and MEN2. The RET proto-oncogene comprises 21 exons and is located at 10q11.2. Mutations of RET may also lead to papillary thyroid carcinoma, lung cancer, chronic myelomonocytic leukemia, and familial Hirschsprung's disease. In this study, we investigated *RET* mutation spectrum in patients who were referred to our laboratory for *RET* molecular analysis. Between the period of 2009-2014, 155 patients with MTC were referred to our molecular genetics laboratory for *RET* mutation analysis. Exons 10, 11, 13, 14, 15, 16 of the RET proto-oncogene were sequenced using Sanger sequencing method. 12 different *RET* mutations were detected in 32 cases (20.6%). The mutations detected and their frequencies were as follows: 28% C634Y (9 cases), 25% C634R (8 cases), 6% D631Y, S891A, M918T, C618S, V804M (2 cases), and 3% C618G, L790F, C611Y, K710R, S649L (1 case). As a conclusion, the majority of patients with hereditary MTC showed *RET* mutations located at exon 11. The most frequent two mutations in Turkish MTC patients were found in codon 634 which was consistent with the literature. The K710R mutation in *RET* gene was defined for the first time in this study.

Key words: Medullary thyroid carcinoma, *RET* gene, DNA sequencing, hereditary disease, mutation