CDH5, a Possible New Candidate Gene for Genetic Testing of Lymphedema

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Abstract

Background: Expressed by endothelial cells, CDH5 is a cadherin involved in vascular morphogenesis and in the maintenance of vascular integrity and lymphatic function. The main purpose of our study was to identify distinct variants of the CDH5 gene that could be associated with lymphatic malformations and predisposition for lymphedema. Methods and Results: We performed Next Generation Sequencing of the CDH5 gene in 235 Italian patients diagnosed with lymphedema but who tested negative for variants in known lymphedema genes. We detected six different variants in CDH5 five missense and one nonsense. We also tested available family members of the probands. For family members who carried the same variant as the proband, we performed lymphoscintigraphy to detect any lymphatic system abnormalities. Variants were modeled in silico. The results showed that CDH5 variants may contribute to the onset of lymphedema, although further in vitro studies are needed to confirm this hypothesis. Conclusions: Based on our findings, we propose CDH5 as a new gene that could be screened in patients with lymphedema to gather additional evidence.

Keywords: CDH5; NGS; genetic diagnostics; lymphedema.