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ROLE OF CELL ADHESION MOLECULES NECTINS 1 AND 4 IN THE PATHOGENESIS OF ECTODERMAL DYSPLASIA SYNDROMES

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Ectodermal dysplasias (EDs) are heterogeneous conditions with more than 200 described forms. The presence of hair and teeth anomalies, alopecia, and cutaneous syndactyly defines the ectodermal dysplasia-syndactyly syndrome (EDSS; OMIM 613573). We have recently identified PVRL4 mutations as the cause of EDSS in two families from Algeria and Italy. PVRL4 encodes nectin-4, a cell adhesion molecule with a relevant role in cadherin-based adherens junctions and belongs to a family of four members. Notably, PVRL1 (encoding nectin-1) mutations cause Cleft Lip/Palate-Ectodermal Dysplasia Syndrome (CLPED1; OMIM#225060) also known as Zlotogora-Ogur syndrome, hence the term “nectinopathies”. A homozygous pathogenic mutation was detected in the Algerian family. In addition we identified a missense and a truncating mutation in the Italian family, confirming PVRL4 as the disease causative gene of EDSS. Interestingly, in most adult human tissues, nectin-4 expression is almost absent. In turn, high levels of protein are present in the hair follicle and in the interdigital regions of mouse embryos, the mainly affected tissues in EDSS. These data outline a relevant role of nectin-4 in hair cycling and morphogenesis and support the existence of a growing group of EDs secondary to defective cell adhesion. We are currently studying the mechanism by which nectins 1 and 4 cooperates towards the regulation and the maintenance of tissue morphogenesis.