variant (p.[Leu91Leu] (p16)/p.[Gly106Arg] (p14ARF)) that has not been previously described in Caucasoid control population was identified. The implication of this variant in melanoma susceptibility is unknown. At least one MCR1 associated risk polymorphism (V60L, R151C, R160W, D294E, V92M, I155T, R163Q, c.86dupA) was identified in 43 patients (74%) with more than one polymorphism in 18 patients (31%). Among CDKN2 A mutation carriers, all of them have one or more MCR1 associated polymorphism.
Discussion: Genetic susceptibility to melanoma is complex. Isolated populations may be carriers of new variants with unknown effect in risk. To better understanding the risk in a given population to be able to offer genetic counselling, it is crucial to perform studies to better understand the diversity of the disease.

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Characterization of the binding of plectin and BPAG1e to intermediate filaments gives insights into genetic diseases affecting these proteins

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Plectin and BPAG1 are members of the plakin protein family, composed of cytolinkers connecting elements of the cytoskeletal system to each other and to various membrane sites, conferring to cells critical resilience to mechanical stress in various tissues, such as the epidermis. Mutations in genes coding for plectin, BPAG1, the basal epidermal intermediate filament (IF) proteins keratin 5 (K5), keratin 14 (K14) and the muscle-specific desmin, cause phenotypically related diseases, such as epidermolysis bullosa simplex and muscular dystrophies. To gain further insight into the mechanism of these diseases, we have dissected the interaction of plectin and the epithelial isoform of BPAG1 (BPAG1e) with K5 and K14 and other IF proteins by yeast-three hybrid, cell transfection, chemical crosslinking and in vitro binding assays using recombinant proteins encompassing various subdomains of these proteins. The results showed that: 1) plectin interacts much better with K14 than K5 whereas BPAG1e is unable to interact with monomeric keratins; 2) the quaternary structure induced by hetero-polymerization of K5/K14 favors the association with plectin and BPAG1e; 3) the coil 1 domain of K5/14 contains sequences critical for their binding to both plakins; 4) deletion of the COOH extremity of plectin reduces its binding capacity to polymeric K5/K14; and 5) the COOH-terminal portion of plectin contains more than one binding module for K5/K14. Our data unravel the complexity of the binding of plectin and BPAG1e to K5/K14 and provide insights into the molecular basis of plakin- and IF-related human diseases, associated with pathogenic mutations affecting functionally relevant sites within these molecules.