

ADNP Related Syndrome

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Mutations in ADNP have been recently associated with intellectual disability and autism spectrum disorder. However, the clinical features of patients with this syndrome are not fully identified, and no treatment currently exists for these patients. Here, we extended the ADNP syndrome phenotype describing skin abnormalities in both a patient with ADNP syndrome and an *Adnp* haploinsufficient mice. The patient displayed thin dermis, hyperkeratotic lesions in periarticular areas and delayed wound healing. Patient-derived skin keratinocytes showed reduced proliferation and increased differentiation. Additionally, detection of cell cycle markers indicated that mutant cells exhibited impaired cell cycle progression. Treatment of ADNP-deficient keratinocytes with the ADNP-derived NAP peptide significantly reduced the expression of differentiation markers. Sonography and immunofluorescence staining of epidermal layers revealed that the dermis was thinner in the patient than in a healthy control. *Adnp* haploinsufficient mice (*Adnp* +/-

) mimicked the human condition showing reduced dermal thickness. Intranasal administration of NAP significantly increased dermal thickness and normalized the levels of cell cycle and differentiation markers. Our observations provide a novel activity of the autism-linked ADNP in the skin that may serve to define the clinical phenotype of patients with ADNP syndrome and provide an attractive therapeutic option for skin alterations in these patients.