Abstract

Warburg Micro syndrome (WARBM1) is a severe autosomal recessive disorder characterized by developmental abnormalities of the eye and central nervous system and by microgenitalia. We identified homozygous inactivating mutations in RAB3GAP, encoding RAB3 GTPase activating protein, a key regulator of the Rab3 pathway implicated in exocytic release of neurotransmitters and hormones, in 12 families with Micro syndrome. We hypothesize that the underlying pathogenesis of Micro syndrome is a failure of exocytic release of ocular and neurodevelopmental trophic factors