MYH11

Myosin-11 is a protein that in humans is encoded by the MYH11 gene.

Myosin-11 is a smooth muscle myosin belonging to the myosin heavy chain family. Myosin-11 is a subunit of a hexameric protein that consists of two heavy chain subunits and two pairs of non-identical light chain subunits.

It is a major contractile protein, converting chemical energy into mechanical energy through the hydrolysis of ATP.

Alternative splicing generates isoforms that are differentially expressed, with ratios changing during muscle cell maturation.

Clinical significance

Thoracic aortic aneurysms leading to acute aortic dissections (TAAD) can be inherited in isolation or in association with genetic syndromes, such as Marfan syndrome and Loeys-Dietz syndrome. When TAAD occurs in the absence of syndromic features, it is inherited in an autosomal dominant manner with decreased penetrance and variable expression, the disease is referred to as familial TAAD. Familial TAAD exhibits significant clinical and genetic heterogeneity. Mutations in MYH11 have been described in individuals with TAAD with patent ductus arteriosus (PDA). Of individuals with TAAD, approximately 4% have mutations in TGFBR2, and approximately 1-2% have mutations in either TGFBR1 or MYH11. In addition, FBN1 mutations have also been reported in individuals with TAAD. Mutations within the SMAD3 gene have recently been reported in patients with a syndromic form of aortic aneurysms and dissections with early onset osteoarthritis. SMAD3 mutations are thought to account for approximately 2% of familial TAAD. Additionally, mutations in the ACTA2 gene are thought to account for approximately 10-14% of familial TAAD.

Acute myeloid leukemia

The gene encoding a human ortholog of rat NUDE1 is transcribed from the reverse strand of this gene, and its 3' end overlaps with that of the latter. The pericentric inversion of chromosome 16 [inv(16)(p13q22)] produces a chimeric transcript that encodes a protein consisting of the first 165 residues from the N-terminus of core-binding factor beta in a fusion with the C-terminal portion of the smooth muscle myosin heavy chain. This chromosomal rearrangement is associated with acute myeloid leukemia of the M4Eo subtype.

Intestinal cancer

MYH11 mutations appear to contribute to human intestinal cancer

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Ravindra et al., report the case of a previously healthy 6-month-old girl who presented with right arm and leg stiffening consistent with seizure activity. An initial CT scan of the head demonstrated acute

subarachnoid hemorrhage in the basal cisterns extending into the left sylvian fissure. Computed tomography angiography demonstrated a 7 × 6 × 5-mm saccular aneurysm of the inferior M2 division of the left middle cerebral artery. The patient underwent left craniotomy and microsurgical clip ligation with wrapping of the aneurysm neck because the vessel appeared circumferentially dysplastic in the region of the aneurysm. Postoperative angiography demonstrated a small remnant, sluggish distal flow, but no significant cerebral vasospasm. Fifty-five days after the initial aneurysm rupture, the patient presented again with an acute intraparenchymal hemorrhage of the left anterior temporal lobe. Angiogram revealed a circumferentially dysplastic superior division of the M2 branch, with a new 5 × 4-mm saccular aneurysm distinct from the first, with 2 smaller aneurysms distal to the new ruptured aneurysm. Endovascular parent vessel occlusion with Onyx was performed. Genetic testing revealed a mutation of the MYH11. To the authors' knowledge, this is the first report of rapid de novo aneurysm formation in an infant with an MYH11 mutation. The authors review the patient's clinical presentation and management and comprehensively review the literature on this topic [1].

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Ravindra VM, Karsy M, Schmidt RH, Taussky P, Park MS, Bollo RJ. Rapid de novo aneurysm formation after clipping of a ruptured middle cerebral artery aneurysm in an infant with an MYH11 mutation. J Neurosurg Pediatr. 2016 Oct;18(4):463-470. PubMed PMID: 27367753.