The Tails of the Transgelin Family

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The transgelin family is a group of 22 kDa actin-associated proteins that belong to the calponin superfamily and have one 26 a.a. calponin-like repeat at their C-terminus. Transgelin and transgelin homologs have been identified across the eukaryotic genomes from yeasts to humans. Three isoforms, designated transgelin 1, 2, and 3, have been identified in humans, rats, and mice, and share high-grade sequence identity with one another. In mice, these isoforms are encoded by three separate genes, *Tagln 1, 2, and 3*, located on chromosomes 9, 1, and 16, respectively. Of all three isoforms, transgelin 1 is the best characterized. Transgelin 1, also known as SM22alpha, is a specific marker for differentiated smooth muscle cells. Arterial specificity of SM22alpha expression is critically dependent on the integrity of the two binding sites for serum response factor (SRF) and the presence of a cofactor called myocardin. SM22alpha-deficient mice appeared phenotypically normal except for a subtle ultrastructural defect in the actin filament organization and decreased contractility in vascular smooth muscles. Several extracellular factors and mechanical stimuli also modulate SM22alpha expression through RhoA-mediated actin polymerization, JNK and p38 MAPK pathways, and Smads proteins. Furthermore, down-regulation of SM22alpha expression has been implicated Énin the oncogenic transformation and atherogenesis. Transgelin 2, also known as SM22beta, is expressed in both smooth muscle and non-smooth muscle cells in a temporally and spatially-regulated pattern that is distinct from that of SM22alpha. In vascular smooth muscle cells, SM22beta co-localizes with SM22alpha to stress fibers. Because these two cytoskeletal proteins are structurally similar but have different tissue distribution, we postulate that SM22beta plays an essential role in organ formation during embryonic development by maintaining the cell shape and basal function in both muscle and non-muscle cells. Transgelin 3, also known as NP25, is only found in highly differentiated neuronal cells, with strong signals in the hippocampus, frontal cortex, cerebellum and midbrain. The human homolog called hNP22 is upregulated in alcoholic brains. Its biological function is unknown. These three transgelin isoforms share high-grade sequence homology with a *Drosophila* muscle-specific protein, mp20, and the *C.elegans* body wall protein, unc-87. Mutation of *unc*-87 and *mp*20 results in paralysis of the C. elegans body wall and Drosophila flight muscle, respectively. It would be interesting to speculate that the transgelin family has evolved from a common ancestral gene encoding a protein resembling mp20 through duplication and divergence to serve specialized functions in specific cell lineages such as smooth muscle cells, neurons, and skeletal myocytes.