Formin-like 1 (FMNL1) is regulated by N-terminal myristoylation and induces polarized membrane blebbing.

Abstract:
The formin protein formin-like 1 (FMNL1) is highly restrictedly expressed in hematopoietic lineage-derived cells and has been previously identified as a tumor-associated antigen. However, function and regulation of FMNL1 are not well defined. We have identified a novel splice variant (FMNL1gamma) containing an intron retention at the C terminus affecting the diaphanous autoinhibitory domain (DAD). FMNL1gamma is specifically located at the cell membrane and cortex in diverse cell lines. Similar localization of FMNL1 was observed for a mutant lacking the DAD domain (FMNL1DeltaDAD), indicating that deregulation of autoinhibition is effective in FMNL1gamma. Expression of both FMNL1gamma and FMNL1DeltaDAD induces polarized nonapoptotic blebbing that is dependent on N-terminal myristoylation of FMNL1 but independent of Src and ROCK activity. Thus, our results describe N-myristoylation as a regulative mechanism of FMNL1 responsible for membrane trafficking potentially involved in a diversity of polarized processes of hematopoietic lineage-derived cells.