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Vangl2 regulates membrane-protrusive activity in migrating gastrula cells

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Our lab works to determine the mechanism whereby the planar cell polarity (PCP) protein Vang-Like 2 (*Vangl2*) regulates cell migration during embryogenesis. We focus on the gastrula stage of zebrafish development as the cells naturally undergo PCP-dependent migration. Loss of *Vangl2* in trilobite mutant embryos results in a strong convergence and extension phenotype characterized by shortened and broadened body axes. Here, both ectodermal and mesodermal cell populations fail to polarize. Previous data established migrating *vangl2* mutant cells lack directionality and meander compared to wild type. We have also shown *vangl2* mutants have increased matrix metalloproteinase activity and decreased fibronectin extracellular matrix (ECM). We hypothesize defective cell-ECM interactions underlie the *vangl2* mutant phenotype. Using time-lapse confocal imaging, we have now analyzed the membrane protrusive activity of ectodermal cells from wild-type and PCP mutant embryos. Our current data suggest *vangl2* mutant ectodermal cells exhibit increased membrane protrusive activity and have significantly fewer polarized protrusions. Our data suggest filopodia are concentrated at the trailing edge in wild-type cells, while *vangl2* mutant cells have more filopodia at the leading edge. We also found that *vangl2* mutant ectodermal cells have reduced directness compared to wild type. To determine the requirement for fibronectin during protrusion formation, we used morpholinos to knockdown fibronectin protein expression in wild-type embryos. The data showed that fibronectin morpholino injected cells exhibited increased formation of non-polarized membrane protrusions similar to *vangl2* mutant cells, suggesting defective cell-ECM interactions contributing to at least a portion of the mutant phenotype. Our preliminary studies suggest decreased *Vangl2* protein localization to filopodia and larger membrane protrusions. Together, our data suggest a model whereby *Vangl2*-dependent regulation of cell-ECM interactions is required to suppress inappropriate proper membrane protrusive activity.

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