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Coordinating epithelial cell proliferation and migration in corneal wound healing

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Corneal epithelial stem cells at the limbus in response to wound are triggered to migrate and suppress proliferation at leading edge. Increased proliferation of basal epithelial cells containing stem cells and concomitant stratification occurs leading to migration of epithelial cell sheet. The extracellular and intracellular signaling pathways that regulate these processes in corneal epithelium by modulating the cell-cell matrix and cell-cell adhesion are less understood. In order to understand the maintenance and functioning of stable cell-cell junctions in corneal epithelium, we studied the protein CDK5 at cell-cell and cell-matrix adhesions during migration. Immuno fluorescence showed co-localization of CDK5, p35, and CDK5(pY15, active form of CDK5) with E-cadherin at cell-cell boundaries indicating that they form an intracellular complex. Inhibiting CDK5 activity with olomoucine (pharmacological inhibitor of CDK5) increased the degradation of surface-biotinylated E-cadherin, generating a degradation product of 29KDa. In contrast, p120 catenin levels were increased two-fold. Similar changes in E-cadherin and p120 expression were seen in cells treated with the CDK5 inhibitor, olomoucine. Reduced E-cadherin immunofluorescence intensity in ShCDK5 was similar to olomoucine treated cells. TIRF analysis of pEGFP-E cadherin in live transfected cells revealed trafficking of cadherin was reduced as opposed to p120. Suppression of CDK5 expression with Sh RNA confirmed previous results obtained with olomoucine and indicating a role for CDK5 in stabilizing cell-cell junctions. CDK5 Kinase is therefore required preventing the dissociation, degradation and cadherin-catenins with, indicating that CDK5 was required for maintaining stable epithelial cell-cell adhesions, homeostasis and tissue repair.

Biography

Arpitha Parthasarathy completed her Ph.D. from Aravind Eye Hospitals, India and Postdoc from National Institutes of Health, Maryland. She had her short postdoctoral stints at GWU and University of Kentucky in corneal wound healing and angiogenesis of retina and cornea. She has published in many peer reviewed ophthalmic journals and is now the "Director of Translational and Molecular Biology Research" at Jerome Canady Research Institute for advanced Biological and Technical Sciences, US Medical Innovations, Takoma Park, Maryland.

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