Anti-angiogenic activity of kidney derived endothelial cells

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Abstract:

The identification of novel endogenous mediators of angiogenic/vasculogenic processes may provide for novel therapeutic targets to modulate blood vessel growth in disease states, such as cardiovascular disease or cancer. Studies in our lab have shown that blood vessels in kidney have little endogenous regenerative capacity. Kidney derived microvascular endothelial cells (KEC) were isolated from rat kidney or from transgenic mice bearing the temperature sensitive SV40 mutant (and subsequently grown at non-permissive temperature, 37^{o}C). Both rat and mouse KECs manifested significantly reduced growth rates when compared with several commonly used EC lines (rat pulmonary EC, HUVEC and human cord blood colony forming ECs). In 2D matrigel assays, all commonly used ECs faithfully formed characteristic branching structures; while all KECs failed to form stabile branching structures. Time-course analysis of branching activity demonstrated that KEC initially formed primitive branching nodes within 3 hours of culture, but these structures regressed such that no branched structures were observed between 6-12 hours. Co-culture of KECs with any branching competent EC impaired branching dose dependently. When co-cultured with ECFC, labeled KECs incorporated into primitive ECFC branches within the first 3 hours of plating. However, when compared with ECFC branches, ECFC-KEC mixed branches showed a more rapid regression of the branched structures between 12-24 hrs. Interestingly, conditioned media from KEC did not affect branching of competent ECFC. Taken together, these data indicate that KEC have anti-angiogenic activity that may destabilize ECs during angiogenesis. The anti-angiogenic activity requires cell-cell contact, suggesting the possible presence of an angio-inhibitory molecule on the cell surface of KECs. Current and future studies seek to generate additional KEC lines, and will determine if KEC cell fractions mediate the anti-angiogenic effect. In addition, we will seek to determine if KECs mitigate progression of angiogenic dependent tumor formation in vivo.