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Anti-angiogenic activity of the mutant Dutch A[•] peptide on human brain microvascular endothelial cells.

Daniel Paris, Ghania Ait-Ghezala, Venkatarajan S. Mathura, Nikunj Patel, Amita Quadros, Vincent Laporte, Mike Mullan. *Brain Res Mol Brain Res.* 2005 May 20;136(1-2):212-30.

<http://www.ncbi.nlm.nih.gov/pubmed/15893605?dopt=Abstract>

Cerebral amyloid angiopathy, the deposition of A^{\bullet} -amyloid (A^{\bullet}) in the cerebrovasculature, characterizes a rare disorder called hereditary cerebral hemorrhage with amyloidosis-Dutch type (HCHWA-D). A single point mutation of the A^{\bullet} -amyloid precursor protein leads to HCHWA-D, resulting in recurrent hemorrhagic stroke at middle age, vascular dementia, and fatal cerebral bleeding.

Wild-type A^{\bullet} has been shown to be anti-angiogenic, and both structural and functional cerebrovascular abnormalities are associated with Alzheimer's disease. This study found Dutch A^{\bullet} to be an even more potent inhibitor of angiogenesis. To better understand the molecular mechanisms that cause the anti-angiogenic activity of Dutch A^{\bullet} , researchers profiled genes that were differentially expressed in human brain microvascular endothelial cells exposed to an anti-angiogenic dose of Dutch A^{\bullet} . The genes affected by Dutch A^{\bullet} were uploaded to IPA and network analysis revealed that exposure to Dutch A^{\bullet} dysregulates networks involved in cellular migration, cellular proliferation, angiogenesis, atherosclerosis, and tumorigenesis.