Molecular changes in penumbra after focal photothrombotic stroke in the rat cerebral cortex

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In ischemic stroke cell damage propagates from infarct core to surrounding tissue. To reveal proteins involved in neurodegeneration and neuroprotection in penumbra, we studied biochemical consequences of focal photothrombotic infarct (PTI) in the rat cerebral cortex. Photosensitizer Bengal Rose does not cross blood brain barrier and remains in vasculature. Following laser irradiation induces focal vessel occlusion and brain cortex infarct. Using proteomic microarrays "Panorama Ab Microarray, Cell Signaling" and "Panorama Ab Microarray, Neurobiology" (Sigma-Aldrich), we studied expression of 448 proteins in penumbra at 1, 4 or 24 hours after PTI as compared with untreated contralateral cortex. Diverse cellular subsystems were involved in penumbra response to PTI: (1) Proteins initiating, regulating or executing various apoptosis stages (caspases 3, 6, 7, SMAC/DIABLO, Bcl-10, Par4, E2F1, p75, p38, JNK, p53, NMDAR2a, c-myc); (2) Anti-apoptotic proteins (Bcl-x, p63, MDM2, p21WAF-1, ERK1/2, ERK5, PKCα, PKCβ, PKCμ, RAF1, phosphatases 1α and MKP-1, calmodulin, CaMKIIα, CaMKIV, estrogen and EGF receptors), (3) Signaling proteins (protein kinases Bα, GSK-3, PKC, DYRK1A, TDP43, phospholipase Cγ1, S-100, axin1, GSK-3, FRAT1, NUMB); (4) Proliferation regulators (Cdk6, Cdc7 kinase, Trf1, topoisomerase-1); (5) Axon outgrowth and guidance (NAV-3, CRMP2, PKCβ2); (6) Intercellular interactions (N-cadherin, PMP22); (7) Regulation of actin (cofilin, actopaxin, p120CTN, α-catenin, p35, neurofilament 68, neurofilament-M, ezrin, tropomyosin, spectrin (α+β), myosin Va and pFAK) and microtubule cytoskeleton (βIV-tubulin, polyglutamated β-tubulin, doublecortin, Tau, MAP1); (8) Vesicular transport and synaptic transmission (syntaxin-8, TMP21, Munc-18-3, synip, ALS2, VILIP1, syntaxin, synaptophysin, synaptotagmin, syntaxin, AP2β/γ, adaptin β1/2); (9) Biosynthesis of neuromediators (tryptophan hydroxylase, monoamine oxidase B, glutamate decarboxylase, tyrosine hydroxylase, DOPA decarboxylase, dopamine transporter); (10) ubiquitin-mediated proteolysis (ubiquilin-1, UCHL1, NEDD8); (11) Mitochondria quality control (Pink1, parkin, HtrA2); (12) Cytoprotection (AOP-1, MAKAPK2, chaperons Hsp70, Hsp90); (13) APP-related proteins (APP, β-amyloid, nicastrin). These data provide the integral view on cellular response in penumbra to PTI. They are involved either in neurodegeneration, or neuroprotection. These changes were highest at 4 h after PTI and reduced at the next day. Some of these proteins may serve as potential targets for ischemic stroke therapy.

Speaker Biography

Anatoly B. Uzdensky is a Professor in Biophysics and the Head of the Laboratory of Molecular Neurobiology at the Southern Federal University (Rostov-on-Don, Russia). He is the author of more than 120 journal papers and three books. His current research interests include stroke and neurotrauma, neurodegeneration and neuroprotection, cell biology, and proteomics.

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