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## Biochemical processes in penumbra after photothrombotic stroke in the rat cerebral cortex

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In focal ischemic stroke, vessel occlusion rapidly induces local infarct of the brain tissue. During next hours, injurious factors (glutamate, $Ca^{2+}$ and others) propagate to surrounding tissue and form the transition zone, penumbra, where both, neurodegeneration and neuroprotection processes are developed. Cell protection in penumbra is the aim of neurologists, but effective neuroprotectors are not found yet. So, deeper studies of biochemical processes in penumbra are needed. Neuronal and signaling antibody microarrays (Panorama, Sigma-Aldrich) were used to study changes in expression of >400 signaling and neuronal proteins in penumbra surrounding photothrombotic infarct core in rat cerebral cortex 1, 4 or 24h after impact comparing with untreated contralateral cortex. The greatest changes were observed at 4h after photothrombosis. They included simultaneous upregulation of proteins involved in diverse subcellular systems: proapoptotic (caspases 3, 6 and 7, Bcl-10, AIF, SMAC/DIABLO, p53, E2F1, p38, JNK, NMDAR2a, c-myc, Par4, p75, GADD153, GAD65/67, PSR) and anti-apoptotic (Bcl-x, p63, p21WAF-1, MDM2, ERK5, MKP-1, NEDD8, estrogen receptor) proteins. Various signaling proteins (calmodulin, CaMKIIα, CaMKIV, ERK1/2, MAKAPK2, PKCα, PKCβ, PKCμ, RAF1, protein phosphatase 1α, ATF2, EGF receptor, DYRK1A) were upregulated, whereas others (phospholipase Cγ1, S-100, GSK-3, Axin1, NUMB, TDP-43, FRAT1) - downregulated. Proteins involved in mitochondria quality control (Pink1, parkin), proteolysis (ubiquilin-1, UCHL1), intercellular interactions (N-cadherin, PMP22), neurite integrity and guidance (Nav3, CRPM2, PKCβ2) were overexpressed. Proteins associated with actin cytoskeleton (cofilin, actopaxin, p120CTN, α-catenin, p35, myosin Va and pFAK) were upregulated, whereas other cytoskeleton components (ezrin, tropomyosin, spectrin (α+β), βIV-tubulin, polyglutamated β-tubulin, doublecortin, neurofilaments 68 and M, cytokeratins 7 and 19) - downregulated. Downregulation of syntaxin, synaptophysin, synaptotagmin, VILIP, ALS2, and adaptin β1/2 indicated impairment of vesicular transport and synaptic processes. Enzymes that mediate dopamine biosynthesis (tyrosine hydroxylase, DOPA decarboxylase, dopamine transporter) were downregulated, whereas proteins involved in biosynthesis of serotonin and GABA (tryptophan hydroxylase, MAO-B, glutamate decarboxylase) - upregulated. Down-regulation of CDK6, CDC7 kinase, TRF1, and topoisomerase-1 suppressed proliferation. Levels of mitochondrial antioxidant protein AOP-1, chaperons Hsp70 and Hsp90 were reduced. Amyloid precursor protein, nicastrin and β-amyloid were upregulated. These data provide the integral view on neurodegeneration or neuroprotection processes in penumbra after photothrombotic infarct. Some of these proteins can be considered as potential targets for anti-stroke therapy. Supported by Russian Science Foundation (14-15-00068) and Russian Ministry of Education and Science (6.4951.2017/6.7).

### Biography

Anatoly Uzdensky has completed his PhD in 1980 from Rostov State University (Russia). He is the Principal Investigator and Head of the Laboratory of Molecular Neurobiology in the Sothern Federal University (Rostov-on-Don, Russia). He has published more than 120 papers in reputed journals.

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