Ser^{396} and Ser^{404}) which are commonly used in the molecular diagnosis of AD. We demonstrate here, that Tau protein is hyperphosphorylated at sites Ser^{199}, Ser^{202}, Ser^{262}, Ser^{396} and Ser^{404} in the cortex of 6 month old hypertriglyceridemic transgenic mice. Neuronal apoptosis was monitored in transgenic brains using FluoroJade staining. Significantly increased degenerated neurons were counted in the cortical and hippocampal regions of adult transgenic versus wild-type mice. Furthermore, using electrophysiological recordings (long-term potentiation and paired pulse facilitation) we demonstrated severe impairment in presynaptic function of transgenic brains.

These results indicate that chronic hypertriglyceridemia can induce neurodegeneration possibly via hyperphosphorylation of tau protein. Beyond of theoretical observations we aim to develop a novel mouse model of age-related neurodegeneration, providing a useful tool for the development of efficient therapies against neurodegenerative diseases.

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Examination of real-time effects of different cytotoxic and cytoprotective compounds with a novel cell-microelectronic sensing technique

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Real-Time Cell Analyzer (RTCA) DP is a novel cell migration and invasion assay system that uses the Boyden Chamber principle but does not involve any fixation, labeling or counting of the cells. The core of the system is the CIM-Plate device, composed of an upper chamber and a lower chamber. The upper chamber has 16 wells that are sealed at the bottom with a micro-pore-containing polycarbonate or polyester membrane. The membrane contains microelectronic sensor arrays that are integrated on its bottom surface. Migration of cells will occur through these electrodes, which changes impedance, and will increase cell index. The more cells migrate the higher the cell index will be. RTCA SP is also a microelectronic cell sensor method, where microlectrodes are integrated in the bottom of a microtiter plate (96-well E-plate) and measures adhesion, proliferation or cytoxicity. The real-time measurement can detect changes continuously, which means that the system can give information at any stages of the experiment.

We examined the effects of cytotoxic compounds on the migration and proliferation properties of human glioblastoma, liver carcinoma and melanoma cells with a novel cell microelectronic sensing technique. We tested the migration potential of several tumor cell lines in a trans-well migration system. In addition we examined the effects of neuro/cytoprotective compounds on the viability of primary rat neuronal cultures with RTCA-SP system. During the cytotoxicity and cytoprotection screenings *in vitro* cytotoxicity or cytoprotectivity was elicited by numerous compounds synthesized by Avidin Ltd.

In our experiment we examined the migration properties of different tumor cells. GBM3 human glioblastoma cells migrated the fastest. A549 human adenocarcinomic lung cancer cells also showed a relatively high cell index increase, probably due to its small size, enabling it to pass easily through the membrane. Ac929 treatment decreased migration ability of Hep3B hepatoma cells dose-dependently. The highest concentration used (1 μM) resulted the lowest cell index. U87-MG human glioblastoma-astrocytoma cells were treated with Ac1041and Ac915 compounds. The treatment caused dose-dependent decrease of cell index, where 500 nM and 1 μM concentrations were ineffective. 5 μM showed a slight change in migration, and higher doses (20-50 μM) were cytotoxic. Cell index data were calculated 24 hours after treatment. The experiments clearly shows the dose-dependent effect of Ac-compounds. Effects of Ac1041, Ac929 and Ac915 were validated by the RTCA SP system.

During the cytoprotective screenings in vitro cytotoxicity was elicited by hydrogen peroxide in primary rat neuronal cultures. Cells were either pre-treated 5 min before oxidative stress or post-treated at 30 min with novel cytoprotective compounds. Cell Index of Q2 treated cells started to rise as high as absolute control and remained elevated for hours, showing a long-term cytoprotective effect. Vehicle-control cells (which received H_2O_2 and vehicle, but no treatment with cytoprotective compounds), showed a rapid decline of cell index. Pre-treatment with compound 9791 or post-treatment of the cells with the fatty acid derivative 9528 prevented the cells from the toxic effects of oxidative stress dose-dependently.

The cell-microelectronic sensing technique (RT-CES) method is suitable for the screening of molecular libraries to identify molecules or molecule combinations that attenuate oxidative stress-induced cell damage and can also be useful for screening of agents with antitumor properties.

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