REF: HCS-05

HIGH CONTENT NEUROTOXICITY ASSAY

CELL BASED ASSAYS

Service:	High Content Neurotoxicity Assay
Available Host Cells:	Human / Rat / Mouse Neurons
	Human Progenitor Neural Cells
	Rat Dorsal Root Ganglion Neurons
Stimulation:	Compounds to be tested

Background

Neurotoxicity is the capacity of certain compounds to affect the normal activity of the neurons. There are many types of neurotoxins such as heavy metals, pesticides, food additives, solvents or cosmetics, but drugs are a huge source of neurotoxins. Mainly anticancer drugs like cisplatin or paclitaxel that are very efficient like anticancers but produce neuronal damage. The mechanism involved in the neuron citotoxicity can be several: oxidative stress, DNA damage, cytoskeleton dysfunction or apoptosis.

Outcome Parameters

- Oxidative stress
- Genotoxicity-DNA damage
- Neurite outgrowth
- Apoptosis

Compound testing

In this assay we measure described parameters previously which frequently appear in the neurotoxicity induced by drugs. The oxidative stress is measured using the CM probe and the other three parameters are measured by inmunocytochemistry. The Tuj protein is used to mark the neurites and measure the neurite outgrowth. There are compounds that affect the cytoskeleton and disestablish the microtubules affecting the cellular architecture and functionality. An antibody against phosporilated H2AX protein is used to measure the DNA damage. The H2AX is a member of the histone H2A family which phosphorilate when the double strand of DNA is broken. The presence of phosphorilated H2AX is correlated with DNA damage and subsequently with genotoxic agents presence. Finally the measurement of active caspase 3 shows the capacity of the compound to activate the apoptotic pathway and produce the neuronal death. These four parameters are measured and compared with negative controls and when the difference respect to controls of one of the parameters is statistically significant, the drug is considered neurotoxic.

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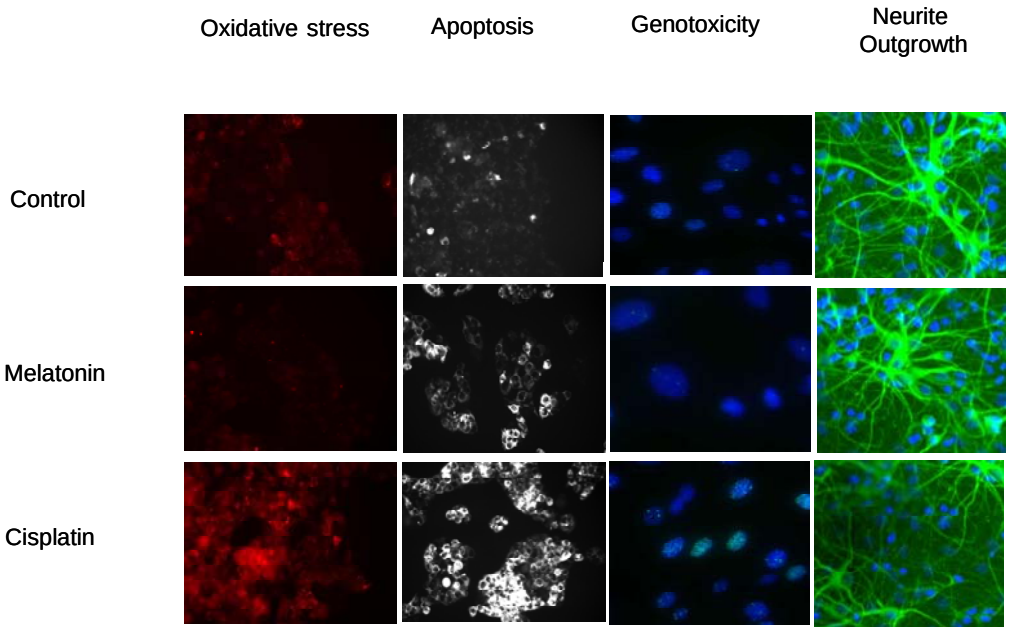
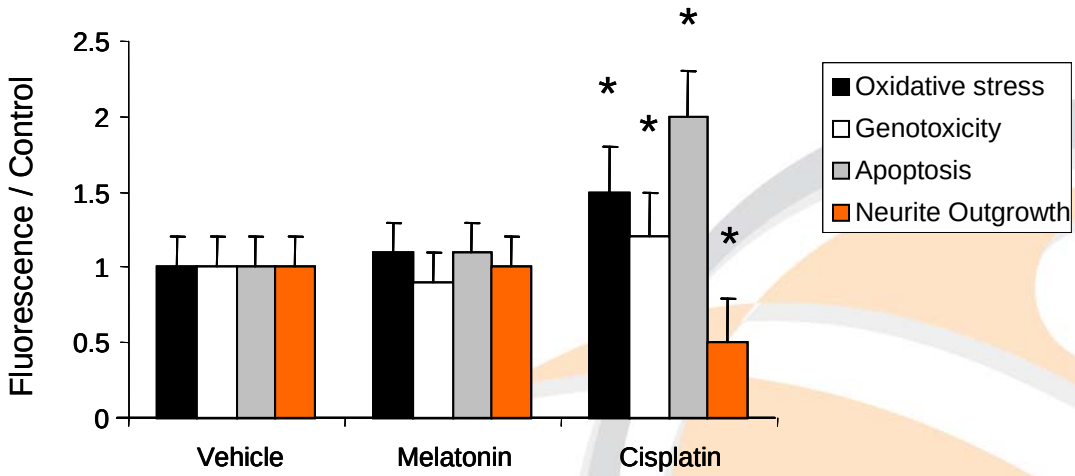
Sample Assay

The human/animal neurons or rat Dorsal Ganglion are treated with the compounds during 24 hours at different concentrations; and after the treatment the probe is added to measure the oxidative stress; after the probe the inmunocytochemistry and measurement for H2AX phosphorilation, caspase 3 activation and Tuj marking are performed.





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