Measurement of phosphorylated proteins in lymphocytes to assess lymphocyte activation during drug toxicity tests

Date: 19th February 2011

Clinical problem: Patients receiving new biologic drugs and need to be monitored for the activation of lymphocytes

Clinical question: Is the phosphorylation of proteins in lymphocytes suitable to assess lymphocyte activation in subjects undergoing drug toxicity tests?

Search strategy:
Cochrane Library search: phosphorylation, kinases, lymphocytes, activation, drug toxicity OR phosphoproteins, lymphocytes, activation, drug toxicity

Pubmed search
1. phosphoproteins(MeSH term), lymphocytes(MeSH term), activation, drug toxicity (MeSH term)
Limits: humans

2. Phosphorylated, proteins (MeSH term), lymphocytes (MeSH term), activation, drug toxicity (MeSH term)
Limits: humans

Search outcome:
Cochrane Library: 120 reviews, none relevant
Medline 1st search outcome: 18 papers, none relevant
Medline 2nd search outcome: 11 papers, none relevant

Comments:
Most of the reviews found in the Cochrane library are comparisons of the toxicity /efficacy of different drugs used for a specific disease. There are not systematic reviews on the activation of lymphocyte specific phospho-proteins following drug treatment.

Most of the papers found in Pubmed are not appropriate to answer the original question, as they are basic research studies on intracellular phospho signalling triggered by a specific compound in lymphocytes. Besides, all the experiments are performed *in vitro* using lymphocytic cell lines, while this CAT is looking mainly for primary immune cells examined *ex vivo*.

Examples:
a) "Activation of mitogen-activated protein kinases by tributyltin in CCRF-CEM cells: role of intracellular Ca(2+)" (*Toxicol Appl Pharmacol. 2000*)
Yu ZP et al. investigate the effects of tributyltin chloride (TBT) and other organotin compounds on mitogen-activated protein kinases (MAPKs) in CCRF-CEM human T lymphoblastoid cells.

b) 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD)-induced activation of mitogen-activated protein kinase signaling pathway in Jurkat T cells. (*Pharmacol Toxicol. 2003*)
Kwon MJ et al. examine mitogen-activated protein kinase associated pathways in mediation of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)-induced cell apoptosis in cultured Jurkat T cells.

Bottom Line:
Phosphorylation of proteins in lymphocytes as a marker of lymphocyte activation to assess drug toxicity/safety has not been systematically explored.

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