



POSTER PRESENTATION

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# Drugs inducing T-cell mediated cutaneous adverse reactions and contact sensitizers evoke similar responses in THP-1 cells

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## Background

Contact sensitizers induce an innate immune response in dendritic cells (DC) enhancing antigen presentation and T cell response. Little is known concerning the effect of systemic drugs causing T-cell mediated cutaneous adverse drug reactions (CARDs). Therefore, we studied the in vitro effect of drugs on THP-1 cells, a monocyte cell line widely used to show activation by contact sensitizers.

## Methods

THP-1 cells were stimulated for 24h with allopurinol (ALP), oxypurinol (OXP), ampicillin (AMP), amoxicillin (AMX), carbamazepine, sodium valproate (VAP), lipopolysaccharide (LPS), a DC maturation stimulus, and the strong contact sensitizer, 1-fluoro-2,4-dinitrobenzene (DNFB), at concentrations that reduced cell viability to 70%, evaluated by the Alamar Blue test. We studied p38 MAPK activation by Western Blot and the expression of DC maturation markers, pro-inflammatory cytokine/chemokines and heme oxygenase 1 (HMOX-1) genes by real-time RT-PCR.

## Results

All drugs significantly upregulated HMOX-1 gene (mean log<sub>2</sub> values varying from 1.842 ± 0.164, p<0.01 for AMP to 3.096 ± 0.575, p<0.05 for OXP). All drugs, but the anti-epileptics, increased the pro-inflammatory chemokine IL-8/CXCL8 (mean log<sub>2</sub> values varying from 0.959 ± 0.154, p<0.05 for AMX and 4.729 ± 0.508, p<0.05 for OXP). Both DC maturation markers (CD83 and CD40) were significantly upregulated by VAP and AMP

(respectively 1.594±0.672, p<0.05 and 0.999±0.226, p<0.05) and CD83 was also upregulated by VAP. Other genes studied were irregularly activated. Moreover, like DNFB, all drugs activated p38 MAPK. In general, allopurinol and oxypurinol showed the most intense effect, very similar to DNFB and inferior to LPS. The concomitant stimulation of THP-1 cells by OXP and AMP had no additive effect on the endpoints studied.

## Discussion

Like contact sensitizers, systemic drugs activate THP-1 cells in vitro. Direct activation of monocyte or DC that participate in antigen presentation may be an important step in the pathophysiology of delayed immune mediated CARDs. Drugs use different signalling pathways and affect these cells with a different intensity that may reflect the frequency and severity of the CARDs they cause. The effect of systemic drugs on THP-1 cells needs to be further studied in order to confirm the usefulness of this in vitro test to study their sensitizing potential, similarly to its use for contact sensitizers.

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