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Hepatic cells derived from human skin progenitors show a typical phospholipidotic response upon exposure to amiodarone

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Highlights

- Hepatic cells derived from human skin (hSKP-HPC) are evaluated as an *in vitro* model for liver drug-induced phospholipidosis (DIPL).
- Accumulation of intracellular phospholipids and lamellar bodies are found in hSKP-HPC in presence of amiodarone, a reference compound inducing phospholipidosis.
- Upon amiodarone exposure, phospholipidosis-related genes are strongly modulated in hSKP-HPC compared to HepG2 where only a marginal effect is observed.
- hSKP-HPC represent a useful *in vitro* tool to screen phospholipidogenic compounds.

Abstract

Phospholipidosis is a metabolic disorder characterized by intracellular accumulation of phospholipids. It can be caused by short-term or chronic exposure to cationic amphiphilic drugs (CAD). These compounds bind to phospholipids, leading to inhibition of their degradation and consequently to their accumulation in lysosomes. Drug-induced phospholipidosis (DIPL) is frequently at the basis of discontinuation of drug development and post-market drug withdrawal. Therefore, reliable human-relevant *in vitro* models must be developed to speed up the identification of compounds that are potential inducers of phospholipidosis. Here, hepatic cells derived from human skin (hSKP-HPC) were evaluated as an *in vitro* model for DIPL. These cells were exposed over time to amiodarone, a CAD known to induce phospholipidosis in humans. Transmission electron microscopy revealed the formation of the typical lamellar inclusions in the cell cytoplasm. Increase of phospholipids was already detected