HepaRG-CAR: a new human liver cell line

HepaRG cells outperform all other proliferative sources of human hepatocytes in liver functions. Now we modified the HepaRG cell line by stable lentiviral overexpression of the constitutive androstane receptor (CAR), a regulator of e.g. detoxification and energy metabolism, which has the following advantages:

- High liver functionality & increased mitochondrial energy metabolism in monolayer, particularly in 1.7% dimethylsulfoxide (DMSO)
- Low costs: expandable in culture medium with only 2.5% fetal bovine serum
- Highly resistant to 1.7% DMSO toxicity, used for hepatic differentiation

Transcript levels of HepaRG-CAR monolayers either treated with 1.7% DMSO or not, expressed as % of the level of two human liver samples

Gene	Description	HepaRG-CAR -DMSO	HepaRG-CAR +DMSO
	Transcription factor		
AHR	Aryl hydrocarbon receptor	133 ±22	308±123
CAR	Constitutive androstane receptor	108 ±25	208±26
FXR	Farnesoid X receptor	89±5	94±21
HNF4α	Hepatocyte nuclear factor 4 alpha	140 ±76	209±80
PXR	Pregnane X receptor	18 ±11	25±16
	Phase 1 drug metabolism		
AOX1	Aldehyde oxidase 1	58 ±8	128±28
CYP1A2	Cytochrome P450 1A2	0.04 ±0.05	0.5±0.4
CYP2B6	Cytochrome P450 2B6	136 ±93	874±548
CYP2C8	Cytochrome P450 2C8	22 ±1.2	28±3
CYP3A4	Cytochrome P450 3A4	16 ±24	160±101
POR	Cytochrome P450 reductase	78 ±17	180±38
	Phase 2 drug metabolism		
UGT1A1	Uridine diphosphate glucuronosyltransferase 1 family. Polypeptide A1	135 ±76	1595±866

Applications

- Testing metabolism and safety new medicines
- Studying liver biology & disease
- Treating liver failure patients with HepaRG-CAR-bio-artificial liver

Patent information

Patent filed in July 2016, now in national phase in EU and US

Publications

Van der Mark et al. (2017) Drug. Metab. Dis. 45, 56-67.