

## Publication

### Role of HNF4 $\alpha$ in regulation of cell proliferation and drug response

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Mammalian nuclear receptors are a superfamily of highly conserved transcription factors that affect diverse biological functions, including carbohydrate and lipid metabolism, due to their regulation of the expression of various target genes. Nuclear receptors are commonly known to regulate various metabolizing enzymes and transporters which may lead to an altered regulation of drug response. One of member of this family is the orphan hepatocyte nuclear factor 4 $\alpha$  (HNF4 $\alpha$ ), which has been associated with metabolic and cancerous diseases. This transcription factor is suggested to act as tumor suppressor and to inhibit cell proliferation.

In this work we studied the impact of HNF4 $\alpha$  on cell proliferation by counting cells using a capillary based resistance measurement method after a fixed period of time and we confirmed the antiproliferative effect of HNF4 $\alpha$  in HeLa and Caki-1 cells. Furthermore, we investigated potential target genes of HNF4 $\alpha$  such as cell cycle regulators by quantitative real-time PCR and identified the transcription factor NF $\kappa$ B1 as a potential target gene. Further investigation of the interaction between HNF4 $\alpha$  and NF $\kappa$ B1 is not part of this work. Additionally, we tested if one of the pharmaceutical compounds – canreonic acid, chenodeoxycholic acid, chlorambucil, myristic acid or myristoleic acid – is able to affect the nuclear receptor HNF4 $\alpha$  using a cell based dual reporter gene system. We have found that none of these compounds is able to regulate the activity of HNF4 $\alpha$ .

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