



# Modeling of early hepatocellular carcinoma

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Recently, Stefan Hoehme and colleagues from Leipzig University published a study simulating the spatiotemporal development of early hepatocellular cancer (Hoehme et al. 2018). Research on tumor initiation and development of hepatocellular cancer represents a major field of research in toxicology (Grasl-Kraupp et al. 2000; Braeuning and Schwarz 2016; Williams et al. 2016; Rennert et al. 2017; Braeuning et al. 2016; Amereh et al. 2017; Moghbel et al. 2016). However, little is known about early tumor development, when single-initiated cells gain a selection advantage over their neighbours, e.g., increased proliferation or resistance to cell death. Intuitively, one may assume that a tumor that originates from a single-initiated hepatocyte will grow with a spherical shape (Hoehme et al. 2018). Interestingly, the spatiotemporal model of Hoehme and colleagues came to another prediction. Rather, early hepatocellular tumors grow in extremely elongated cell arrangements. Only later, when tumors reach cell numbers of approximately 4000 elongated arrangements, they transform into spherical structures. Importantly, this model prediction could be experimentally confirmed. A rat liver tumor initiation study with single dose of 250 mg/kg *N*-nitrosomorpholine showed that small clusters of glutathione-transferase-P-positive cells showed an elongated, columnar architecture and only adopted a spherical shape, when they grew larger (Hoehme et al. 2018). The simulation of Hoehme and colleagues was based on previous work, where techniques of spatiotemporal tissue modeling have been developed (Hoehme et al. 2017; Ghallab et al. 2016; Friebel et al. 2015; Hammad et al. 2014; Schliess et al. 2014; Vartak et al. 2016). It has been shown that the hepatocytes arrange themselves in the orientation of the closest sinusoid, a mechanism also named ‘hepatocyte–sinusoid-alignment’ (HSA) (Hoehme et al. 2010; Höhme et al. 2007). If one assumes that HSA is maintained for some time even

after initiation of tumor cells, elongated patterns of early hepatocellular cancer are inevitable. The work of Stefan Hoehme et al. adds some important details to our knowledge on the behavior of hepatocytes early after initiation.

## Compliance with ethical standards

**Conflict of interest** The author declares that he has no conflict of interest.

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