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The role of the gaseous signaling molecule hydrogen sulfide in chronic liver disease

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PROPOSITIONS

Stellingen behorende bij het proefschrift:

**The role of the gaseous signaling molecule hydrogen sulfide in chronic liver disease
with special emphasis on non-alcoholic fatty liver disease**

1. Non-alcoholic fatty liver disease (NAFLD) is a chronic liver disease triggered by unique and different factors at different stages. Treatment therefore has to be stage-specific and aimed at various triggers. (*This thesis*)
2. Hydrogen sulfide (H₂S) is a unique gaseous signaling molecule that has many physiological functions. Impaired homeostasis of hydrogen sulfide is observed in various diseases including NAFLD and therefore it is an attractive target for the treatment of NAFLD. (*This thesis*)
3. Serum free thiols (R-SH) are a promising marker of systemic redox status and may be used to determine the severity of NAFLD in the general population. (*This thesis*)
4. Although an anti-fibrogenic effect of H₂S has been reported, the role of endogenously synthesized H₂S is essential for the activation and proliferation of hepatic stellate cells (HSCs) via increasing cellular bio-energetics. (*This thesis*)
5. Cystathionine γ -lyase (CTH) is the major enzyme responsible for the synthesis of H₂S during hepatic stellate cells activation. (*This thesis*)
6. Hydrogen sulfide has anti-senescent properties and promotes stellate cell activation. Inhibition of endogenous H₂S reduced HSCs activation and proliferation via cellular senescence. (*This thesis*)
7. An anti-fibrotic strategy based on an induction of senescence in HSCs, e.g. esculetin, should be combined with a senolytic agent, e.g. the natural flavonoid derivative quercetin.
8. Measure seven times before you cut (Mongolian proverb), measure seven times before you conclude (scientific translation).
9. Satisfaction lies in the effort, not in the attainment (Mahatma Gandhi).
10. To raise new questions, new possibilities, to regard old problems from a new angle, requires creative imagination and marks real advance in science (Albert Einstein).