Soluble guanylate cyclase as a novel target for cognition enhancement

Stellingen behorende bij het proefschrift

Soluble guanylate cyclase as a novel target for cognition enhancement

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1) The different pathological processes associated with Vascular Cognitive Impairment produce a vicious circle of neurovascular dysregulation and cerebrovascular damage. (*this dissertation*)

2) Neurovascular coupling at the level of the neurovascular unit and the blood-brain barrier together form the interface at which the cardiovascular and neuronal NO-sGC-cGMP systems collide and intertwine, and it is exactly at this interface where VCI pathology manifests (*this dissertation*)

3) Neurovascular dysregulation has detrimental effects on sGC functionality via (I) reduced NO availability leading to decreased sGC stimulation, and (II) oxidation of sGC leading to decreased sGC activity (*this dissertation*)

4) sGC stimulators and sGC activators have potential to enhance cognition, while the effects on the underlying plasticity mechanisms may be different and could determine disease-specific effectiveness. (*this dissertation*)

5) Academia and Pharma should consider that brain penetrance of sGC stimulators may actually not be required for an effective treatment of VCI. (*this dissertation*)

6) sGC modulators may not only provide a symptomatic treatment, i.e. cognition enhancement, but may also repair/prevent damage and treat VCI at the core of its processes (*this dissertation*)

7) "The highly innovative pharmacological principles of sGC stimulation and activation seem to have a very broad therapeutic potential. Therefore, in both academia and industry, intensive research and development efforts have been undertaken to fully exploit the therapeutic potential of these new compound classes" (*Sandner et al., 2018; HEP book series, volume 264*)

8) "If pro- and mature neurotrophins can produce opposing cellular responses – yin and yang effects – the proteolytic processing of proneurotrophins provides a powerful means to control the direction of action of neurotrophins" (*Lu et al., 2005; Nat Rev Neurosci*)

9) "In art, as in science, reductionism does not trivialize our perception – of color, light, and perspective – but allows us to see each of these components in a new way" (*Eric Kandel*)

10) "Le meilleur travail n'est pas celui qui te coûtera le plus mais celui que tu réussiras le mieux." (The best work is not what is most difficult for you, it is what you do best) *(Jean-Paul Sartre)*