Development and preclinical evaluation of radioligands for the PET studies of cerebral adenosine A1 and A2A receptors

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Propositions

belonging to the thesis

"Development and Preclinical Evaluation of Radioligands for the PET Studies of Cerebral Adenosine A_1 and A_{2A} Receptors"

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1. PET is a sensitive, non-invasive in vivo imaging technique for quantitative measurements of biochemical processes but specificity of a radioligand for a single, unique target (or biochemical process) may be hard to prove (Chapter 3, 4, and 6 of this thesis).
2. As the length of the fluoroalkyl chain of SCH442416 derivative increases (from methyl to fluoropropyl), tracer uptake in skull bone also increases. (Chapter 3 of this thesis)
3. Even though preladenant failed to demonstrate clinical efficacy in phase III studies for the treatment of Parkinson's disease, its properties (subtype selectivity, high affinity, regional distribution in brain) could still make it a potential PET tracer for in vivo imaging of cerebral A_{2A}Rs – although its slow kinetics results in long scanning times. (Chapter 4 of this thesis)
4. Increases of the cerebral uptake of the adenosine A_1 receptor ligand [^{11}C]MPDX after treatment of rodents with ethanol and an adenosine kinase inhibitor (chapter 6) or N^6-cyclopentyl adenosine (Paul et al., 2014) may be due to the fact that the radiotracer is an inverse agonist.
5. Since the negative findings of chapter 5 could either be due to failure of the blood-brain barrier to open after an adenosinergic stimulus in anesthetized rats or to inappropriate kinetics of the tested tracer, further studies with RatCap tomograph-which allow molecular imaging of rodent brain in the awake condition – is highly relevant (Baba. JS et al. J Nucl Med.2013; 54:969-976 and Schulz. D et al. Nat. Methods. 2011; 8:347-352)
6. "Gold standard" does not have to be necessarily the "truth": it can include known or unknown systematic errors, as long as the same errors exist in the results that are going to be compared with the gold standard.
7. In the Netherlands, you are super lucky if you have two things for a long time: your bike and sunny weather.
8. The mind is beautiful, but thoughts decide to what degree.
9. A man is known by the company he keeps.
10. To increase the productivity in science, brainstorm as much as you can, and only test the most probable ideas. You may miss the possibility of the rare accidental discovery, but your approach is more logical than being dependent on pure luck.
11. "*Arise, awake and stop not till the goal is reached*"- Swami Vivekananda (Great Indian Philosopher)
12. *"You must be the change you wish to see in the world"*- Mahatma Gandhi (Father of the Indian nation)