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Monitoring the Function of the P-glycoprotein Transporter at the Blood Brain Barrier

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1. The foundation of a successful experiment lies in the design of the study, its initial approach, and well-described planning.
2. PET imaging is a technique that assesses biological processes in vivo whose changes can be measured by Standard Uptake Value (SUV). However, the use of kinetic modeling is crucial since it relates the radioactivity measured in the blood to the one measured by PET in the target tissue, providing kinetic parameters that describe the underlying biological mechanism more precisely (Chapter 1).
3. Longitudinal studies allow the monitoring of animals at different time points and reduce the variability between subjects (inter-individual variability) because each animal serves as its own control and thus it minimizes the number of animals used which also contributes to the principle of 3Rs (Replacement, Reduction, and Refinement) (Chapter 3).
4. We used to say, “The Simpler, The Better”. However, the simpler is not always the faster or the easier way. Even though a one-step synthesis could reduce the synthesis time and facilitate the automation of the reaction, other complications may occur, for instance, the kinetics of the reaction of the one-step could be slower than the kinetics of the two-step synthesis (Chapter 7).
5. [18F]MC225 may allow the detection of increases and decreases of the P-gp function at the Blood-Brain Barrier which may help in the diagnoses of patients with different neurodegenerative diseases and predict drug resistance issues (Chapter 8).
6. P-gp transporters may be involved in the efflux of different brain proteins of which its accumulation may be related to the development of several brain disorders. However, it remains unclear if this abnormal aggregation of proteins causes the P-gp dysfunction or if the alterations in the P-gp functionality results in the accumulation and aggregation of proteins which leads to neurotoxicity (Chapter 9).
7. To date, P-gp inhibitors have shown low potency and poor sensitivity. Thus, they must be chronically administered and at high doses to efficiently block the P-gp function and improve brain delivery which may also increase the risk of side effects.
8. Association does not always imply causation; thus, it is needed to adequately analyze all potential confounders and fully understand the process under evaluation.
9. “Experience is the universal mother of science”. Miguel de Cervantes Saavedra.
10. “Stay Hungry Stay Foolish”. Steve Jobs, Stanford Commencement address on June 12th, 2005.