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PET Radiotracer Discovery and Development for Neuroimaging

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The discovery and development of a successful CNS radiotracer is challenging and is akin to a mini drug discovery and development process itself, although with a different set of criteria (e.g. fast clearance and low bioavailability are not good for drugs but are often ideal for radioligands). Key parameters guiding tractability have previously centered on labeling feasibility, lipophilicity (to predict brain entry) and affinity (to predict a target signal). However, these factors alone are not sufficient to satisfactorily de-risk putative compounds initially selected for labelling with factors such as non-specific binding (which can obscure the target signal) and irreversible kinetics (leading to flow limitation problems) not accounted for. Recently, biomathematical techniques have been introduced that provide a more comprehensive and quantitative approach to radiotracer discovery. These methods are able to de-risk the process by using mathematical equations that describe the tracer's kinetics in conjunction with in silico and in vitro data. Finally, the development of all successful radiotracers requires suitable validation with appropriate in vivo experiments and the selection of optimal analysis methods.

Presenter: GUNN, Roger (Imperial College)

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