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Click chemistry for PET and SPECT

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Nuclear imaging modalities such as PET and SPECT have become indispensable tools for pre-clinical and clinical research. Interests in PET and SPECT start to spread beyond the oncology, neurology and cardiology into new areas such metabolic diseases, immunology etc. Thus, new, potential targets and targeting molecules come in the focus of academic and industrial research. New radiotracers are required and thus efficient a versatile radiolabelling methods. The Cu(I) catalyzes cycloaddition of azides and terminal alkynes, termed 'click' reaction, could become such a method.(1, 2) The reaction is characterised by: i) formation of stable 1,4-difunctionalized 1,2,3-triazoles linkage ii) high yields obtained in organic and aqueous media; iii) the potential for use in many diverse applications. In fact 'click' chemistry has been adopted in radiotracer development.(3)

Suitable 18F-labeled alkyne and azide containing prosthetic groups have been prepared for subsequent labelling of peptides and nucleosides.(4, 5) Our group has investigated the use of click chemistry in the development of chelating systems for the 99mTc(CO)3-core for SPECT. In this case the triazole linkage is elegantly employed as a stable coupling group but also as an integral part of the metal chelator.(6) Using a repertoire of molecular building blocks we were able to identify the first 99mTc-labelled thymidine derivatives which are substrates of the human TK1 in a matter of a few hours.(7) Other groups use click chemistry for coupling macrocyclic DOTA-type chelating systems to azide-peptide derivatives.(8)

'Click' chemistry can also aid the parallel development of SPECT, PET, MRI and NIR tracers staring from a single azide precursor. This concept could be proven for folic acid. Reaction of an azido folate with different alkyne-functionalised imaging probes afforded compounds in high yields, which targeted the tumor associated folate receptor. However, significant differences in targeted and non-targeted uptake of the various folate tracers for nuclear and optical imaging could be observed in xenografted mice.

This presentation will give a comprehensive overview of the potential and limitation and the future perspectives of 'click' chemistry for molecular imaging.

References

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