DEVELOPING NOVEL PET TRACERS FOR HYPOXIA

Francesco Angelucci and Hans-Réne Bjørsvik

Department of Chemistry, University of Bergen, Allègaten 41, 5007 Bergen, Norway

Hypoxia is a condition of inadequate oxygen supply that can arise in solid tumors as a consequence of their unorganized cell growth and inadequate vascularization. The affected cancerous tissues show an increased resistance to radiotherapy and they have been shown to be at a higher risk of becoming malignant [1]. The discovery that 2-nitroimidazoles had the optimal reductive potential to be selectively retained in hypoxic tissue has led to their use as radiolabeled PET tracers that allow to identify the affected tissue and adapt the therapy accordingly [2]. However, the available radiotracers are limited in their potential by the unreactivity of 2-nitroimidazole. This has left us with a class of substantially similar tracers that suffer from a less than ideal signal to noise ratio with significant margins for improvement. In this project we decided to investigate the possibility of expanding the library of available 2-nitroimidazole radiotracers by exploring the role of different substitution patterns on the backbone of the imidazole. This will be achieved mainly via cross-coupling (Suzuki [3], Sonogashira [4] and Heck) reactions on the imidazole backbone aimed at modifying the hydro/lipophilicity character of the tracers and thus their distribution patterns *in vivo*. The nitro moiety will be introduced only in the final step before radiolabeling by introducing first an azide and converting it to amine and then, via diazotization, to nitro.

The ^{18}F labeled tracers will then be tested *in vivo* to ascertain the ideal distribution characteristics for optimal hypoxia imaging.

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