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Title:
Radiosynthesis of [11C](S,S)-SAM by biocatalytic methodologies as a potential prostate cancer imagen agent

Purpose/Background:

Prostate cancer (PCa) is the second most diagnosed cancer in man and represents the fifth leading cause of cancer mortality. The understanding of this pathology and the new biomarkers are allowing an improvement in the management of this disease. Being able to identify those patients with a high degree of malignancy constitutes a challenge and paths the way to precision medicine.

Sarcosine (N-methyl glycine) has been identified as a differential metabolite that is highly increased during PCa progression. This increase is associated to high levels of glycine N-methyltransferase (GNMT), enzyme that catalyzes the production of sarcosine using (S, S)-adenosylmethionine ((S, S) isomer of SAM) as co-enzyme. (S, S)-SAM acts as a natural ligand for GNMT, so this molecule labelled with ^{11}C can constitute a potential radiotracer~~s~~ for PCa diagnosis.

An enzymatic method to produce [^{11}C](S,S)-SAM, using methionine adenosyl transferase (MAT), [^{11}C]methionine and ATP was previously described (1). This method was optimized manually and the enzyme was obtained from rat liver extract.

The present study proposes the development of an immobilized biocatalytic system for the radiosynthesis of [^{11}C](S, S)-SAM in an automatically module.

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Methods:

The synthetic process began with the production of [^{11}C]CO_2 in the cyclotron (GE PETtrace 16.5MeV) via the ^{14}N(p, α)^{11}C nuclear reaction. [^{11}C]CO_2 was delivered from the target to the automated synthetic platform (GE) TRACERlab® FX C Pro, where it was trapped for purification and further reduction to [^{11}C]CH_4. Then, it was iodinated to yield [^{11}C]CH_3I, in order to react with the precursor, L-homocysteine thiolactone to generate [^{11}C]methionine. This molecule was incubated with different amounts of MAT immobilized system and ATP to produce

[^{11}C](S,S)-SAM. Furthermore, several assays were performed testing reaction time and reaction vessel volume. To purify the crude product, different conditions of SPE cartridge were tested.

Results:

The optimum conditions for the labelling reaction were: 300 mg of enzyme, 0,2 mg of ATP and 5 min of reaction time. The optimal volume of the reaction vessel was 20mL. For ~~the~~ purification a strata X-C cartridge was selected. With these conditions [^{11}C](S,S)-SAM was obtained with a conversion percentage [^{11}C]methionine/[^{11}C](S,S)-SAM of (82 ± 6)% and a radiochemical purity of (97 ± 2)%.

Conclusion:

It was possible to optimize the [^{11}C](S,S)-SAM radiosynthesis using an immobilized enzyme derivative produced by bioengineering in an automatically radiosynthesis module. Further studies must be performed in order to obtain a deeper and complete biological characterization of this compound in a prostate cancer model.

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