Substance P – a possible PET diagnostic agent

Katarina Smilkov[1], Darinka Gjorgieva Ackova[1], Adriano Duatti[3], Giovanni Di Domenico[3], Remo Guerrini[2], Emilija Janevik-Ivanovska[1]

[1] Faculty of Medical Sciences, Goce Delcev University, Stip, Macedonia
[2] Department of Chemical and Pharmaceutical Sciences, University of Ferrara, 44121 Ferrara, Italy
[3] Laboratory of Nuclear Medicine, Department of Experimental Medicine, University of Ferrara, Via L. Borsari, 46, 44121 Ferrara, Italy

Background

Supstance P (SP) is the most prominent member of tachykinine family and has been known to trigger biological responses by linking to (mostly) NK 1 receptors. The presence of functional NK1 receptors has already been documented in malignant brain tumors of glial origin, medullary thyroid cancer, non-small cell lung cancer and pancreatic carcinoma. Also, some studies have confirmed the presence of Substance P receptors in breast cancer, colon cancer and lymphomas. Development of diagnostic equivalents to Substance P, may allow easier localization of primary cancers and targeting a therapeutic radioisotopes to these receptors may be used for the treatment of malignancies that express them, through possible reduction of the blood supply and tumor draining.

Methodology

^{99m}Tc and ^{188}Re radiolabeled Substance P was tested for cell surface binding after incubation with NK1 receptor expressing U-87 MG cells, and negative controll cell line L-929. The cell culture was incubated for 15 min with the radiolabeled Substance P and the activity was measured in gamma counter. The results were performed in triplicate and were presented as a percentage of initial activity added.
The preliminary whole-body biodistribution studies were carried out with ^{99m}Tc labeled SP using a hybrid SPECT/CT YAP(S)PET (small-animal tomography scanner).

Table 1. Cell uptake, expressed as a percentage of the initial activity added.

Cell line	% of initial added activity [^{99m}Tc(N)(Cys-Cys-SP)(PCN)]	% of initial added activity [^{188}Re(N)(Cys-Cys-SP)(PCN)]
U-87 MG	58,49 ± 0,35	61,37 ± 1,02
L-929	2,95 ±1,17	1,96 ± 0,95

Results

Our results using ^{99m}Tc and ^{188}Re radiolabeled Substance P, demonstrated that the affinity of these radioconjugates for NK1 receptor expressing cells, showed pronounced cell surface binding after incubation with U-87 MG cells, compared to the negative control cell line L-929 (Table 1). Further preliminary whole-body biodistribution studies with ^{99m}Tc labeled SP using a hybrid SPECT/CT YAP(S)PET small-animal tomography scanner, showed a predominant kidney elimination 60 min post injection, which is expected for peptides, and an uptake in a region associated with the thymus. Although cardiac uptake was suspected in this region, it was excluded with *ex-vivo* measurement of the thymus gland, which after 60 min. showed high, detectable uptake of 0.0132%IA/g. This finding confirmed the previous findings about the localization of specific SP binding sites.

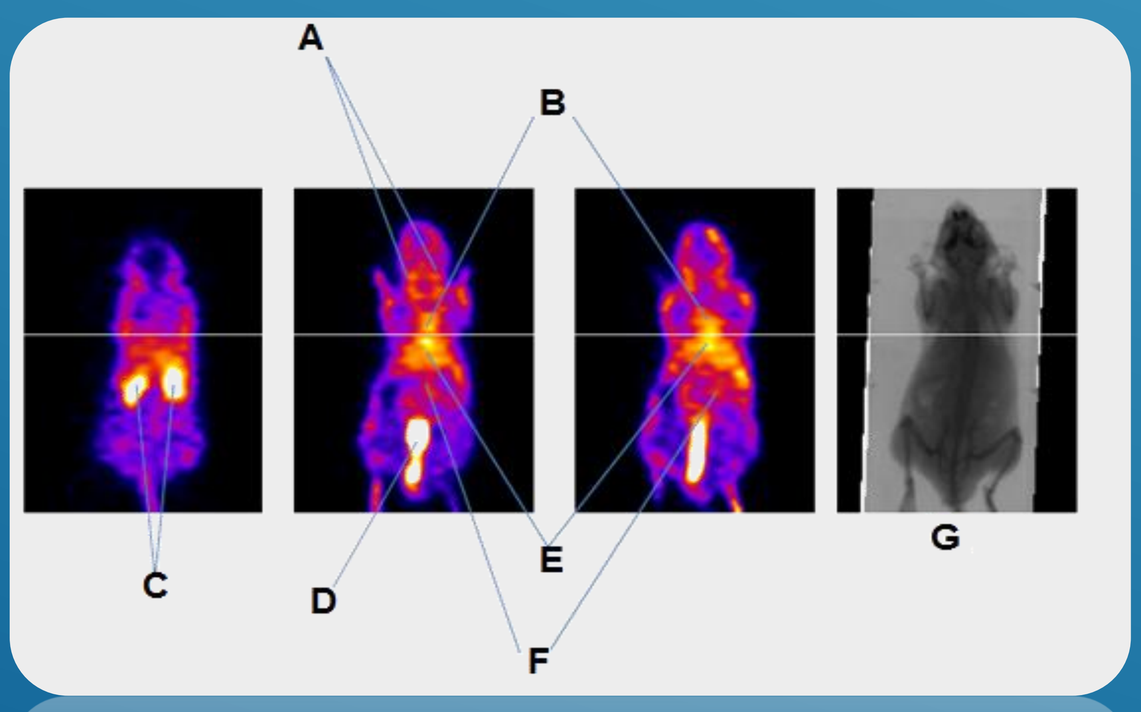

Fig. 1. Representative coronal sections recorded 20 minutes after administration of [^{99m}Tc(N)(Cys-Cys-SP)(PCN)] in mouse:
A) salivary glands, B) heart and/or thymus, C) kidney, D) bladder, E) liver, F) digestive system, G) X-ray image of the test mice.

Conclusion

Following the success of ^{68}Ga-DOTATOC, and knowing that receptor targeted imaging may provide better diagnostic outcomes in comparison with registering a high glucose uptake in the affected area using [^{18}F]FDG, we believe that it would be interesting to consider new radiochemistry approaches of radiolabeling Substance P with ^{68}Ga. ^{68}Ga (or other PET radionuclides) may provide better screening and possible detection of malignant brain tumors of glial origin, but also other diseases known to express NK1 receptors.

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