^{123}I-Interleukin-2

^{123}I-IL-2

Kam Leung, PhD[1]

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Chemical name:	^{123}I-Interleukin-2	
Abbreviated name:	^{123}I-IL-2	
Synonym:	T cell growth factor	
Agent Category:	Polypeptide	
Target:	IL-2 receptors	
Target Category:	Receptor binding	
Method of detection:	SPECT, planar	
Source of signal:	^{123}I	
Activation:	No	
Studies:	• *In vitro* • Rodents • Humans	Click on protein, nucleotide (RefSeq), and gene for more information about IL-2.

Background

[PubMed]

Interleukin-2 (IL-2) is a T-cell growth factor secreted by T lymphocytes (1). It stimulates the growth and differentiation of T cells, B cells, NK cells, LAK cells, monocytes, macrophages, and oligodendrocytes (2-4). High-affinity receptors are expressed mainly on activated T cells and macrophages (5), which infiltrate tumors, inflammatory tissues, and autoimmune tissues (6). Peripheral blood cells normally express very low levels of IL-2 receptor (7). ^{123}I-IL-2 has been developed as a single photon emission computed tomography (SPECT) tracer for imaging activated immune cells in tumors and pathological tissues (8, 9).

[1] National Center for Biotechnology Information, NLM, NIH; Email: micad@ncbi.nlm.nih.gov.

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Synthesis

[PubMed]

IL-2 was commonly labeled with sodium [^{123}I]iodide by electrophilic radioiodination using the chloramine-T method (8). This method gave a radiochemical yield of 16% and a radiochemical purity of >98% in a specific activity of 3.0-4.4 MBq/65 pmol (80-120 μCi/65 pmol). IL-2 was later labeled with lactoperoxidase and glucose oxidase (10) to provide a radiochemical yield of 23.8 ± 9.8% and a radiochemical purity of >98% in a specific activity of 3.7-6.1 MBq/65 pmol (100-165 μCi/65 pmol). [^{123}I]IL-2 was purified by column chromatography or high-performance liquid chromatography (HPLC).

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

^{123}I-IL-2 (200 nM) was able to inhibit 90% of the binding of FITC-labeled anti-CD25 (IL-2 receptor) antibody to activated T cells as compared with unlabeled IL-2 (10). The receptor binding capacity of [^{123}I]IL-2 was decreased only slightly by the labeling procedure. ^{123}I-IL-2 induced proliferation of mitogen-activated human peripheral blood lymphocytes and a murine cytotoxic T lymphocyte cell line, CCTL-2, in a dose-dependent manner (3.7 fM to 1.8 pM). Two classes of ^{123}I-IL-2-binding sites (B_{max1} = 2,200 sites/cell, K_{d1} = 500 pM and B_{max2} = 45,000 sites/cell, K_{d2} = 60 nM) were found on the cell surface of activated lymphocytes (11).

Animal Studies

Rodents

[PubMed]

No significant accumulation of ^{123}I-IL-2 was observed in major organs except from kidneys and, to a lesser extent, in liver and spleen in normal mice and rats (10). Two animal models to study human autoimmune diabetes were BB/W diabetic rats and Non Obese Diabetic (NOD) mice. In NOD mice receiving injections of labeled IL-2 (65 pmol, 1.2 MBq, 30 μCi per mouse), the pancreatic uptake was 4% injected dose (ID)/g at 2 min after injection and reached a plateau of 8% ID/g at 60 min (12). This trend was not observed in the pancreas of normal mice or in NOD mice receiving injections of labeled α-lactalbumin (65 pmol, 1.2 MBq, 30 μCi per mouse). On the other hand, the uptake in the kidneys and liver decreased with time from the 2-min radioactivity in NOD mice. There was a moderate accumulation of radioactivity in the spleen and thymus with time because of presence of activated lymphocytes in these organs. Planar imaging of NOD and normal mice after ^{123}I-IL-2 (130 pmol, 6 MBq, 150 μCi per mouse) injection showed a significant accumulation in the pancreatic region of NOD mice but not in normal mice. Pretreatment of NOD mice with 100 μg of AMT13, an anti-IL-2R antibody, inhibited 30% of pancreatic IL-2 uptake (9). Histological examination of pancreas from NOD and

normal mice reveled that there was a significant correlation between the degree of lymphocyte infiltration and radioactivity in the pancreas.

Gamma camera images showed a maximum uptake of ^{123}I-IL-2 between 5 and 15 min in pancreas of BB/W rats (10). The other organs with visible uptake were the kidneys and urinary bladder. The retention of radioactivity in the pancreas of BB/W rats was three times higher than the heart at 20 min. In contrast, there was no significant difference between the heart and the pancreas in normal rats. Radioactivity in the spleen was also higher in the BB/W rats than in the normal rats. Histological staining of the pancreas and spleen of BB/W rats confirmed that the degree of infiltration of IL-2R-positive cells was positively correlated with tissue radioactivity.

Infiltrations of activated T cells in rat renal allograft were studied by ^{123}I-IL-2 gamma camera imaging (13). The retention of radioactivity at 4 h after injection was 77% of peak activity in rejecting allografts but only 45% in control syngeneic grafts. Retention of radioactivity by rejecting allografts after injection of ^{123}I-α-lactalbumin was 36% as nonspecific uptake. Histological and autoradiographic studies showed a positive correlation of the degree of infiltrations of IL-2R-positive cells between allografts and syngeneic controls.

Other Non-Primate Mammals

[PubMed]

No publication is currently available.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

Biodistribution of ^{123}I-IL-2 was studied in 10 normal volunteers, 10 newly diagnosed, type 1 diabetes patients, 10 coeliac disease patients, and 10 Hashimoto's thyroiditis patients (11). [^{123}I]IL-2 was rapidly cleared from plasma after intravenous injection with $t_{1/2}$ (1) of 1.8 ± 0.7 min and $t_{1/2}$ (2) of 139 ± 26 min. No significant uptake in the thyroid, liver, or gastrointestinal tissues was detectable 1 h after the ^{123}I-IL-2 injection in normal subjects. A variable degree of spleen uptake was observed. Significant uptake was detected in the thyroid of all the patients with Hashimoto's thyroiditis, in the bowel of all the coeliac disease patients, and in the pancreas of all the diabetic patients. ^{123}I-IL-2 scintigraphy may be a useful tool for the *in vivo* assessment of activated mononuclear cell infiltration in various pathological tissues. Internal dosimetry data for ^{123}I-IL-2 in humans is not available in the literature.

Figures, Tables and Boxes Appendix (do not delete)

References

1. Smith K.A. Interleukin 2. Annu Rev Immunol. 1984;**2**:319–33. PubMed PMID: 6443342.
2. Miyajima A., Miyatake S., Schreurs J., De Vries J., Arai N., Yokota T., Arai K. Coordinate regulation of immune and inflammatory responses by T cell-derived lymphokines. FASEB J. 1988;**2**(9):2462–73. PubMed PMID: 2836253.
3. Muraguchi A., Kehrl J.H., Longo D.L., Volkman D.J., Smith K.A., Fauci A.S. Interleukin 2 receptors on human B cells. Implications for the role of interleukin 2 in human B cell function. J Exp Med. 1985;**161**(1):181–97. PubMed PMID: 2981952.
4. Smith K.A. Interleukin-2. Curr Opin Immunol. 1992;**4**(3):271–6. PubMed PMID: 1418705.
5. Smith K.A. The interleukin 2 receptor. Annu Rev Cell Biol. 1989;**5**:397–425. PubMed PMID: 2688708.
6. Signore A., Procaccini E., Annovazzi A., Chianelli M., van der Laken C., Mire-Sluis A. The developing role of cytokines for imaging inflammation and infection. Cytokine. 2000;**12**(10):1445–54. PubMed PMID: 11023659.
7. Robb R.J., Munck A., Smith K.A. T cell growth factor receptors. Quantitation, specificity, and biological relevance. J Exp Med. 1981;**154**(5):1455–74. PubMed PMID: 6975347.
8. Signore A., Beverley P.C., Parman A., Negri M., Pozzilli P. Labelling of interleukin-2 (IL-2) with 123-iodine with retention of its capacity to bind to activated lymphocytes. Exp Clin Endocrinol. 1987;**89**(3):301–6. PubMed PMID: 3499331.
9. Signore A., Chianelli M., Toscano A., Monetini L., Ronga G., Nimmon C.C., Britton K.E., Pozzilli P., Negri M. A radiopharmaceutical for imaging areas of lymphocytic infiltration: 123I-interleukin-2. Labelling procedure and animal studies. Nucl Med Commun. 1992;**13**(10):713–22. PubMed PMID: 1491835.
10. Signore A., Chianelli M., Ronga G., Pozzilli P., Beverley P.C. In vivo labelling of activated T lymphocytes by i.v. injection of 123I-IL2 for detection of insulitis in type 1 diabetes. Prog Clin Biol Res. 1990;**355**:229–38. PubMed PMID: 2281102.
11. Signore A., Picarelli A., Annovazzi A., Britton K.E., Grossman A.B., Bonanno E., Maras B., Barra D., Pozzilli P. 123I-Interleukin-2: biochemical characterization and in vivo use for imaging autoimmune diseases. Nucl Med Commun. 2003;**24**(3):305–16. PubMed PMID: 12612472.
12. Signore A., Chianelli M., Ferretti E., Toscano A., Britton K.E., Andreani D., Gale E.A., Pozzilli P. New approach for in vivo detection of insulitis in type I diabetes: activated lymphocyte targeting with 123I-labelled interleukin 2. Eur J Endocrinol. 1994;**131**(4): 431–7. PubMed PMID: 7921233.
13. Abbs I.C., Pratt J.R., Dallman M.J., Sacks S.H. Dynamics of the expression of the interleukin-2 (IL-2) receptor in rat renal allografts analyzed by immunohistology, autoradiography, and nuclear imaging using radioiodinated IL-2 probes. Transplantation. 1994;**58**(11):1284–7. PubMed PMID: 7992378.