Tumor Specific Three Dimensional 'Katti Peptides' in SPECT Imaging of Breast Tumors

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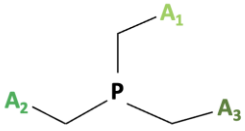
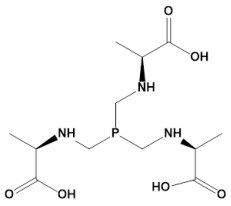
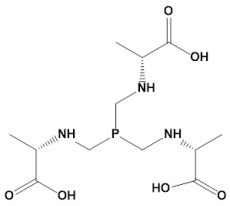
Most of the protein, peptide and small molecule drugs used for diagnostic and therapeutic applications (for the diagnosis and therapy) of various diseases are based upon simple two dimensional (2D) or monolayer architectures. The mismatch of two-dimensional drug molecules with the three-dimensional microenvironments of intricate cell-cell and cell-tissue matrix interactions can result in inadequate and inefficient drug-cell or drug-tissue/drug DNA interactions. Such mismatch of three-dimensional biological vectors (cells, tissue and DNA) with simple two-dimensional drug geometries has created inefficient representations of interactions of drugs to cells or tissue interactions within the complex biological environment, thus making it difficult to accurately predict, diagnose and treat various diseases.

Trimeric Amino Acid Motif





L-Trimeric Alanine Katti Peptide



D-Trimeric Alanine Katti Peptide

We have discovered a new class of three-dimensional amino acid motif as shown above (1-2). These trimeric amino acids (referred to as **'Katti Peptides'** by the United States National Academy of Inventors) comprise of three-dimensional spatial juxtaposition of amino acids as shown above. Mitochondrial dysfunction of cancer cells results in loss of the ability to synthesize essential, as well as specific non-essential, amino acids adequately to support their rapid growth, metastases and proliferation. This results in increased demand from cancer cells for amino acids through upregulation of amino acid transporters which are over expressed on the surface of tumor cells. For example, two amino acid transporters, SLC7A5 and SLC7A11, have been shown to be essential for the growth and proliferation of breast tumor cells. We have radiolabeled both D- and L-Trimeric Alanine Katti Peptides with Technetium-99m (^{99m}Tc), either after the reduction of $Na^{99m}TcO_4^-$ with $SnCl_2$ or via the tricarbonyl precursor $[^{99m}Tc][Tc(H_2O)_3(CO)_3]^+$. The prepared diagnostic and therapeutic radiopharmaceutical were then evaluated for their radiolabeling efficiency and stability in the presence of PBS and human serum. Finally, biodistribution studies were performed in tumor-bearing SCID mice bearing 4T1 breast cancer xenografts, to compare the in vivo kinetics of the radiolabeled amino acids. Radiolabeling yield and bench stability results can be seen below:

Sample	Radiolabeling yield	Bench stability (24h)
D-Ala	95.62±2.08	92.34±1.81
L-Ala	95.32±3.23	94.48±2.56

In this presentation, we will discuss Full details of breast tumor specificity through detailed SPECT images of $[^{99m}Tc](CO)_3]$ D- and L-Trimeric Alanine Katti Peptides.

1. Katti et al: Characterization of Supramolecular $(H_2O)_{18}$ Water Morphology and Water-Methanol $(H_2O)_{15}(CH_3OH)_3$ Clusters in a Novel Phosphorus Functionalized Trimeric Amino Acid Host; J. Am. Chem. Soc. 2003, 125, 23, 6955–6961.
2. Katti et al: Conjugate and method for forming aminomethyl.. US Patent 5,948,386, 1999