【Grant-in-Aid for Transformative Research Areas（B）】

Creation of novel theranostics using nuclear-multimolecular interaction probes by quantum entangled photon pair（Photon Pair Theranostics）

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Research Area Information	Number of Research Area：22B202　Project Period (FY)：2022-2024 Keywords：RI, probe, Laser spectroscopy, gamma-ray, dynamics calculation

Purpose and Background of the Research

●Outline of the Research

The goal in cancer research is to develop therapeutic drugs with few side effects for advanced cancer that has spread in the body with metastasis. There is a need for an epoch-making diagnostic method for selecting the optimal therapeutic drug for each patient. In this research, we bring together experts from all academic fields, from the nucleus to the individual hierarchy, to create and demonstrate the world's first whole-body intermolecular interaction imaging method using quantum entangled photon pair emitting nucleus-intermolecular interaction probes. The purpose is to create photon pair diagnostic therapeutics, which visualize in vivo chemical environment for diagnosis and treatment of malignant tumors.

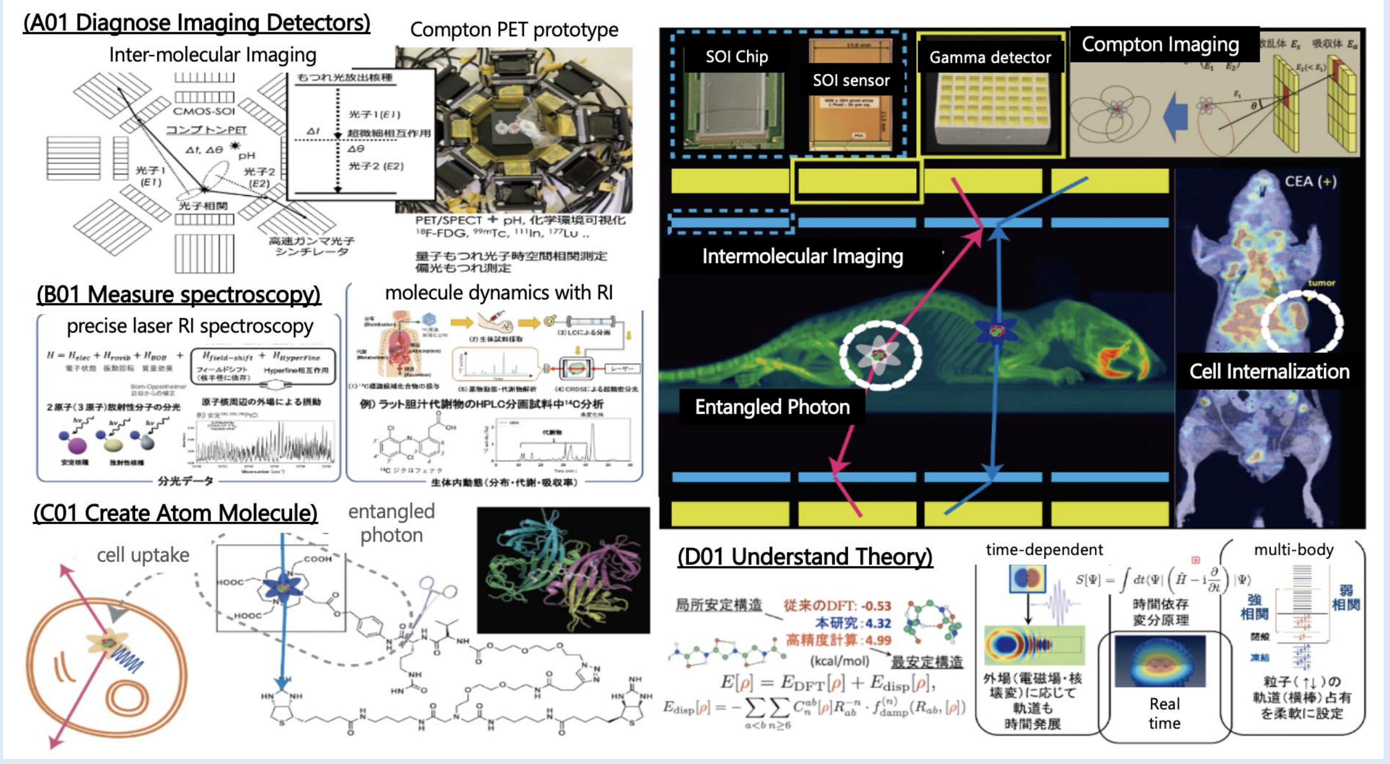

Figure 1. Image of entire research and content of each group

●Research groups

A01 Diagnose (Engineering/Medical Group), B01 Measure (Physics/Experimental Group), C01 Create (Chemistry/Pharmaceutical/Medical Group), D01 Understand (physics/theory group) will work together to conduct research that crosses the hierarchy from atomic nuclei to individuals.

(A01 Diagnose) Multi-molecular interaction imaging based on entangled photon pairs

Conventional nuclear medicine such as PET was only capable of visualizing the accumulation of radioisotopes (RI). Using the principle of observing chemical states such as pH using entangled gamma rays discovered in the JST PRESTO "quantum biology" area research and Compton camera visualizing broadband gamma. We aim to develop a device that non-invasively captures the chemical state of cells from outside the body.

● **Research groups (continuation)**

(B01 Measure) Ultraprecise spectroscopy and in vivo dynamics of radioactive molecules

In order to construct theoretical model, we will establish an ultra-sensitive laser spectroscopy and clarify the energy state of radioactive molecules by experiments. In addition, we will develop in vivo pharmacokinetic evaluation methods based on radioactive molecular spectroscopy for the design of molecular probes for RI diagnosis and treatment. We will develop isotope separation for evaluating pharmacokinetics of molecules with radionuclides and stable isotopes.

(C01 Create) Medical diagnosis of in vivo chemical environment by creation of entangled photon-pair emitting nuclei and molecular probes

Using the RIKEN accelerator, we will develop a method for mass production of entangled photon pair-emission. In addition, we will design and synthesize molecules labeled with newly manufactured RI and have high sensitivity to changes in the intracellular environment. Introduce the developed RI-labeled molecular probe into a living organism such as a mouse, accumulate it in cancer cells, and observe the in vivo chemical environment and intermolecular interactions.

(D01 Understand) First-principles calculation of quantum entangled gamma-ray probe

A detailed understanding of the behavior of radioactive molecules in vivo is essential to realize photon-pairing diagnostic technology, especially (1) elucidate the initial electronic dynamics induced by nuclear decay of radionuclides and (2) understand the effects of changes in electronic states in biomolecules on nuclear spin dynamics. In this research, we develop a first-principles calculation method for intermolecular probes using quantum entangled gamma-ray.

Expected Research Achievements

A living body is a system with a complex hierarchical structure consisting of organs and cells, cells are molecules, molecules are atoms, and atoms are atomic nuclei and electrons. (Fig. 2)

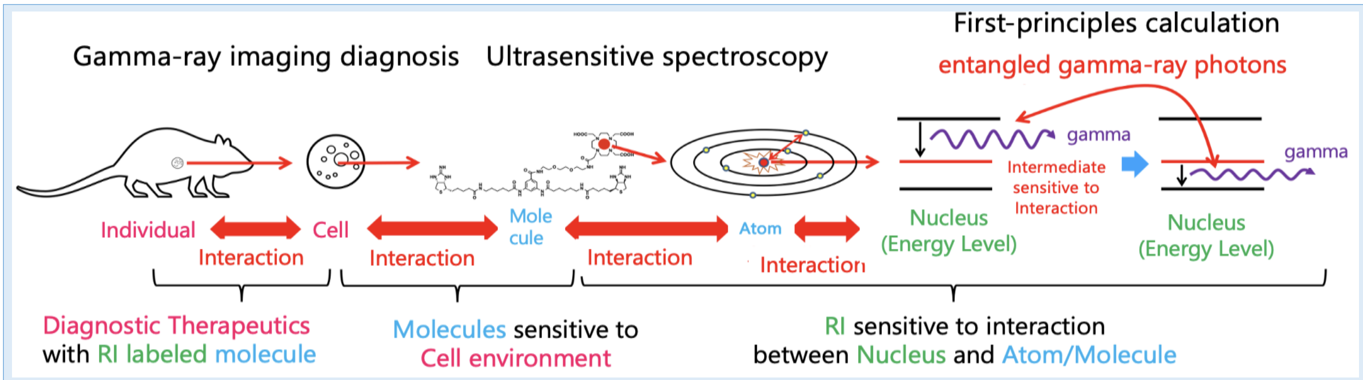

Figure 2. Hierarchical structure of the living body to be studied

We utilize femtometer-sized atomic nuclei, which are 15 orders of magnitude smaller than a human body, and gamma rays that are six orders of magnitude higher than the visible light energy to detect chemical changes.

We conduct research to noninvasively observe weak local electromagnetic fields generated by chemical reaction and validate the applicability of a new diagnostic therapeutics (quantum entangled photon-emitting nucleus-intermolecular interaction probe) (Fig. 3) that connects multiple spatial scales and energy scales of atomic nucleus → biological space, chemical reaction → atomic nucleus.

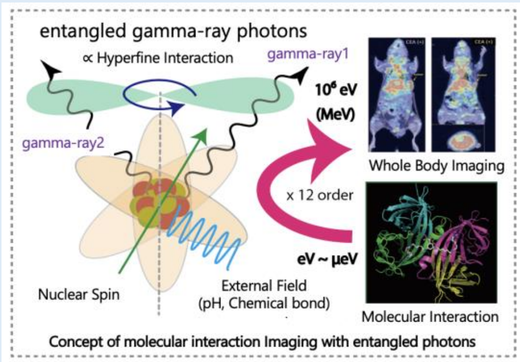

Figure 3. Concept of Photon pair probe

We are working across the hierarchical disciplines of multiple energy scale and spatial scales, working together to form new fusion disciplines. In the future, we also aim to establish a new collaboration with emerging and fusion areas with academic fields such as new nuclear control engineering, medicine, radiotherapy, nuclear physics, quantum biology, and quantum life science.

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