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

Section II

Title of Project： Deuterium Science

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Number of Research Area：20B204　Researcher Number：70431517

【Purpose of the Research Project】

Deuterium (^{2}H, D) is a non-radioactive, stable isotope of hydrogen (protium, ^{1}H) (Figure 1, left). Most properties of protium and deuterium are similar; however, there are major physical differences between the two isotopes which make their substitution with one another an interesting research field and they are: (1) D is twice as heavy as ^{1}H and (2) C−D bonds are stronger than C−^{1}H bonds. As a result, deuterated materials occasionally show quite different properties in comparison with their non-deuterated analogs. For example, the metabolic rate of C−D bond cleavage is slower by ten times or more as compared with that of C−^{1}H bond. This difference has led to the development of a heavy drug (deuterium-labeled medicines, namely, deutetrabenazine) approved by FDA (USA) as a new pharmaceutical in 2017 (Figure 1, right). Deuterium-control (isotope-control) on the material properties is an emerging yet immature concept in material design worldwide. The effect of deuterium substitution in materials can have positive or negative effect on the material properties depending on the position of the deuterium atoms and the metabolic pathways of the drug or the reaction mechanisms involved.

The purpose of this research project is to cultivate a deep understanding of the properties of deuterated materials and to explore the research field "deuterium science". Through this research activity, we wish to propose a new material design concept "Deut-Switch", which aims to maximize the material functions by precise and logical deuteration of materials and accurate prediction of the isotopic effect.

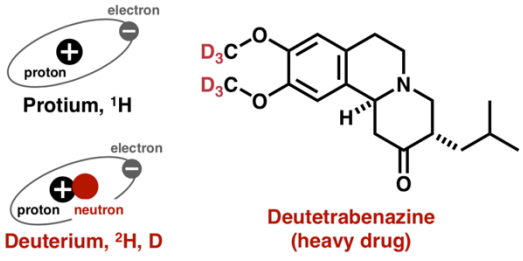

Figure 1. Isotopes of hydrogen (left) and heavy drug (right).

【Content of the Research Project】

To achieve our objectives, we promote the following four research items and collaborate closely with each other (Figure 2).

(1) **A01 Synthesis.** Development of synthetic methodology of deuterated materials;

(2) **A02 Calculations.** Understanding of the properties of deuterated materials by computational methods;

(3) **A03 Measurements.** Exploration of the reactivity of deuterated materials using spectroscopic measurements;

(4) **A04 Applications.** Application of deuterated drugs for metabolic research.

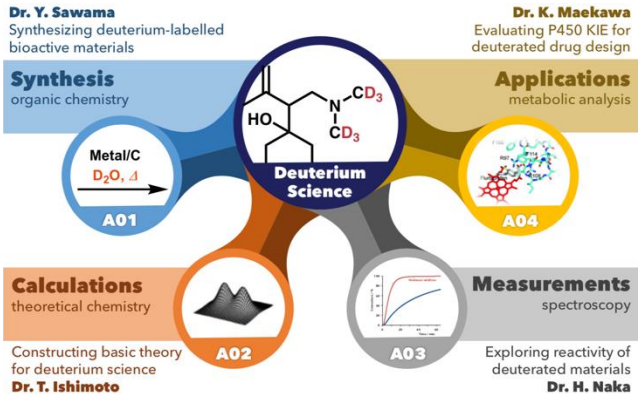

Figure 2. Framework of the project “deuterium science”.

【Expected Research Achievements and Scientific Significance】

This project will establish efficient methods for the synthesis and measurement of deuterated materials. New guides for the rational design of deuterated pharmaceuticals and agrochemicals will be provided.

Knowledge established in this project will be of high value in various academic and industrial fields. Examples include neutron scattering analysis of macromolecule structures, NanoSIMS isotopic imaging, organic electroluminescent display, solar battery, petroleum identification agent, nuclear-fusion power generation, and optical fiber.

【Key Words】

Heavy drug: medicine labeled with deuterium at specific molecular sites. The replacement of specific C−^{1}H bonds of medicine with the more stable C−D bonds results in better metabolic stability (isotopic effect). This effect contributes to reducing the frequency of taking medications and the occurrence of side effects as a result of unfavorable metabolic degradation pathways

【Term of Project】

FY2020-2022

【Budget Allocation】

121,800 Thousand Yen

【Homepage Address and Other Contact Information】

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