

World Premier International Research Center Initiative (WPI)

Summary of Research Center Project

* Compile in English within A4 2 pages.

Center name: Institute for the Advanced Study of Human Biology

Host institution: Kyoto University

Head of host institution: Juichi Yamagiwa, President

Prospective Center Director: Mitinori Saitou, Professor, Graduate School of Medicine

Prospective Administrative Director: Tadashi Ogawa, Specially appointed Professor/Program Manager, Center for Enhancing Next-generation Research

1) Overall Framework of the Center Project

The **Institute for the Advanced Study of Human Biology** will elucidate the design principles of human traits, including disease states, using multidisciplinary integrative strategies, and create a basis for developing innovative therapeutic opportunities. The Institute will inaugurate with 13 principal investigators (PIs): 9 PIs investigating key individual themes in human biology with an intense focus on genome regulation/evolution and disease modeling, 2 PIs that will respectively direct essential interdisciplinary science between life sciences and mathematics, and between life sciences and humanities, and 2 PIs organizing research development cores for cutting-edge single-cell genome information analysis and primate genome editing, respectively. The Institute will recruit 3 young PIs to accelerate its mission. The Institute will establish a link with international institutions such as the EMBL, University of Cambridge, and Karolinska Institute, creating a stratified organization for research promotion and strengthening its international profile. Thus, the Institute will realize the advanced study of human biology as a forefront life science in the coming decades and provide a foundation for medical innovation.

2) Content of Research

The Institute will target humans and non-human primates as major research subjects in an effort to uncover the design principles of human beings and disease states, through a multi-disciplinary science approach. The key goals are: 1) to achieve outstanding research in key individual themes in human biology in the area of reproduction, development, growth and aging as well as heredity and evolution; 2) to elucidate the principles for the emergence of species differences among humans, non-human primates, and rodents for proper extrapolation of the findings in model organisms to humans; 3) to generate primate models for key gene functions and intractable diseases, particularly those affecting the central nervous system and kidney; 4) to reconstitute key human cell lineages and tissues in vitro and validate their properties based on integrative information; and 5) to formalize an ethics for the use of human/non-human primate materials and create a philosophy to direct the values of the Institute's research outcomes.

3) Interdisciplinary Research

The Institute will establish two lines of interdisciplinary science that are highly integral to its mission and goals. First, the Institute will promote fusion between the life sciences and mathematics, such as topological data analysis and machine learning. Based on multi-species/multi-cell type/multi-hierarchical omics information, the Institute will define the principles of the emergence of species differences in phenotypes of homologous cells among humans, non-human primates, and rodents, allowing better

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extrapolation of the knowledge from model organisms to humans as well as providing insights into the principles for the creation of organismal diversity through evolution. This analysis will be extended into the identification of the principles for the species differences on the scales of time and physical dimensions in development and growth. Second, by integrating life sciences with the humanities, the Institute will contribute to the creation of a world-standard bioethics for the proper use of human/non-human primate materials and create a natural philosophy regarding the values of its key research outcomes (e.g., artificial gametes/cerebral cortexes, genome-edited monkeys).

4) International Research Environment

To realize an international research effort, the Institute will provide the PIs from overseas with adequate budget support for building teams of professional research staff: one associate professor as co-PI, 2 postdoctoral fellows, 200 m² research space, and 30 million JPY of start-up funding. The co-PIs will communicate closely with their PIs and work full-time at the Institute to run the PI group efficiently, particularly when the PIs are absent from the Institute. All the staff and postdoc positions will be called by open international recruitments through the Institute's web site, advertisements in major journals, and other opportunities. All the PIs will recruit at least one non-Japanese staff/postdoc to their group. The Institute will appoint Professor Edith Heard, who is the incoming Director General of EMBL, as senior consultant to advise the Institute's research direction and management, enhancing the ability of the Institute to attain international standards both in science and management. The Institute will also establish links with other prominent international institutions for collaborative efforts. Finally, the Institute will hold international symposia, workshops, and seminars, by inviting world-leading researchers, and will provide full administrative support for researchers and their families joining from overseas.

5) Center Management and System Reform

The Director will have the authority to make the final decision on key issues, such as choice of research direction, personnel affairs, and budgetary concerns, in consultation with an Executive Board consisting of a director, 2 vice directors, 2 PIs, and an administrative director. A PI board comprising 16 PIs and 4 co-PIs, according to the direction of the executive board, will make concrete decisions and action plans concerning the Institute. The Administrative Office will consist of the administrative director, 13 staffs (bilingual), and 2 URAs (PhDs). The URAs of the Institute, assigned to the strategical research support section, will play a key role in planning and implementing international meetings, younger-researcher fostering programs, and academic-industry cooperation, receiving strong support from the Kyoto University URA organization (KURA) and the University's next-generation researcher fostering projects (HAKUBI). Kyoto University will conduct 2 major system reforms. First, to enhance its competitiveness, the Institute will strategically establish world-leading research core facilities, which will play unique and highly specialized roles in Japanese research. The specialty of the core facilities (ultra-performance instruments and robust analysis technologies) and the employment of technical specialists will enable them to grow as a global research hub. Based on the experiences of the Institute, Kyoto University will construct a generalized core-facility model for utilization throughout the university and Japan. Second, to ensure the independence of the Institute after the end of the WPI grant period, it will be essential to secure appropriate funds to cover indirect costs (e.g., management personnel expenses, depreciation in facilities). To this end, Kyoto University will newly create an indirect-cost estimation model to secure indirect costs of an appropriate scale and will verify this model at the Institute as a test bed.