**Initiative on Rare and Undiagnosed Diseases (IRUD)**

[Research background] Since 2015, the Initiative on Rare and Undiagnosed Diseases (IRUD) was launched (hereinafter referred to as 1st IRUD) and a system collecting undiagnosed cases and their samples has been established throughout Japan. [Purpose] 1) To establish a coordinating center managing the IRUD activities. 2) To organize the diagnosis centers, the analysis centers, the data center and the bio-repository center. 3) To manage the IRUD promotion conference and assess the project achievement with AMED. 4) To promote utilization of Central Institutional Review Board (CIRB). 5) To cooperate with other research projects to enhance the diagnostic rate. 6) To facilitate the bio-repository and its utilization. 7) To promote international collaboration. [Advantages over similar researches and projects] As the PI of the 1st IRUD, the applicant has achieved satisfactory results as planned. Specifically, we analyzed more than 7640 specimens and 2212 families, and made diagnoses at about 35% of all cases, identified many new mutations, new genes and even new diseases. We and this proposal have big advantages over others because we have lots of experiences to manage the 1st IRUD directly and via the IRUD Promotion Conference as PI with the big achievements. [Standing position of our project with respect to international research projects] Researches for rare and undiagnosed diseases have been global trends. In the 1st IRUD, we have pursued international collaboration by hosting international meetings and sharing data with IRUD Exchange system using HPO. IRUD is not only a research project but also utilize the national medical system so that contributes to patients’ clinical situations. [Necessity] IRUD Coordinating Center is essential to coordinate or manage the whole system including many clinical, analysis, data and repository centers throughout Japan. [Expected achievement and future prospects] The next IRUD, a unique research and medical project, much more developed than before will be established. Close collaboration and governance of the clinical centers, analysis centers, data center and repository center will be achieved by management of the IRUD Promotion Conference and group conferences of the project. The establishment and operation of CIRB facilitates IRUD as well as other researches with many institutes. The achievements of IRUD would be further developed and contributed to elucidation of disease mechanisms and development of treatments.