



PRESS RELEASE (2018/11/01)

### Discovery of novel proteins essential for DNA break repair

Immunodeficiency, centromeric instability, and facial anomalies (ICF) syndrome is an autosomal recessive disorder characterized by reduced immunoglobulin levels in the serum and recurrent infection. The patients' chromosomes are fused via centromeric and/or pericentromeric regions, which are composed of repeat sequences.

In the present study, Dr. M. Unoki and H. Prof. Sasaki in the Medical Institute of Bioregulation, Kyushu University, and Prof. H. Funabiki in the Rockefeller University revealed that CDCA7 and HELLS proteins, which are mutated in ICF syndrome patients, are essential for non-homologous end joining (NHEJ), one of the major repair pathways of DNA breaks. Homologous recombination (HR), the alternative pathway, is unsuitable for repairing repeat sequences, because it includes a process of strand exchange between the DNA molecule with the same or similar sequences.

The research group speculates that, in ICF patients, a defect in NHEJ could lead to the distinctive chromosome configuration via the use of HR. Because defects in DNA repairs are the major triggers of carcinogenesis and mutations of proteins involved in NHEJ cause immunodeficiency, the research group believes that this study deepens the insights into these diseases.

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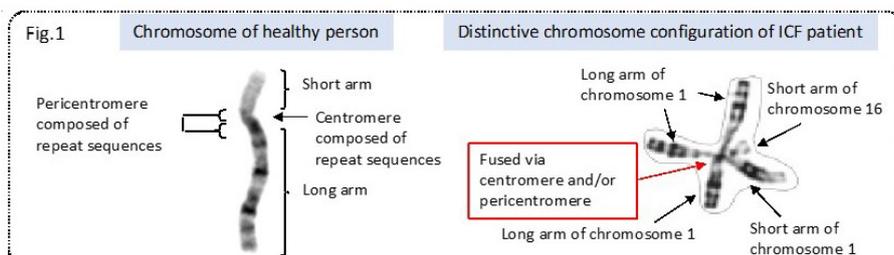


Figure 1. Representative chromosomes of healthy person and ICF syndrome patient.

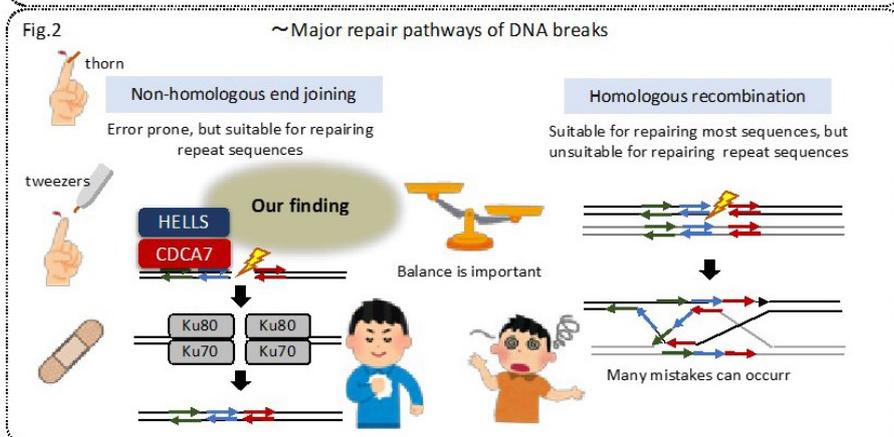


Figure 2. Schematic representation of major repair pathways of DNA breaks and our finding. The research group found that HELLS and CDCA7 proteins serve as a pair of tweezers to remove nucleosomes and help Ku80 to access and protect DNA break ends like a band-aid.

**【Contact】**  
Motoko Unoki, Assistant professor  
Division of Epigenomics and Development/Medical Institute of Bioregulation  
Tel : +81-92-642-6761 / Fax: +81-92-642-6799  
Email : unokim@bioreg.kyushu-u.ac.jp