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スマート・エイジング学際重点研究センター  
Smart-Aging Research Center

環境ストレス応答研究センター  
Environmental Stress Response Research Center



日時：2019年10月2日（水）17:00-18:30

October 2, 2019 from 5:00 to 6:30pm

場所：スマートエイジング研究センター国際会議室

Center for Smart-Aging Research Center, 1F Auditorium

講師：Professor Paul-Henri Romeo (CEA, France)

演題：Macrophage production and functions in inflammatory diseases and regulated by TRIM33.

## Abstract

Macrophages are regulators of both tissue homeostasis and acquired diseases such as cancer, inflammatory diseases and bacterial and viral infections. The macrophage specific transcriptional programs are dictated by the transcription factor PU.1 that primes distal regulatory elements for macrophage identities and makes chromatin competent for activity of stimuli-dependent transcription factors. Although the functions of macrophage-specific distal regulatory elements that bind PU.1 have been elucidated, the underlying mechanisms of action of these cis-acting sequences are not characterized.

The tripartite motif (TRIM) family of proteins plays important roles in innate immunity and antimicrobial infection but none of these proteins has been shown to directly regulate transcription of genes in macrophage. We will show that TRIM33 is recruited by PU.1 in a subset of macrophage specific regulatory sequences of genes involved in the inflammatory response and that sequestering of SPT16/FACT by TRIM33 at PU.1-bound distal regions might represent a new regulatory mechanism for RNA Pol II recruitment and transcription output in macrophages. Functionally, we will show that expression of TRIM33 in immature myeloid cells is necessary for efficient production of small peritoneal macrophages and bone marrow derived macrophage, that TRIM33 regulates macrophage function during inflammatory diseases such as Crohn's disease and a previously unknown mechanism of macrophage-specific regulation of *Ifnb1* transcription whereby TRIM33 is critical for *Ifnb1* gene transcription shut down.