

分子腫瘍学セミナー・基盤医学特論開講通知
Molecular Oncology Seminar, Information on Special Lecture Tokuron

RNA methylation and control of RNA and cellular fates

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The most common reversible post-transcriptional mRNA modification on mRNA is N6-methyladenosine (m6A). The presence of m6A alters mRNA metabolism including mRNA stability, mRNA splicing, and translation efficiency. The deposition of transcriptome-wide m6A marks depends on the METTL3-METTL14-WTAP-VIRMA-ZC3H13-RBM15 protein complex, in which METTL3 serves as the catalytic subunit. We previously found that m6A is required for YTHDC1 to undergo liquid-liquid phase separation and form nuclear YTHDC1-m6A condensates. These nuclear bodies are increased in number in acute myeloid leukemia (AML) cells compared to normal CD34 cells. Furthermore, we found that YTHDC1 can protect oncogenic mRNAs including MYC from being degraded by the exosome machinery. However, the functional regulators of these nuclear bodies and how they mediate control of RNA fate remains unclear. In more recent studies, we identify novel mechanisms downstream of m6A and how RNA methylation control is mediated through these nuclear bodies. We propose that targeting nuclear bodies and their associated factors provide new therapeutic strategies to targeting the RNA methylation program.

造血幹細胞・造血器腫瘍における RNA 研究の大家である Michael G. Kharas 先生をお招きしてセミナーを開催します。ふるってご参加ください。

Publications

- 1) Vu L, et al., and Kharas MG*. "Functional screen of MSI2 interactors identifies an essential role for SYNCRIP in myeloid leukemia stem cells." *Nature Genetics*. 2017 Jun;49(6):866-875.
- 2) Vu L, et al., and Kharas MG*. "The N6-methyladenosine (m6A)-forming enzyme METTL3 controls myeloid differentiation of normal hematopoietic and leukemia cells." *Nature Medicine*. 2017 Nov;23(11):1369-1376.
- 3) Park S-M, et al., and Kharas MG*. "IKZF2 drives leukemia stem cell self-renewal and inhibits myeloid differentiation." *Cell Stem Cell*. 2019 Jan 3;24(1):153-165.e7.
- 4) Minuesa G, et al., and Kharas MG*. "Small-molecule targeting of MUSASHI RNA binding activity 1 in acute myeloid leukemia." *Nat. Comm.* 2019 Jun 19;10(1):2691.
- 5) Cheng Y, et al., and Kharas MG*. "N6-methyladenosine on mRNA facilitates a phaseseparated nuclear body that suppresses myeloid leukemic differentiation" *Cancer Cell*. 2021 Jul 12;39(7):958-972.e8.

日時	2023年9月25日(月) 17:00 – 18:30
Date	September 25, 2023 (Mon), 17:00 – 18:30
場所	基礎研究棟 第1講義室
Venue	Lecture Room No.1, Basic Medical Research Building
言語	発表: 英語
Language	Talk: English
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