大学院特別セミナー

Mechanisms of target drug tolerance in lung cancer

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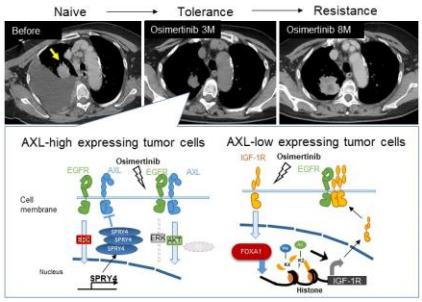

EGFR mutated lung cancer responds to EGFR-tyrosine kinase inhibitors (EGFR-TKIs), but cancer cells acquire resistance sooner or later. Drug tolerance is the basis for acquired resistance to targeted drugs, including the 3rd generation EGFR-TKI osimertinib. We have uncovered that osimertinib tolerance occurs by a different mechanism depending on the presence or absence of AXL (a receptor tyrosine kinase) expression. In AXL-high expressing cells, osimertinib stimulated AXL by inhibiting a negative feedback loop with SPRY4, resulting in maintaining cell survival and inducing the emergence of tolerant to osimertinib. Moreover, a population of AXL-low expressing cells exposed to osimertinib also became tolerant by increasing IGF-1R expression and phosphorylation via increased expression of the transcription factor FOXA1. These results suggest that optimal inhibition of tolerant signal combined with osimertinib may cure EGFR mutated lung cancer.

1. Taniguchi H, et al. AXL confers intrinsic resistance to osimertinib and advances the emergence of tolerant cells. **Nat Commun** 2019 Jan 16;10(1):259.
2. Wang R, et al. Transient IGF-1R inhibition combined with osimertinib eradicates AXL-low expressing EGFR mutated lung cancer. **Nat Commun** 2020 Sep 14;11(1):4607.

11月5日（金）17：00～　Zoom開催

申し込み

本セミナーは、大学院の単位認定の対象となります。

受講希望の際は、医薬系学務課へご連絡ください。

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