

## ROR1: Novel Therapeutic Target for Lung Adenocarcinoma

### Background:

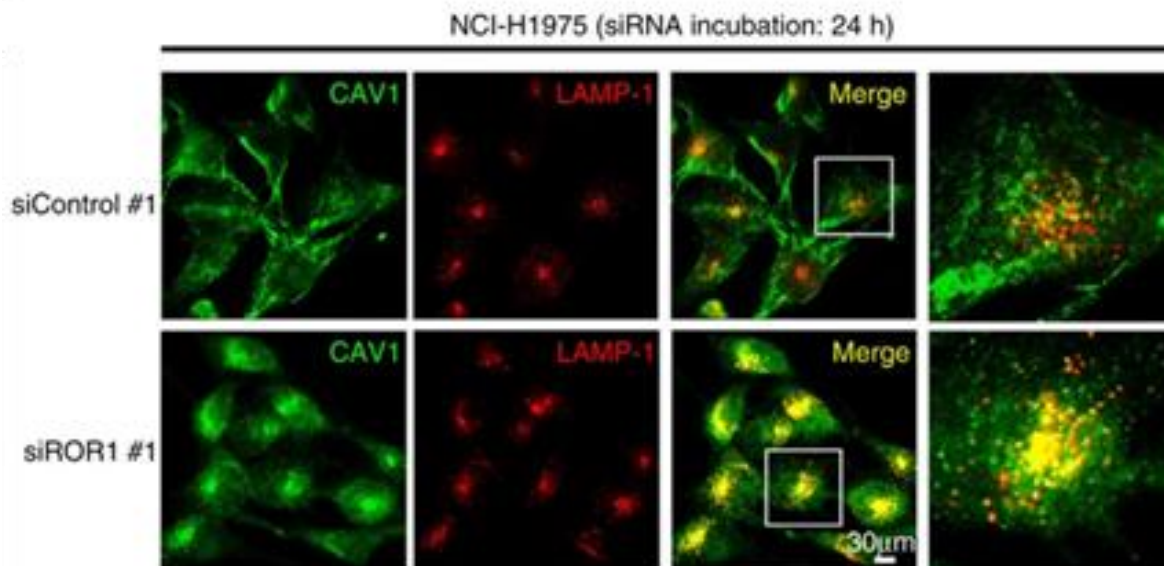
Lung cancer has long been the leading cause of cancer death and lung adenocarcinoma is the most prevalent among the four major histologic types. For lung adenocarcinoma patients, epidermal growth factor receptor (EGFR) inhibitors such as Gefitinib and Erlotinib are highly effective in initial treatment. In the course of treatment, however, therapeutic resistance is still a major clinical challenge.

### Technology Overviews:

Nagoya University researchers have successfully elucidated functional molecular mechanism of the receptor tyrosine kinase-like orphan receptor 1 (ROR1) to develop molecular targeted drugs of lung adenocarcinoma. Previously it has been reported that ROR1 plays an essential role in sustaining survival signaling from mutant EGFR in pulmonary adenocarcinoma cells. Furthermore, the newest results provide mechanistic insight into how ROR1 inhibition can overcome EGFR-tyrosine kinase inhibitor (TKI) resistance due to bypass signaling via diverse RTKs such as MET and IGF-IR. Therefore, ROR1 inhibition is an attractive approach to defeat lung adenocarcinoma including even those with acquired resistance to EGFR -TKI treatment, which is currently a major clinical obstacle of this devastating cancer.

### Figures:

**Figure 1. ROR1 is required for the prevention of CAV1 being routed to the lysosome.** Two-color immunofluorescence analysis showing significant colocalization of CAV1 with LAMP-1 24 h after siROR1 treatment.



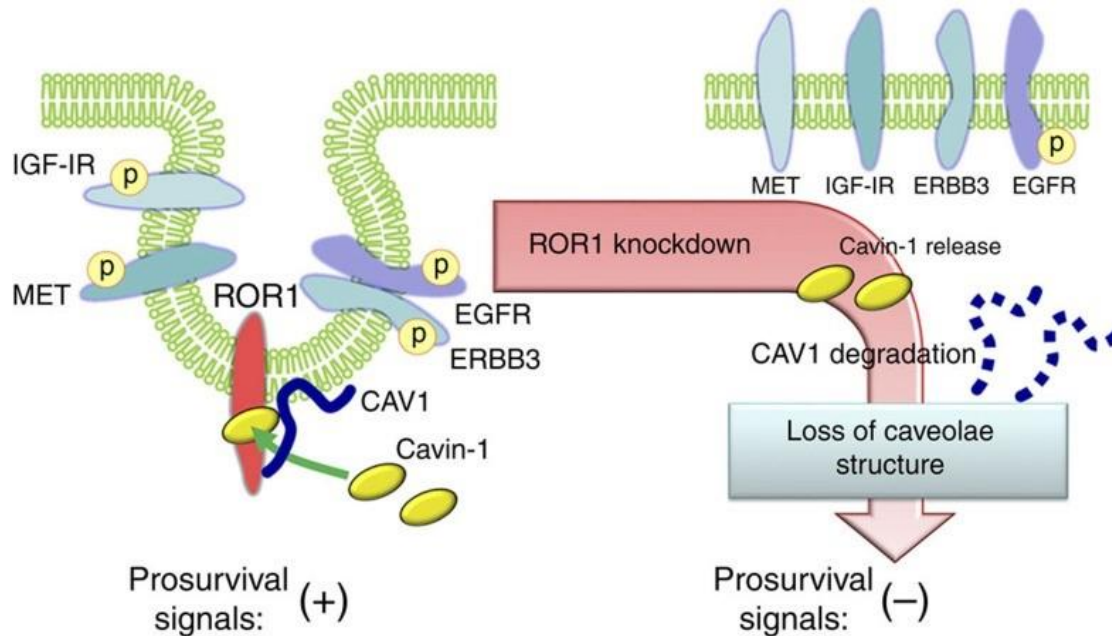
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Figure 2. Schematic diagram of proposed model showing how ROR1 sustains caveolae formation.



**Further Details:**

Yamaguchi T. et al., ROR1 sustains caveolae and survival signaling as a scaffold of cavin-1 and caveolin-1. *Nat Commun.* 2016 Jan 4;7:10060.

Ida L. et al., Receptor tyrosine kinase-like orphan receptor 1, a target of NKX2-1/TTF-1 lineage-survival oncogene, inhibits apoptosis signal-regulating kinase 1-mediated pro-apoptotic signaling in lung adenocarcinoma. *Cancer Sci.* 2016 Feb;107(2):155-61.

Yamaguchi T. et al., NKX2-1/TTF1/TTF-1-Induced ROR1 is required to sustain EGFR survival signaling in lung adenocarcinoma. *Cancer Cell.* 2012 Mar 20;21(3):348-61.

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