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IN BRIEF

COLORECTAL CANCER

Editing an invasion

Sae-Won Han, Hwang-Phill Kim and colleagues investigated RNA editing in colorectal cancer (CRC) samples. Whole genome and transcriptome sequence data showed an increase in adenosine-to-inosine editing in RAS homologue family member Q (*RHOQ*), which resulted in a substitution of asparagine with serine at residue 136 (RHOQN136S). The RHOQN136S protein had increased activity compared with wild-type RHOQ, and this was associated with a reorganization of the actin cytoskeleton and increased invasive potential of cells *in vitro*: invasive growth *in vitro* was further increased in the presence of mutant *KRAS*. In patients with CRC, edited *RHOQ* transcripts and mutant *KRAS* were associated with disease recurrence.

ORIGINAL RESEARCH PAPER Han, S.-W. *et al.* RNA editing in *RHOQ* promotes invasion potential in colorectal cancer. *J. Exp. Med.* http://dx.doi.org/ 10.1084/jem.20132209 (2014)

DEDIFFERENTIATION

A point of return

Research in *Drosophila melanogaster* has shown that loss of Lola-N, a splice variant of the Lola transcription factor expressed in differentiated neurons, results in brain tumour formation. Lola-N represses the expression of stem cell-associated genes and its loss results in dedifferentiation of neurons, derepression of neural stem cell genes and proliferation. Thus, fully differentiated neurons are capable of tumour formation in fruit flies if an essential mediator of stem cell gene repression is lost.

ORIGINAL RESEARCH PAPER Southall, T. D. *et al.* Dedifferentiation of neurons precedes tumor formation in *lola* mutants. *Dev. Cell* **28**, 685–696 (2014)

LUNG CANCER

Overcoming crizotinib resistance

Two papers have reported on the efficacy of the second-generation anaplastic lymphoma kinase (ALK) inhibitor ceritinib in patients with and animal models of non-small-cell lung cancer (NSCLC). In a Phase I dose-escalation trial in 59 patients with tumours that had genetic alterations in *ALK*, ceritinib was given at once-daily doses between 50 mg and 750 mg (established as the maximum tolerated dose (MTD)). In the expansion phase of the trial, an additional 71 patients were treated with the MTD. Of the 80 patients with NSCLC who had previously received the ALK inhibitor crizotinib, the overall response rate (ORR) was 56% (95% confidence interval (CI) 45 to 67). Of the 114 patients with NSCLC treated with more than 400 mg per day of ceritinib, the median progression-free survival was 7 months (95% CI 5.6 to 9.5) and the ORR was 58% (95% CI 48 to 67). Responses were evident in patients with mutations in *ALK* that confer resistance to crizotinib. Friboulet and colleagues used *in vitro* and *in vivo* models to show that ceritinib is active in NSCLC cell lines with L1196M, G1269A, I1171T and S1206Y substitutions in ALK, which confer resistance to crizotinib. However, ceritinib remains ineffective against cell lines that have G1202R and F1174C substitutions in ALK, and one of these substitutions was present in 5 of 11 biopsies taken from patients with resistance to ceritinib. Both of these papers indicate that although ceritinib should be effective in some patients who have developed resistance to crizotinib, resistance is likely to remain a relevant hurdle.

ORIGINAL RESEARCH PAPERS Friboulet, L. *et al.* The ALK inhibitor ceritinib overcomes crizotinib resistance in non-small cell lung cancer. *Cancer Discov.* http://dx.doi.org/10.1158/2159-8290.CD-13-0846 **(2014)** | Shaw, A. T. et al. Ceritinib in ALK-rearranged non–small-cell lung cancer. *New Eng. J. Med.* **370**, 1189–1197 (2014)