CANCER DISCOVERY

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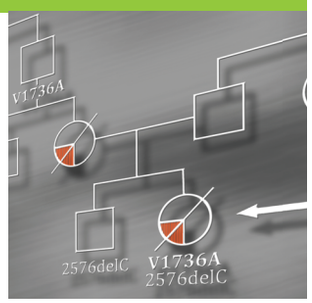

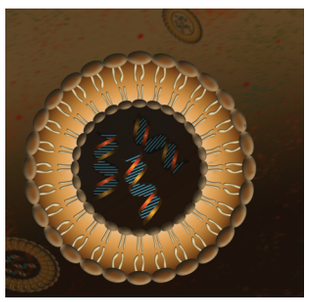

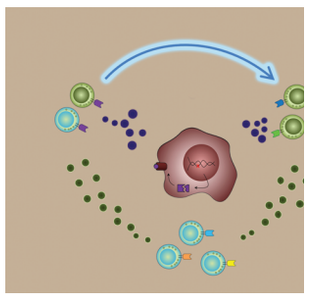

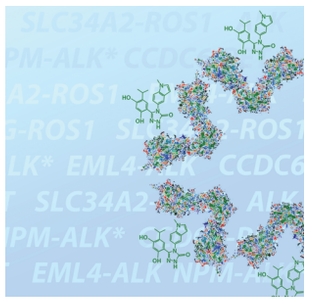

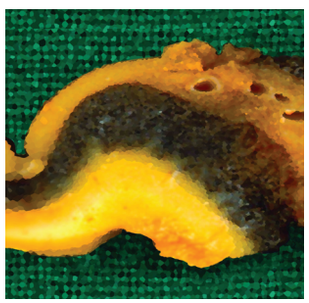

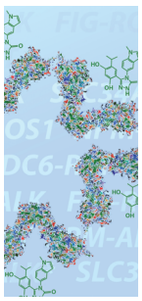

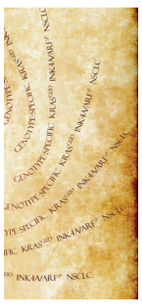

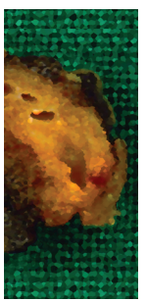

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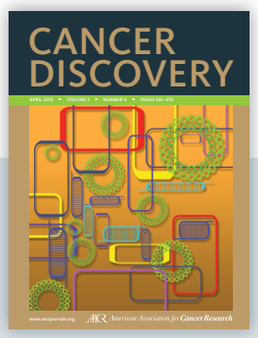

ON THE COVER Tabernero and colleagues report the results of a phase I dose-escalation and expansion study assessing the safety, activity, and pharmacodynamics of ALN-VSP, a lipid nanoparticle containing siRNAs against vascular endothelial growth factor A (*VEGFA*) and kinesin spindle protein (*KSP*), in patients with advanced solid tumors with liver involvement. One patient with metastatic endometrial cancer had a complete response and 3 patients (2 with metastatic renal cell carcinoma and 1 with metastatic pancreatic neuroendocrine tumor) experienced disease stabilization. Post-treatment tumor biopsies showed evidence of intratumoral delivery, increased *VEGFA* mRNA cleavage, and decreased *VEGFA* and *KSP* mRNA levels compared with pre-treatment biopsy samples, consistent with an on-target response and an RNAi mechanism of action. For details, please see the article by Tabernero and colleagues on page 406.