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ON THE COVER

McKie and colleagues show that OPCML expression is silenced in multiple tumor types, including the vast majority of high-grade serous ovarian tumors, and correlates with poor prognosis. They further establish an extracellular mechanism of OPCML-mediated tumor suppression through negative regulation of a specific group of receptor tyrosine kinases (RTK). Through binding to RTK extracellular domains, OPCML induces RTK membrane redistribution, internalization, and degradation. Recombinant OPCML down-regulated the same RTKs in vivo and inhibited ovarian cancer cell growth, suggesting that extracellular protein therapy may be useful in the treatment of OPCML-deficient tumors. For details, please see the article by McKie and colleagues on page 156.