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Sommario/riassunto	Neuroblastoma, the most common extra-cranial pediatric solid tumor, is responsible for 9-15% of all pediatric cancer deaths. Its intrinsic heterogeneity makes it difficult to successfully treat, resulting in overall survival of 50% for half of the patients. Here we analyze the role in neuroblastoma of the adaptor protein p140Cap, encoded by the SRCIN1 gene. RNA-Seq profiles of a large cohort of neuroblastoma patients show that SRCIN1 mRNA levels are an independent risk factor inversely correlated to disease aggressiveness. In high-risk patients, SRCIN1 was frequently altered by hemizygous deletion, copy-neutral loss of heterozygosity, or disruption. Functional assays demonstrated that p140Cap is causal in dampening both Src and Jak2 kinase activation and STAT3 phosphorylation. Moreover, p140Cap expression decreases in vitro migration and anchorage-independent cell growth, and impairs in vivo tumor progression, in terms of tumor volume and number of

spontaneous lung metastasis. p140Cap also contributes to an increased sensitivity of neuroblastoma cells to chemotherapy drugs and to the combined usage of doxorubicin and etoposide with Src inhibitors. Overall, we provide the first evidence that SRCIN1/p140Cap is a new independent prognostic marker for patient outcome and treatment, with a causal role in curbing the aggressiveness of neuroblastoma. We highlight the potential clinical impact of SRCIN1/p140Cap expression in neuroblastoma tumors, in terms of reducing cytotoxic effects of chemotherapy, one of the main issues for pediatric tumor treatment.