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ON THE COVER Killian and colleagues found that gastrointestinal stromal tumors (GIST) with mutations in succinate dehydrogenase (SDH) complex genes exhibited a distinct methylation signature relative to the profile of KIT-mutant tumors and normal reference tissues. This methyl-divergent profile was distinguished by increased global DNA hypermethylation, particularly at DNase hypersensitive sites, and was also present in other SDH-mutant tumor lineages, including paraganglioma and pheochromocytoma, supporting the oncogenotype dependence of this signature. In addition, a similarly perturbed methylation profile was detected in gliomas harboring mutations in another Krebs cycle enzyme, isocitrate dehydrogenase (IDH). These findings identify a strong association between the mitochondrial Krebs cycle and cancer epigenomic reprogramming. For details, please see the article by Killian and colleagues on page 648.