Decoupling genetics, lineages, and microenvironment in IDH-mutant gliomas by single-cell RNA-seq.

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Public Summary:
Tumor subclasses differ according to the genotypes and phenotypes of malignant cells as well as the composition of the tumor microenvironment (TME). We dissected these influences in isocitrate dehydrogenase (IDH)-mutant gliomas by combining 14,226 single-cell RNA sequencing (RNA-seq) profiles from 16 patient samples with bulk RNA-seq profiles from 165 patient samples. Differences in bulk profiles between IDH-mutant astrocytoma and oligodendroglioma can be primarily explained by distinct TME and signature genetic events, whereas both tumor types share similar developmental hierarchies and lineages of glial differentiation. As tumor grade increases, we find enhanced proliferation of malignant cells, larger pools of undifferentiated glioma cells, and an increase in macrophage over microglia expression programs in TME. Our work provides a unifying model for IDH-mutant gliomas and a general framework for dissecting the differences among human tumor subclasses.

Scientific Abstract:
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