

SUPPLEMENTARY FIGURES LEGENDS

Figure S1. DNA methylation profiling distinguishes sinonasal carcinomas, including *IDH2* mutants, from lymphoma, melanoma and Ewing sarcoma. t-SNE analysis of the sinonasal tumors and select tumors of mesenchymal origin shows a clear separation of sinonasal carcinomas, including all sinonasal *IDH2* mutants (group 1) from Ewing sarcomas, lymphoma and melanoma. The tumors are color-coded according to the legend and groups are numbered. Group 4 in this plot represents sinonasal carcinomas where a small number of samples in each histologic category was a possible limiting factor for definitive respective clusters formation, including moderately-differentiated intestinal type adenocarcinoma. SMARCB1-deficient sinonasal carcinoma (group 2) is in a proximity of atypical teratoid/rhabdoid tumor-MYC subgroup (group 5). Methylation data on tumors used for comparison with our cohort were previously published [22].

Abbreviations: SNUC=sinonasal undifferentiated carcinoma, LCNEC= large cell neuroendocrine carcinoma, PD non-ITAC= poorly-differentiated carcinoma non-intestinal type adenocarcinoma, SMARCB1-def=SMARCB1-deficient sinonasal carcinoma, ONB=olfactory neuroblastoma, MD ITAC= moderately-differentiated intestinal type adenocarcinoma, HG non-ITAC=high-grade non-intestinal type adenocarcinoma, PDCA-GL= poorly-differentiated carcinoma with focal glandular/acinar differentiation, PDCA-NE-GL=poorly-differentiated carcinoma with neuroendocrine and glandular differentiation, SCNEC=small cell neuroendocrine carcinoma, SCNEC-SQCC=combined small cell neuroendocrine carcinoma and squamous cell carcinoma, ATRT=atypical teratoid/rhabdoid tumor, CNS NB= central nervous system neuroblastoma.

Figure S2. t-SNE analysis supports the sinonasal tumors segregation in respect to *IDH2* mutations status.

Figure S3. Pathway analysis of *IDH2* mutant SNUC and large cell neuroendocrine carcinoma. Both *IDH2* mutant tumor types show enrichment for MAPK, Hippo and mTOR signaling pathways in both tumor types. X-axis represent gene ratio and Y-axis represents different signaling pathways enriched based on KEGG database.

Figure S4. Morphology and INSM1 immunoexpression in high-grade sinonasal carcinomas with neuroendocrine differentiation. Large cell neuroendocrine carcinoma (SN_31, A-B), poorly-differentiated carcinoma with neuroendocrine and glandular differentiation (SN_58, C-D) are depicted. Foci of keratinization (E, left) were distinct from small cell component (E, right) in a combined small cell carcinoma and squamous cell carcinoma. Only small cell component was positive for INSM1 (F, SN_53) in a small cell neuroendocrine carcinoma (SN_51, G-H). H&E images are on the left and INSM1 immunostain on the right, at 200X magnification.