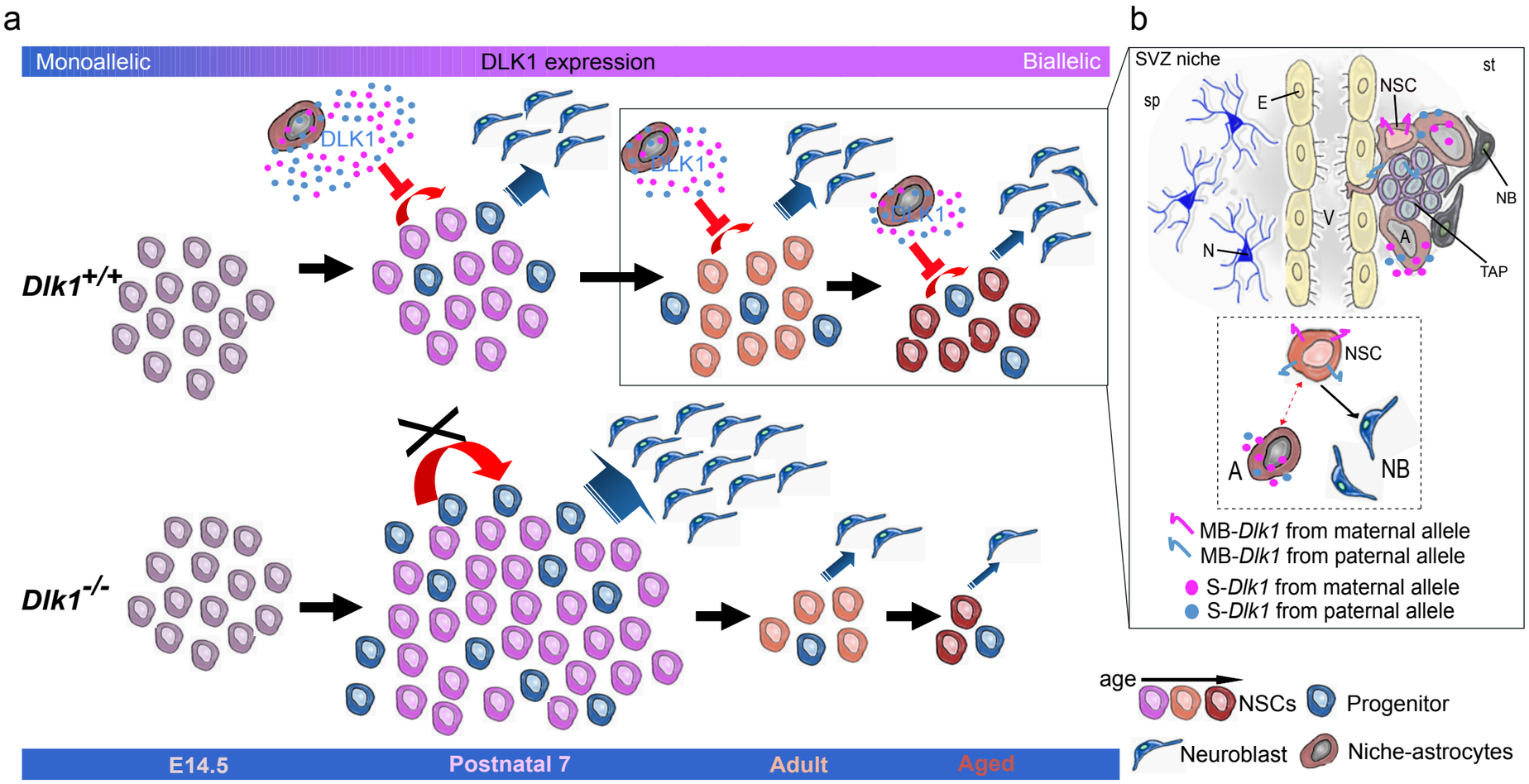
Supplementary Figure 8



Supplementary Figure 8. DLK1 secreted by niche-astrocytes is required for the maintenance of the stem cell pool within the radial-glial lineage. (**a**) Under normal circumstances in vivo, a considerable amount of developmental activity is found in the SVZ at early postnatal periods. Neural stem cells (NSCs) increase proliferation in association with their differentiation into the transit amplifying progenitors (TAP) to subsequently give rise to neuroblasts. DLK1 secreted by surrounding niche-astrocytes, contributes to maintaining NSC in a more undifferentiated and slow-dividing state, preserving the stem cell pool size. This requirement for DLK1 in NSC maintenance continues throughout adulthood albeit within a more restricted and smaller pool of adult stem cells. In the absence of DLK1, early postnatally, the stem cell pool increases proliferation as it prematurely enters the transit amplifying differentiation programme. This early increase in proliferation and differentiation results in an exhaustion and reduction in the size of the stem cell pool which is reflected in fewer neurospheres generated in mutant culture throughout the lifetime of the animal. Exogenous treatment with DLK1 abrogates this effect. Therefore DLK1 continuously regulates the maintenance of the stem cell pool over the lifetime of the animal. Maternally and paternally inherited expression of the gene is required in both NSCs and niche-astrocytes to contribute to this maintenance process. (**b**) Within the neurogenic niche, the niche-astrocytes secrete DLK1 to maintain the NSCs while the stem cells themselves require membrane-bound DLK1 to respond to secreted DLK1. This relationship between the niche-astrocytes and the NSCs, which some have suggested to be reversible, can be characterized by the expression of the two different isoforms of DLK1 in the two cell types, and this regulates the developmental pathway leading to the continued production of new neurons in the olfactory bulb. N, neuron; NB, neuroblast; A, niche-astrocyte; E, ependymal cells; V, ventricle lumen; sp, septum; st, striatum.