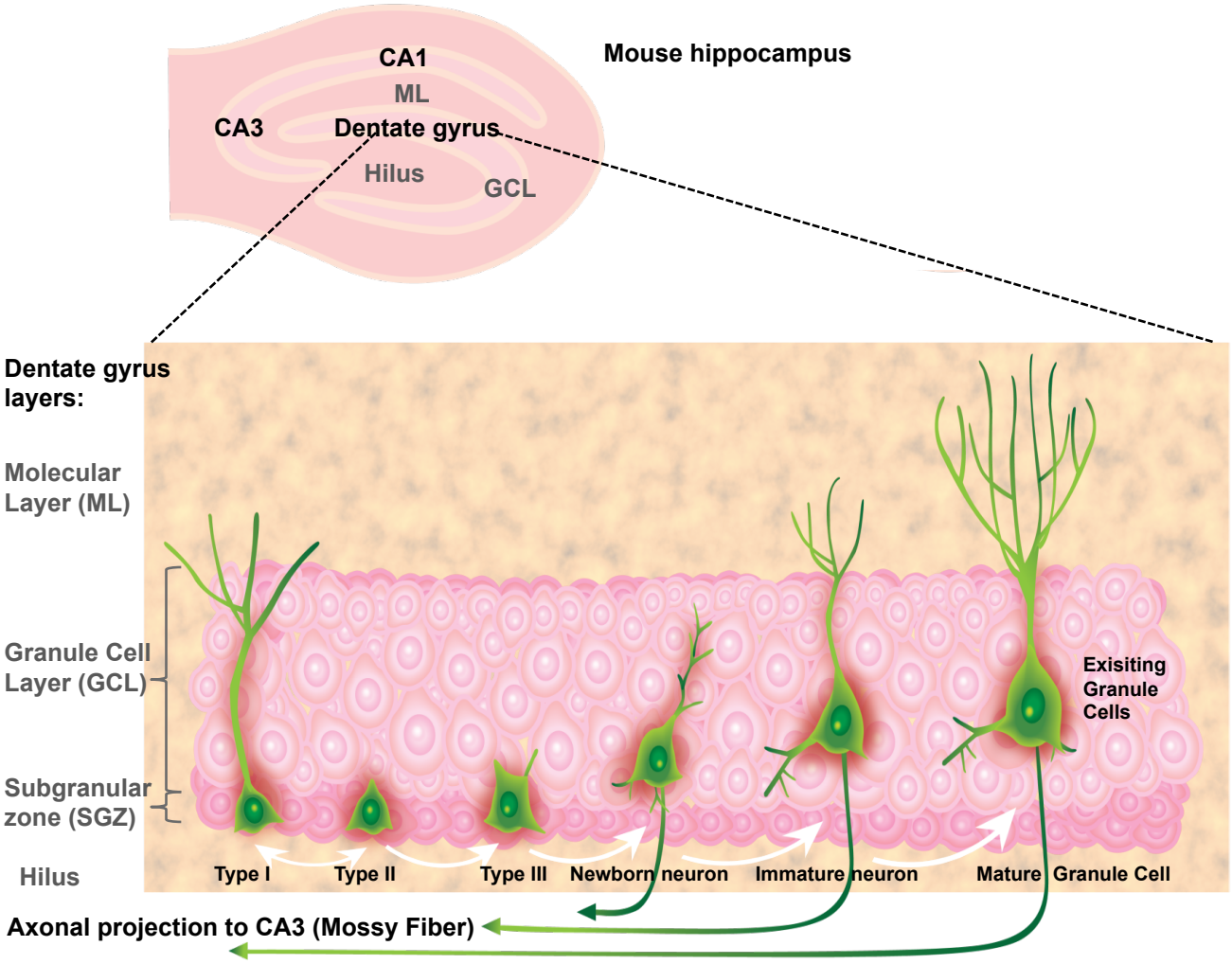
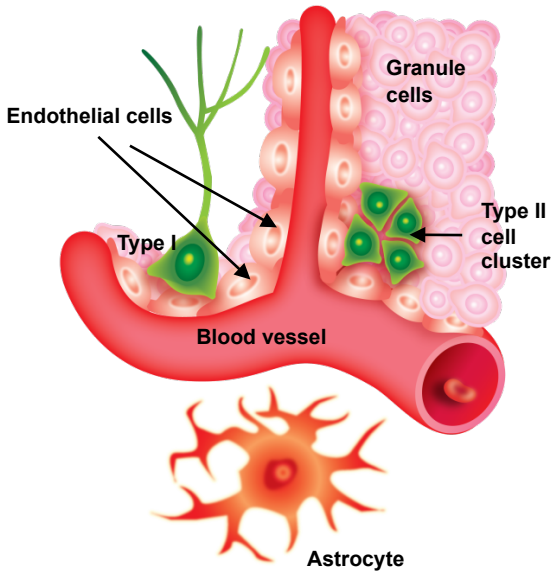
SUPPLEMENTARY INFORMATION 2



Phases of Adult Hippocampal Neurogenesis in the Mouse Model. The development of newborn granule cells in the dentate gyrus can be divided into specific stages – defined by morphological, electrophysiological and antigenic characteristics. Type I cells are multipotent (having the potential to differentiate into various lineages e.g. neurons, astrocytes or oligodendrocytes) and self-renewing (possessing the ability to produce identical daughter cells)[1]. These radial glial-like cells enter the cell cycle, becoming highly proliferative Type II cells[2]. They receive their first tonic GABA inputs from local interneurons, which facilitate neuronal fate decision[3, 4]. Within three to five days of birth at least 50% of newborn cells undergo programmed cell death[5] and typically 60 - 70 % of the surviving progenitors go on to adopt a neuronal lineage[6]. The post-mitotic Type III neural fate-committed progenitors then migrate radially from the subgranular zone into the granule cell layer[7]. Axonal outgrowth occurs through the hilus into the hippocampal CA3 region through the mossy fiber pathway, making its first contacts by the third week; dendrites sprout into the molecular layer and continue to elaborate over the next few weeks[8-10]. Newborn cells are first tonically activated by ambient GABA from local interneurons[11, 12]. Over time, they receive inhibitory GABAergic inputs and glutamatergic inputs via axosomatic, axodendritic, and axospinous synapses that aid in their maturation and synaptic integration process[7, 11-13]. Immature neurons have membrane properties and input connectivities that make them more excitable than their neighbouring mature neurons, with lower thresholds for long-term potentiation[7, 11, 12]. By two to three months, contacts made by the young adult-born neurons with multiple synaptic partners such as interneurons, hilar mossy cells and CA3 pyramidal cells are stabilized, and these neurons have the same morphological and functional characteristics of existing mature dentate granule cells[9, 10].

The hippocampal neurogenic niche. Within the subgranular zone of the rat dentate gyrus, dense clusters of Type II cells lie close to blood capillaries and astrocytes, which in turn regulate their maturation[14, 15]. The dentate gyrus is also richly innervated[16], with various neurotransmitters and neuropeptides dynamically governing adult hippocampal neurogenesis[17].



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