

Published in final edited form as:

*Glia*. 2008 October ; 56(13): 1463–1477. doi:10.1002/glia.20712.

## Morphogenesis and regulation of Bergmann glial processes during Purkinje cell dendritic spine ensheathment and synaptogenesis

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### Abstract

Astrocytes have an important role in synaptic formation and function but how astrocytic processes become associated with synaptic structures during development is not well understood. Here we analyzed the pattern of growth of the processes extending off the main Bergmann glial (BG) shafts during synaptogenesis in the cerebellum. We found that during this period BG process outgrowth was correlated with increased ensheathment of dendritic spines. In addition, two-photon time-lapse imaging revealed that BG processes were highly dynamic, and processes became more stable as the period of spine ensheathment progressed. While process motility was dependent on actin polymerization, activity of cytoskeletal regulators Rac1 and RhoG did not play a role in glial process dynamics or density, but was critical for maintaining process length. We extended this finding to probe the relationship between process morphology and ensheathment, finding that shortened processes result in decreased coverage of the spine. Furthermore, we found that areas in which BG expressed dn-Rac1, and therefore had a lower level of synaptic ensheathment, showed an overall increase in synapse number. These analyses reveal how BG processes grow to surround synaptic structures, elucidate the importance of BG process structure for proper development of synaptic ensheathment, and reveal a role for ensheathment in synapse formation.

### Keywords

Bergmann Glia; dendritic spines; synaptogenesis; Purkinje cell; Cerebellum; Rac1

### Introduction

Although glia are more numerous than neurons, their vital roles in complex brain functioning are poorly understood. Studies spanning the last decade revealed new aspects of the neuron/glia relationship beyond maintenance of the milieu, especially in synaptic function, plasticity, and spine and dendrite development (Amateau and McCarthy, 2002; Araque et al., 1998; Christopherson et al., 2005; Ge et al., 2006; Laming et al., 2000; Lin and Bergles, 2004; Lordkipanidze and Dunaevsky, 2005; Murai et al., 2003; Pfrieger and Barres, 1997; Takatsuru et al., 2006; Takayasu et al., 2006; Ullian et al., 2001; Yang et al., 2003; Zhang et al., 2003). The intimate morphological relationship between glial processes and synapses provides an