

**Weekly Colloquium**

Tuesday, 9/26/2017, 12:30pm, Billings Building – Rosedale Conference Room

**“The role of immune cells in neural degeneration and regeneration: New Perspectives”**

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The text book description of the role of macrophages in peripheral nerve injury is as follows: After a nerve injury, Schwann cells express and secreted the chemokine CCL2/MCP-1 and that acts on circulating monocytes through the receptor CCR2. The monocytes enter the distal nerve segment and differentiate into macrophages. These macrophages are thought to be essential for clearing myelin and axonal debris. Given this view, it was quite surprising that we found that clearance of this debris is entirely normal in CCR2 knockout (KO) mice even though there is a substantial decrease in the accumulation of macrophages in these animals. In our search for what cell accounts for this compensatory phagocytosis, we discovered that neutrophils play an important role in myelin clearance both in wild type and in CCR2 KO mice. Depletion of neutrophils leads to a reduction of myelin clearance. In 1995, we reported that in addition to accumulating in the distal nerve segment after an injury, macrophages accumulate in peripheral ganglia around axotomized neurons; however, for a number of years we were puzzled as to what role these phagocytic cells might play at this novel site. We subsequently found that, in two mouse mutants in which macrophages do not accumulate in dorsal root ganglia, the conditioning lesion response in sensory neurons was abolished. Infections of WT uninjured dorsal root ganglia neurons with AAV5 containing the coding region for CCL2 led to expression of CCL2 by these neurons, accumulation of macrophages in the DRG, and a stimulation of the intrinsic growth capacity of these neurons. We conclude that macrophages and neutrophils clear a pathway for regeneration by acting on the distal nerve segment after an injury and that macrophages enhance regeneration further by acting directly or indirectly on axotomized neuronal cell bodies.

**Recent Publications:**

Niemi JP, DeFrancesco-Lisowitz A, Roldan-Hernandez L, Mandell D, Zigmond RE. A critical role for macrophages near axotomized neuronal cell bodies in stimulating nerve regeneration. *J Neurosci* **33**:16236-16248, 2013.

Niemi JP, DeFrancesco-Lisowitz A, Cregg JM, Howarth M, Zigmond RE. Overexpression of the monocyte chemokine CCL2 in dorsal root ganglion neurons causes a conditioning-like increase in neurite outgrowth and does so via a STAT3-dependent mechanism. *Exp Neurol* **275**: 25-37, 2016.

DeFrancesco-Lisowitz A, Lindborg JA, Niemi JP, Zigmond RE. The neuroimmunology of degeneration and regeneration in the peripheral nervous system. *Neuroscience* **302**:174-203, 2015.

