PERICYTE, A NOVEL NEW ADULT STEM CELL, AMELIORATES AUTOIMMUNE ENCEPHALOMYELITIS

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Background: Rouget described the pericyte (PC) in 1873 as a contractile motile cell that surrounds the capillary in a tunic-like fashion. PCs are regulatory cells in the blood-brain barrier. They regulate capillary blood flow, vascular integrity, and angiogenesis. They are also a possible source of adult stem cells. Myelin oligodendrocyte glycoprotein (MOG)–immunized experimental autoimmune encephalomyelitis (EAE) mice were injected intravenously (IV) with 3- to 7-day-old PCs labeled with a fluorescent (IF) probe.

Objectives: We hypothesize that PCs can be used in therapeutic methods in central nervous system (CNS) diseases (eg, multiple sclerosis). To investigate the use of PCs in stem cell replacement therapy, we used an animal model of chronic CNS inflammation: EAE.

Methods: MOG-induced EAE: Female C57BL/6 mice were immunized with 100 μL (200 μg) of MOG in complete Freund’s adjuvant (CFA). Control mice received CFA without MOG. All mice were injected intraperitoneally with 200 μL of pertussis toxin (200 ng) after immunization and 2 days later. Mice were scored daily: 0 = no symptoms; 1 = flaccid tail; 2 = paresis of hind limbs; 3 = paralysis of hind limbs; 4 = quadriplegia; 5 = death. Isolation of microvessels (MVs) and PCs: Mouse CNS capillaries were prepared as described previously. Homogenized tissue was centrifuged and the pellet resuspended in DMEM/dextran. The suspension was centrifuged and the pellet resuspended and filtered through a series of meshes. MVs were collected, resuspended, and incubated overnight. PC pellet was resuspended in DMEM and plated. PC labeling and injection: PCs were removed from culture dishes, washed, pelleted, and resuspended with IF probe. The labeled PCs were injected IV (1–2 x 10⁵) into the mice. Tissue was harvested after 24 hours and prepared for fluorescence-activated cell sorting (FACS) analysis. FACS analysis: Single cell suspensions were incubated with antibody directed against indicated markers.

Results: 1) When injected into the blood, PCs migrate to all organs tested in small numbers. 2) PCs migrate in larger numbers to injured tissues. 3) PCs reduce clinical symptoms in EAE mice; preliminary data indicate that they did not relapse for at least 40 days.

Conclusions: The results confirm early work by the Dore-Duffy lab indicating that PCs have stem cell activity and a potential therapeutic role. The mechanism(s) of action is unknown and is currently being investigated.

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