

*EDITORIAL***RE-REDISCOVERY OF THE BRAIN'S LYMPHATIC SYSTEM**

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As we nursed our first colony of “crispr’d” [Science’s 2015 #1 Breakthrough, (1)] mice, we were equally excited to see the discovery of lymphatics in the brain as second runner-up (#3) on the People’s Choice top 10 list (2). However, this rediscovery (3) should really be considered a “re-rediscovery” of detailed research performed and reviewed from the 1960’s to 1990’s and published largely in the “lymphology” literature (4-6) including all editions of Földi et al’s widely read textbook since 1960, the latest in 2012 (7) and even earlier work from the 19th and 20th centuries (8-10). Nonetheless, non-lymphology texts and the literature ignored these findings, until a relatively recent slew of molecular lymphatic biomarkers were discovered, and continued to reiterate the “a-lymphatic” status of the brain, and, generally, to underestimate the importance of the lymphatic system in health and disease. These earlier studies by Professor Michael Földi himself or interpreted by him established compelling structural and functional evidence, even quantitatively, for the brain’s lymphatic drainage system via the pre-lymphatic perivascular spaces of Virchow-Robin, the subarachnoid space and cerebrospinal fluid, eventually reaching the cervical lymph node network and central

veins. He also was the first to describe “lymphostatic encephalopathy”(4-7), a clinical condition seen in patients with cervical lymphatic obstruction and replicated in experimental animals. In several other ways, 2015 has been the year of the lymphatic system and lymphology, when the discipline celebrated its 50th anniversary at the 25th World Congress of Lymphology in San Francisco (see this issue’s ISL News) and the Nobel Prize in Medicine was awarded for the discovery of ivermectin to treat the millions suffering from lymphatic filariasis in the endemic areas. Lucid at 96, with no evidence of impaired CNS lymph drainage, lymphologist extraordinaire Michael Földi is doubtless pleased to see Louveau et al’s exquisite molecular delineation of the brain’s lymphatic system and the renewed impetus to explore its role in human disease.

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