

Stanford

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Bio

ACADEMIC APPOINTMENTS

- Emeritus Faculty, Acad Council, Pathology

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Astrocytes make up a substantial proportion of the central nervous system (CNS) and participate in a variety of important physiologic and pathologic processes. They are characterized by vigorous response to diverse neurologic insults and induction of the glial fibrillary acidic protein (GFAP) gene, a feature that is well conserved across a variety of different species. The prominence of astroglial reactions in various diseases, the rapidity of the astroglial response and the evolutionary conservation of reactive astrogliosis indicate that reactive astrocytes fulfill important functions of the CNS. It is important to identify the essential molecular mechanisms which activate metabolic responses in astrocytes in order to understand astrogliosis. Our experimental models include:

- 1) Primary dissociated rodent brain astrocyte cultures,
- 2) Growth factor transfected astrocytes transplanted into contused rat spinal cord,
- 3) Brain stab wound. Longitudinal studies are being carried out to determine the induction of cytoskeletal proteins, cytokines, early response genes, and growth factors in the mechanical injury model of rat spinal cord and in a stab wound injury to mouse and rat brains.

The study employs quantitative reverse transcriptase-polymerase chain reaction, immunocytochemistry, in situ hybridization, ELISA assays, Western blot, and Northern blot. Normal and transgenic mice containing a transgenic vector composed of a 2.2 kb 5'-flanking sequence derived from the GFAP gene fused to the E coli lacZ structural gene GFAP null, and GFAP overexpressing mice are being used. Some of the substances to be determined are c-Fos, c-Jun, heat shock protein, IL-1, IL-6, TNF α , NGF β , CNTF, EGF, PDGF, GFAP, LIF, MIP, vimentin, and actin. Identification of those factors that promote and those that inhibit regeneration will allow one to devise therapeutic protocols to treat spinal cord injury. These treatments could employ antisense oligonucleotides, antibodies, growth factors, enzymes, pharmaceutical drugs, and gene therapies.

Publications

PUBLICATIONS

- **Astrocytoma and Schwann cells in coculture** *MOLECULAR AND CHEMICAL NEUROPATHOLOGY*
Lal, P. G., Ghirnikar, R. S., Eng, L. F.
1996; 29 (1): 93-104
- **Astrocyte-astrocytoma cell line interactions in culture** *JOURNAL OF NEUROSCIENCE RESEARCH*
Lal, P. G., Ghirnikar, R. S., Eng, L. F.
1996; 44 (3): 216-222
- **Inflammation in EAE: Role of chemokine/cytokine expression by resident and infiltrating cells** *NEUROCHEMICAL RESEARCH*
Eng, L. F., Ghirnikar, R. S., Lee, Y. L.
1996; 21 (4): 511-525