

Richard A Weisiger, M.D.

Clinical Professor of Medicine
Chief, GI Faculty Gastroenterology and Liver Practices

Academic Office

Division of Gastroenterology
513 Parnassus Avenue, Room S-357
San Francisco, CA 94143-0358
Phone: 415-476-6422
Fax: 415-476-0659
Email: dick.weisiger@ucsf.edu

Clinic

UCSF GI Faculty Practice
350 Parnassus Avenue, Suite 410
San Francisco, CA 94143-0657
Phone: 415-353-2318
Fax: 415-353-2407



Research Program

Investigation of the pathophysiology of functional disorders, with an emphasis on irritable bowel syndrome. Many disorders including depression, fibromyalgia and irritable bowel syndrome are now believed to be caused by inappropriate activation of brain stress pathways. While the stress response was adaptive in the ancestral environment where stress was usually brief (e.g., escaping a fire or flood), stress in modern life may persist for months or years. The resulting activation of stress pathways may cause multiple somatic symptoms (e.g., headache, anxiety, depression, abdominal pain, bloating, constipation, diarrhea) in the absence of organic disease. This is a major and increasing cause of morbidity, absenteeism from work, and health care expenditures in the United States.

Recent animal data indicate that abuse or neglect during early life causes permanent activation of brain stress pathways involving corticotrophin releasing factor (CRF). These changes strongly predispose to functional disorders in adults. The mechanism appears to be permanent inactivation of the promoter for the glucocorticoid receptor in the brain, which normally feeds back to inhibit the stress response. Permanent activation of central stress pathways can be triggered by a single episode of severe abuse or only a few days of neglect. It now appears to be mediated by increased DNA methylation and decreased histone acetylation, both of which lead to decrease expression of the glucocorticoid receptor. This is the first known example of postnatal epigenetic programming of genes by environmental factors, and opens up an entire new field of research. Nearly all of these data come from murine models. I am in the process of sharing these findings with members of the UCSF research community and hope to be able to further test these concepts in humans from my GI clinic.

Education

- 1964-68 Princeton University B.A. Chemistry
- 1968-74 Duke University School of Medicine M.D. Medicine
- 1970-73 Duke University School of Medicine Ph.D. Biochemistry
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Training

- 1974-75 Washington University School of Medicine Intern Medicine
- 1976 Washington University School of Medicine Resident Medicine
- 1976-78 National Institutes of Health Postdoctoral Fellow Biochemistry, Metabolism
- 1978-80 UCSF School of Medicine, Fellow Medicine - Gastroenterology

Certification

- 1977 Diplomate in Internal Medicine The American Board of Internal Medicine
- 1978 Licensed as a Physician and Surgeon State of California
- 1981 Diplomate in Gastroenterology The American Board of Internal Medicine

Memberships and Affiliations

Memberships

- 1980-present American Society for Clinical Research
- 1981-present American Association for the Study of Liver Diseases
- 1983-present Graduate Research Group
- 1983-present American Association for the Advancement of Science

Service to Professional Organizations

- 1984-present Western Society for Clinical Investigation
- 1988-present International Association for the Study of the Liver
- 1989-present American Society for Clinical Investigation
- 1992-98 California Academy of Medicine
- 1992-01 European Society for Clinical Investigation
- 1994-present Western Association of Physicians
- 1994-present American Physiologic Society
- 1996-present American Gastroenterology Association
- 1984-88 Grant review committee, American Liver Foundation Committee Member
- 1984-88 Abstract Selection Committee, AASLD Committee Member
- 1986 Chaired meeting session, Western Society for Clinical Investigation Committee Chair
- 1991-96 American Journal of Physiology Editorial Board
- 1993 Chaired National Meeting session, American Society for Clinical Investigation, Session Chairman
- 1994 Personally wrote and implemented first website for AASLD, American Association for the Study of Liver Diseases
- 1995 Conceived of and Organized FASEB Symposium on Cytoplasmic Transport, Atlanta GA, American Physiology Society
- 1995-97 Training and Education Committee, American Association for the Study of Liver Diseases Committee Member
- 2000 Communications Committee, American Association for the Study of Liver Diseases Committee Member
- 2001-04 Website Committee, American Association for the Study of Liver Diseases Committee Chair
- 2005 Kentucky Science & Engineering Foundation External reviewer

Selected Publications

- Weisiger RA, Ostrow JD, Koehler RK, Webster CC, Mukerjee P, Pascolo L, Tiribelli C. Affinity of human serum albumin for bilirubin varies with albumin concentration and buffer composition: results of a novel ultrafiltration method. *J Biol Chem*, Aug/10/2001;276(32):29953-60.
- Weisiger RA, Zucker SD. Transfer of fatty acids between intracellular membranes: roles of soluble binding proteins, distance, and time. *Am J Physiol Gastrointest Liver Physiol*, Jan/2002;282(1):G105-15.
- Weisiger RA. Cytosolic fatty acid binding proteins catalyze two distinct steps in intracellular transport of their ligands. *Mol Cell Biochem*, Oct/2002;239(1-2):35-43.
- Weisiger, RA. Mechanisms of intracellular fatty acid transport: role of cytoplasmic-binding proteins *J Mol Neurosci*, 2007;33(9):42-44.

- Weisiger RA, Bilhartz LE. Gastrointestinal and Liver Disease, Review and Assessment, 2 Ed. WB Saunders, Philadelphia. 1-240: 2002.
- Weisiger RA. Conjugated hyperbilirubinemia. Editor(s): Gumaste V. Online Textbook of Medicine, OB/GYN, Psychiatry and Surgery: eMedicine, 2005.
- Weisiger RA. Isoniazid hepatotoxicity. Editor(s): Lewis T. Online Textbook of Medicine, OB/GYN, Psychiatry and Surgery: eMedicine, 2005.
- Weisiger RA. Albumin and other plasma binding proteins, 3 Ed. Editor(s): Benhamou et. al. Oxford Textbook of Hepatology: Blackwell Publishing, Oxford. 1-14, 2007.
- Weisiger RA. Isoniazid Hepatotoxicity. Online Textbook of Medicine, OB/GYN, Psychiatry and Surgery: eMedicine.com, 2007.
- Weisiger RA. Conjugated Hyperbilirubinemia. Online Textbook of Medicine, OB/GYN, Psychiatry and Surgery: eMedicine.com, 2007.