Edward Lewis Tobinick, MD Curriculum Vitae June 2015

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Education

1969-73 B.A. Magna Cum Laude, with honors in Biology, Phi Beta Kappa, Brandeis University. 1973-1977 MD, UCSD School of Medicine

1977 Subinternship in Neurology, Memorial Sloan Kettering - New York Hospital Neurology Program (one month rotation)

1977-1978 Internship in Internal Medicine, UCLA 1978-82 UCLA Internal Medicine & Dermatology Residencies

1980 Diplomate, American Board of Internal Medicine

1982 Diplomate, American Board of Dermatology

Academic and Journal Appointments

1984 - 2011 Assistant Clinical Professor of Medicine, UCLA School of Medicine

2008-2010 Editorial Board, *Journal of Neuroinflammation*

2009-2015: Invited ad hoc reviewer for the following journals: Brain Research, CNS Drugs, Current Alzheimer Research, Experimental Neurology, Future Neurology, Journal of Neurochemistry, Journal of Neuroimmunology, Neuroscience and Pharmaceutical Medicine

Specialty Board Certifications/ Licensure

1980-present (2015) Certified, American Board of Internal Medicine

1982-present (2015) Certified, American Board of Dermatology

Active medical licenses: California, Florida

Professional Societies

1984 - 2008: Fellow of the American Academy of Dermatology.1998 - 2010: ASLMS.2010-2015: American Academy of Pain Medicine.

Honors/Certificates

National Honor Society, 1969
Phi Beta Kappa, Brandeis University, 1973
UCLA Department of Medicine Five Year
Teaching Certificate, 1987
UCLA Department of Medicine Ten Year
Teaching Certificate, 1992
Venice Family Clinic Certificate of Appreciation
for Volunteer Teaching, 1992

Venice Family Clinic, Rossman/Davidson Clinical Teaching/Service Award, 2005

Publications - Neurology

Perispinal etanercept for traumatic brain injury(book chapter). Tobinick E, Rodriguez-Romanacce H, Kinssies R, Kim N, in K.A. Heidenreich Editor, New Therapeutics for Traumatic Brain Injury: Prevention of secondary brain damage and enhancement of repair and regeneration, Elsevier, in preparation, publication scheduled for 2016.

Authors' reply to Whitlock: Perispinal etanercept for post-stroke neurological and cognitive dysfunction:scientific rationale and current evidence. Ignatowski TA, Spengler RN, Tobinick E. CNS Drugs, 2014 Dec, 28(12):1207-13.

Perispinal etanercept for post-stroke neurological and cognitive dysfunction:scientific rationale and current evidence. Ignatowski TA, Spengler RN, Dhandapani KM, Folkersma H, Butterworth RF, Tobinick E. <u>CNS Drugs</u> 2014 Dec, 28(12):1207-13.

Immediate neurological recovery following perispinal etanercept years after brain injury. Tobinick E, Rodriguez-Romanacce H, Levine A, Ignatowski TA, Spengler RN. Clinical Drug Investigation, 2014 May; 34(5):361-6.

Author's reply to Page: "Selective TNF inhibition for chronic stroke and traumatic brain injury: an observational study involving 629 consecutive patients treated with perispinal etanercept". Tobinick E. CNS Drugs. 2013 May; 27(5):399-402.

Selective TNF inhibition for chronic stroke and traumatic brain injury: an observational study involving 629 consecutive patients treated with perispinal etanercept. Tobinick E, Kim NM, Reyzin G, Rodriguez-Romanacce H, DePuy V. CNS Drugs. 2012 Dec; 26(12):1051-70. PMID:23100196.

Deciphering the physiology underlying the rapid clinical effects of perispinal etanercept in Alzheimer's disease. Edward Tobinick. Current Alzheimer Research. 2012 Jan; 9(1):99-109. PMID:22191562.

Rapid improvement of chronic stroke deficits after perispinal etanercept: three consecutive cases. Edward Tobinick. CNS Drugs. 2011 Feb; 25(2):145-155. PMID:212547090.

(continued next page)

Publications - Neurology, continued

- Perispinal etanercept: a new therapeutic paradigm in neurology. Edward Tobinick. Expert Review of Neurotherapeutics. 2010 June; 10(6):985-1002. PMID:20518613.
- Tumor necrosis factor modulation for treatment of Alzheimer's disease: rationale and current evidence. Edward Tobinick. CNS Drugs. 2009 Sept; 23(9):713-25. PMID:19689163.
- Perispinal etanercept for neuroinflammatory disorders. Edward Tobinick. Drug Discovery Today, 2009 Feb, 14(3-4): 168-77.
- Rapid intracerebroventricular delivery of 64-Cu-DOTA-etanercept after peripheral administration demonstrated by PET imaging. Edward Tobinick, K. Chen, X. Chen. BMC Research Notes, 2009 Feb 27, 2:28.
- Rapid improvement in verbal fluency and aphasia following perispinal etanercept in Alzheimer's disease. Edward Tobinick, Hyman Gross, BMC Neurology, 2008, 8(1): 27.
- Perispinal etanercept produces rapid improvement in primary progressive aphasia: Identification of a novel, rapidly reversible TNF-mediated pathophysiologic mechanism. Edward Tobinick. Medscape J Med, 2008 10(6): 135.
- Rapid cognitive improvement in Alzheimer's disease following perispinal etanercept administration. Edward Tobinick, Hyman Gross. J Neuroinflammation. 2008 Jan 9:5:2.
- A critique of intradiscal administration for treatment of radiculopathy. Edward Tobinick. Anesthesiology, 2008 108(2): 334; author reply 335.
- New horizons in the treatment of Alzheimer's disease: Immunotherapeutics. Edward Tobinick, U.S. Neurology, 2008; 4(1): 34-36.
- Perispinal etanercept for treatment of Alzheimer's disease. Edward Tobinick, Current Alzheimer Research, 2007 4(5): 550-2.
- Resolution of chronic pain and fingertip ulceration due to hand-arm vibration syndrome following combination pharmacotherapy. Buell, C., E. Tobinick, K. Lamp, H. Arch Derm, 2007 143 (10): p. 1343-4.

- Paradigm Shift: Excess TNF-alpha emerges as a key therapeutic target in Alzheimer's disease. Edward Tobinick, Medscape General Medicine, 2007 9(3): 17.
- TNF Modulation for Treatment of Alzheimer's Disease: A Six Month Pilot Study. Edward Tobinick MD, H. Gross MD, A. Weinberger MD, H. Cohen MD FRCPC, Medscape General Medicine, 2006 April; 8(2): 25.
- Spinal delivery of p38 and TNF-alpha inhibitors. Edward Tobinick, MD, PLoS Medicine, 2006; 3(11): e511.
- Efficacy of etanercept delivered by perispinal administration for chronic back and/or neck disc-related pain: a study of clinical observations in 143 patients. Edward Tobinick, MD, et. al. Current Medical Research and Opinion, 2004 20(7): 1075-85.
- Targeted etanercept for discogenic neck pain:uncontrolled, open-label results in two adults. Edward Tobinick, Clinical Therapeutics, 2003 Apr 1; 25: 1211-1218.
- Perispinal TNF-alpha inhibition for discogenic pain. Edward Tobinick et. al, Swiss Med W. 2003 Mar;133(11-12):170-7.

Abstracts & Presentations - Neurology

- Perispinal TNF-alpha inhibition for discogenic pain.
 Invited presentation by Edward Tobinick MD at the
 2nd Annual Restauracion Neurologica 2004
 International Conference, Havana, Cuba, February
 27, 2004.
- TNF Modulation for Treatment of Alzheimer's Disease:
 A Six Month Pilot Study. Edward Tobinick MD, H.
 Gross MD, A. Weinberger MD, H. Cohen MD FRCPC.
 Accepted abstract for the 10th International
 Conference on Alzheimer's Disease and Related
 Disorders, Madrid, Spain, July 19, 2006.
- TNF Modulation for Treatment of Alzheimer's Disease: Effects on Verbal Function. Edward Tobinick MD, David Shirinyan, H. Gross. Days of Molecular Medicine Conference, Karolinska Institutet, Stockholm, Sweden, May 27, 2006.

Abstracts & Presentations - Neurology

- Perispinal etanercept for treatment of Alzheimer's Disease. Edward Tobinick MD. Invited presentation at the 7th International Conference on Alzheimer's Disease Drug Discovery, NYC, October 12, 2006, published in Alzheimer's and Dementia: the Journal of the Alzheimer's Association, 2 (3), p. S721-782, July 2006.
- Perispinal etanercept for treatment of Alzheimer's Disease. Edward Tobinick MD. Invited presentation at the Best Practices in the Continuum of Care: Advances in Alzheimer's Disease Management conference for University of Arkansas for Medical Sciences, Little Rock, Arkansas, April 16, 2008.
- Perispinal etanercept produces rapid improvement in primary progressive aphasia. Abstract presented at the 11th International Conference on Alzheimer's Disease, Chicago, Illinois, July 30, 2008, published in Alzheimer's and Dementia: the Journal of the Alzheimer's Association, 4 (4) T1-880, July 2008.
- Repurposing of Enbrel for Alzheimer's Disease. Keynote presentation by Edward Tobinick MD Third Annual Drug Repositioning Summit, Boston, Massachusetts, October 6-7, 2008.
- Perispinal etanercept for Alzheimer's Disease. Invited presentation at Restauracion Neurologica 2009 International Conference, Havana, Cuba, March 11, 2009.
- TNF antagonists for neurological disorders: from concept to the clinic. Presentation at GTC bio's 5th Modern Drug Discovery & Development Conference, October 14-16, 2009, San Diego, California.
- TNF modulation for treatment of Alzheimer's disease. Presentation by Edward Tobinick MD at the inaugural Targeting Alzheimer's with Novel Therapeutics Conference at the World Pharmaceutical Congress, Philadelphia, Pennsylvania, June 11, 2009.
- Neuroinflammation as a new therapeutic target in neurology. Presentation by Edward Tobinick MD at University Hospital, Tamarac, Florida, Medical Staff CME Lecture, November 10, 2011.

Presentations - Neurology, continued

TNF inhibition for aphasia after stroke or brain injury. Presentation by Edward Tobinick MD and H. Rodriguez at the Florida Association of Speech Language Pathologists & Audiologists (FLASHA) 2015 Annual Convention, May 30, 2015, Fort Lauderdale, Florida.

Publication - Anatomy/Physiology

The Cerebrospinal Venous System: Anatomy, Physiology, and Clinical Implications. Edward Tobinick, Medscape General Medicine, 2006 February; 8(1): 53.

Publication - Cardiology

Right Ventricular Ejection Fraction in Patients with Acute Anterior and Inferior Myocardial Infarction Assessed by Radionuclide Angiography, Tobinick E, Schelbert H, Henning H, et. al. Circulation 57: 1078-1084, June 1978.

Publications - Dermatology

- **Basal Cell Carcinoma**. Edward Tobinick M.D., American Family Physician, 36:(3)219-224, September, 1987.
- Textbook: *Skin Surgery, A Practical Guide*Usatine R, Tobinick E, Moy R,Siegel D.
 Mosby 1998, 337 pp.

Publication - Immunology/Virology

TNF-alpha inhibition for potential therapeutic modulation of SARS coronavirus infection. Tobinick E, Curr Med Res Opin, 20(1) 39-40, Jan. 2004.

Publication - Oncology/Neurology

Targeted Etanercept for Treatment-Refractory Pain Due to Bone Metastasis: Two Case Reports. Edward Tobinick, MD, Clinical Therapeutics, 2003 August; 25: 2279-2288.

Publication - Pharmacology

The value of drug repositioning in the current pharmaceutical market. Edward Tobinick, <u>Drug News and Perspectives</u>, 2009 Mar; 22(2): 119-125.

U.S. patents issued- Neurology

- [6,015,557 patent reissue, pending 2015] *Tumor necrosis factor antagonists for the treatment of neurological disorders*. Issued January 18, 2000; filed March 23, 1999.
- 6,419,934 B1 TNF modulators for treating neurological disorders associated with viral infection. Issued July 16, 2002; filed September 5, 2000.
- 6,379,666 B1 *TNF inhibitors for the treatment of neurological, retinal, and muscular disorders.* Issued April 30, 2002; filed December 11 2000.
- 6,423,321 B2 *Cytokine antagonists for the treatment of sensorineural hearing loss*. Issued July 23, 2002; filed December 27, 2000.
- 6,471,961 *Interleukin antagonists for the treatment of neurological, retinal and muscular disorders*. Issued October 29, 2002; filed May 2, 2000.
- 6,419,944 *Cytokine antagonists for the treatment of localized disorders.* Issued July 16, 2002, filed April 5, 2001.
- 6,537,549 *Cytokine antagonists for the treatment of localized disorders.* Issued March 25, 2003, filed April 25, 2001.
- 6,982,089 **Cytokine antagonists for neurological and neuropsychiatric disorders.** Issued January 3, 2006.
- 7,214,658 Method of delivering a TNF antagonist to the brain of a human by perispinal administration without direct intrathecal injection. Issued May 8, 2007.
- 7,629,311 Methods to facilitate transmission of large molecules across the blood-brain, blood-eye, and blood-nerve barriers. Issued Dec 8, 2009.
- 8,119,127 *Cytokine antagonists for neurological and neuropsychiatric disorders*. Issued Feb 21, 2012.
- 8,236,306 Methods to facilitate transmission of large molecules across the blood-brain, blood-eye, and blood-nerve barriers. Issued Aug 7, 2012.
- 8,349,323 *Cytokine antagonists for neurological and neuropsychiatric disorders*. Issued January 8, 2013.
- 8,900,583 *Methods for treatment of brain injury utilizing biologics*. Filed October 31, 2011. Issued December 2, 2014.

Note: All issued U.S. patents are assigned to TACT IP, LLC. Additional U.S. and International patents pending.

Foreign patents

758,523 (**Australia**) *TNF antagonists for the treatment of neurological disorders*. Issued July 2003. Multiple additional foreign patents pending.

U.S. patent issued- Opthalmology

6,428,787 B1 **TNF** inhibitors for the treatment of retinal disorders. Issued August 6, 2002; filed September 19, 2000.

U.S. patents issued- Laser

6,080,147; 6,149,645; 6,165,171; 6,168,589; 6,217,572; 6,579,283; 6,595,985.

100 selected scientific articles 2003-2015 citing publications by Edward Tobinick [1-27]:

- Karppinen, J., et al., Tumor necrosis factor-alpha monoclonal antibody, infliximab, used to manage severe sciatica. Spine, 2003. 28(8): p. 750-3.
- 2. Sommer, C. and M. Schafers, *Mechanisms of neuropathic pain: the role of cytokines*. Drug Discov Today: Disease Mechanisms, 2004. **1**(4): p. 441-448.
- 3. Myers, R.R., W.M. Campana, and V.I. Shubayev, *The role of neuroinflammation in neuropathic pain: mechanisms and therapeutic targets.* Drug Discov Today, 2006. **11**(1-2): p. 8-20.
- 4. Pearce, J.M., The craniospinal venous system. Eur Neurol, 2006. 56(2): p. 136-8.
- 5. Mulleman, D., et al., *Pathophysiology of disk-related low back pain and sciatica. II. Evidence supporting treatment with TNF-alpha antagonists.* Joint Bone Spine, 2006. **73**(3): p. 270-7.
- 6. Dana Alliance, *The 2007 Progress Report on Brain Research*. Progress Report on Brain Research 2007, New York: Dana Press.
- 7. DeWitte, M., D.J. Shealy, M.T. Nakada, and G.M. Anderson, *Chapter 4- TNF and Cancer*, in *Cytokines in the Genesis and Treatment of Cancer*, M.A. Caligiuri and M.T. Lotze, Editors. 2007, Humana Press: Totowa, NJ. p. 71-90.
- 8. Tubbs, R.S., A. Hansasuta, M. Loukas, R.G. Louis, Jr., et al., The basilar venous plexus. Clin Anat, 2007. 20(7): p. 755-9.
- 9. Tweedie, D., K. Sambamurti, and N.H. Greig, *TNF-alpha inhibition as a treatment strategy for neurodegenerative disorders: new drug candidates and targets.* Curr Alzheimer Res, 2007. **4**(4): p. 378-85.
- 10. Van Eldik, L.J., W.L. Thompson, H.R. Ranaivo, H.A. Behanna, et al., *Glia Proinflammatory Cytokine Upregulation as a Therapeutic Target for Neurodegenerative Diseases: Function-Based and Target-Based Discovery Approaches*, in *Neuroinflammation in Neuronal Death and Repair*, G. Bagetta, M.T. Corasaniti, and S.A. Liption, Editors. 2007, Elsevier. p. 278-297.
- 11. Perispinal administration of anti-TNF agent results in rapid cognitive improvement in AD. Nature Clinical Practice Neurology, 2008. 5: p. 2.
- 12. Auffray, C., Evaluations for Tobinick, EL and Gross H J of Neuroinflammation. Faculty of 1000 Biology, 2008. 5(1): p. 2.
- 13. Goldberg, R.J., International conference on Alzheimer's disease 2008: Summary of new research: perispinal etanercept improves primary progressive aphasia. Brown University Geriatric Psychopharmacology Update, 2008. 12(10): p. 4.
- 14. Griffin, W.S., Perispinal etanercept: potential as an Alzheimer therapeutic. J Neuroinflammation, 2008. 5: p. 3.
- 15. Ignatowski, T.A. and R.N. Spengler, *Cytokines in Synaptic Function*, in *Cytokines and the Brain*, I. Berczi and A. Szentivanyi, Editors. 2008, Elsevier: Amsterdam, Netherlands. p. 111-143.
- 16. Wang, Y., *P4-266: Modification of synaptic plasticity by TNF and sphingomyelinase: Implications for cognitive impairment in Alzheimer's disease.* Alzheimer's and Dementia, 2008. **4**(4 Supplement): p. T749.
- 17. Zanella, J.M., E.N. Burright, K. Hildebrand, C. Hobot, et al., *Effect of etanercept, a tumor necrosis factor-alpha inhibitor, on neuropathic pain in the rat chronic constriction injury model.* Spine (Phila Pa 1976), 2008. **33**(3): p. 227-34.
- 18. Bruni, J.E. and D.G. Montemurro, *Chapter 4- Blood Supply of the Nervous System*, in *Human Neuroanatomy: A Text, Brain Atlas, and Laboratory Dissection Guide*, J.E. Bruni and D.G. Montemurro, Editors. 2009, Oxford University Press: New York, N.Y. p. 51-64.
- 19. Di Bona, D., G. Candore, C. Franceschi, F. Licastro, et al., Systematic review by meta-analyses on the possible role of TNF-alpha polymorphisms in association with Alzheimer's disease. Brain Res Rev, 2009. **61**(2): p. 60-8.
- 20. Furst, D.E., E.C. Keystone, R. Fleischmann, P. Mease, et al., *Updated consensus statement on biological agents for the treatment of rheumatic diseases*, 2009. Ann Rheum Dis, 2009. **69 Suppl 1**: p. i2-29.
- 21. Kato, K., S. Kikuchi, V.I. Shubayev, and R.R. Myers, *Distribution and tumor necrosis factor-alpha isoform binding specificity of locally administered etanercept into injured and uninjured rat sciatic nerve*. Neuroscience, 2009. **160**(2): p. 492-500.
- 22. Alamin, T.F. and V. Agarwal, *Chapter 5- The Mechanisms of Pain from Intervertebral Discs*, in *The Lumbar Intervertebral Disc*, F.M. Phillips and C. Lauryssen, Editors. 2010, Thieme Medical Publishers.
- 23. Bassi, E. and C. De Filippi, *Beneficial neurological effects observed in a patient with psoriasis treated with etanercept.* Am J Clin Dermatol, 2010. **11 Suppl 1**: p. 44-5.
- 24. Beattie, M.S., A.R. Ferguson, and J.C. Bresnahan, *AMPA-receptor trafficking and injury-induced cell death*. Eur J Neurosci, 2010. **32**(2): p. 290-7.
- 25. Buchhave, P., H. Zetterberg, K. Blennow, L. Minthon, et al., Soluble TNF receptors are associated with Abeta metabolism and conversion to dementia in subjects with mild cognitive impairment. Neurobiol Aging, 2010. 31(11): p. 1877-84.
- 26. Chio, C.C., J.W. Lin, M.W. Chang, C.C. Wang, et al., *Therapeutic evaluation of etanercept in a model of traumatic brain injury.* J Neurochem, 2010. **115**(4): p. 921-9.
- 27. Clark, I.A., L.M. Alleva, and B. Vissel, *The roles of TNF in brain dysfunction and disease*. Pharmacol Ther, 2010. **128**(3): p. 519-48.

100 selected scientific articles 2003-2015 citing publications by Edward Tobinick [28-52]:

- 28. Labbate, L.A., J.F. Rosenbaum, M. Fava, and G.W. Arana, *Chapter 8- Drugs for the treatment of dementia*, in *Handbook of Psychiatric Drug Therapy*, L.A. Labbate, et al., Editors. 2010, Lippincott Williams & Wilkins/Wolters Kluwer Health: Philadelphia, PA. p. 254-264.
- 29. McNaull, B.B., S. Todd, B. McGuinness, and A.P. Passmore, *Inflammation and anti-inflammatory strategies for Alzheimer's disease—a mini-review.* Gerontology, 2010. **56**(1): p. 3-14.
- 30. Shubayev, V.I., K. Kato, and R.R. Myers, *Chapter 8- Cytokines in pain*, in *Translational Pain Research: From Mouse to Man*, L. Kruger and A.R. Light, Editors. 2010, CRC Press/Taylor & Francis: Boca Raton, FL.
- 31. Cavanagh, C., J. Colby-Milley, M. Farso, S. Krantic, et al., Early molecular and synaptic dysfunctions in the prodromal stages of Alzheimer's disease: focus on TNF-alpha and IL-1Beta. Future Neurology, 2011. 6(6): p. 757-769.
- 32. Esposito, E. and S. Cuzzocrea, Anti-TNF therapy in the injured spinal cord. Trends Pharmacol Sci, 2011. 32(2): p. 107-15
- 33. Frankola, K.A., N.H. Greig, W. Luo, and D. Tweedie, *Targeting TNF-alpha to Elucidate and Ameliorate Neuroinflammation in Neurodegenerative Diseases*. CNS Neurol Disord Drug Targets, 2011. **10**(3): p. 391-403.
- 34. Jiang, H., H. Hampel, D. Prvulovic, A. Wallin, et al., *Elevated CSF levels of TACE activity and soluble TNF receptors in subjects with mild cognitive impairment and patients with Alzheimer's disease.* Molecular Neurodegeneration, 2011. **6**(1): p. 69.
- 35. Jicha, G.A. and P.T. Nelson, Management of frontotemporal dementia: targeting symptom management in such a heterogeneous disease requires a wide range of therapeutic options. Neurodegener Dis Manag, 2011. 1(2): p. 141-156.
- 36. Kowall, N.W., Chapter 10- Rational therapeutics for Alzheimer's disease and other dementias, in The Handbook of Alzheimer's Disease and Other Dementias, A.E. Budson and N.W. Kowall, Editors. 2011, Blackwell Publishing: West Sussex, UK. p. 301-311.
- 37. Nathoo, N., E.C. Caris, J.A. Wiener, and E. Mendel, *History of the vertebral venous plexus and the significant contributions of Breschet and Batson*. Neurosurgery, 2011. **69**(5): p. 1007-14; discussion 1014.
- 38. Patterson, J., F-A-S test, in Encyclopedia of Clinical Neuropsychology, J.S. Kreutzer, J. DeLuca, and B. Caplan, Editors. 2011, Springer Science+Business Media: New York, NY. p. 1024.
- 39. Rossi, D., F. Martorana, and L. Brambilla, *Implications of gliotransmission for the pharmacotherapy of CNS disorders*. CNS Drugs, 2011. **25**(8): p. 641-58.
- 40. Roth, J.L., B.R. Ott, J.N. Gaitanis, and A.S. Blum, *Chapter 15- The Neuroimmunology of Cortical Disease (Dementia, Epilepsy, and Autoimmune Encephalopathies)*, in *Clinical Neuroimmunology: Multiple Sclerosis and Related Disorders*, S.A. Rizvi and P.K. Coyle, Editors. 2011, Springer Science + Business Media: New York, NY. p. 275-290.
- 41. Shi, J.Q., W. Shen, J. Chen, B.R. Wang, et al., Anti-TNF-alpha reduces amyloid plaques and tau phosphorylation and induces CD11c-positive dendritic-like cell in the APP/PS1 transgenic mouse brains. Brain Res, 2011. 1368: p. 239-47.
- 42. Simen, A.A., K.A. Bordner, M.P. Martin, L.A. Moy, et al., *Cognitive dysfunction with aging and the role of inflammation*. Therapeutic Advances in Chronic Disease, 2011. **2**(3): p. 175-195.
- 43. Butchart, J. and C. Holmes, *Systemic and Central Immunity in Alzheimer's Disease: Therapeutic Implications.* CNS Neuroscience & Therapeutics, 2012.
- 44. Clark, I., New hope for survivors of stroke and traumatic brain injury. CNS Drugs, 2012. 26(12): p. 1071-2.
- 45. Clark, I., C. Atwood, R. Bowen, G. Paz-Filho, et al., *Tumor necrosis factor-induced cerebral insulin resistance in Alzheimer's disease links numerous treatment rationales*. Pharmacol Rev, 2012. **64**(4): p. 1004-26.
- 46. Delrieu, J., A. Piau, and B. Vellas, *Chapter 78- Drug development and Alzheimer's disease*, in *Pathy's Principles and Practice of Geriatric Medicine*, A.J. Sinclair, J.E. Morley, and B. Vellas, Editors. 2012, John Wiley & Sons: West Sussex, UK.
- 47. Kim, C.T., Stroke Rehabilitation, in Rehabilitation Medicine, ISBN 978-953-51-0683-8, DOI: 10.5772/38499, C.T. Kim, Editor 2012, InTech.
- 48. Maudsley, S. and W. Chadwick, *Progressive and unconventional pharmacotherapeutic approaches to Alzheimer's disease therapy*. Curr Alzheimer Res, 2012. **9**(1): p. 1-4.
- 49. McAfoose, J., L. Kulic, T. Welt, C. Spani, et al., Effects of anti-TNF Therapy on Amyloid Pathology and Neuroinflammation in 12-month old ARCA-beta Transgenic Mice. Alzheimer's and Dementia, 2012. 8(4): p. P394.
- 50. Ooi, L. and e. al., New Drugs Under Development for Alzheimer's Disease, in Advances in Alzheimer's Disease Management, S. Gauthier and P. Rosa-Neto, Editors. 2012. p. 58-67.
- 51. Santello, M. and A. Volterra, TNF-alpha in synaptic function: switching gears. Trends Neurosci, 2012. 35(10): p. 638-47.
- 52. Stringer, M.D., M. Restieaux, A.L. Fisher, and B. Crosado, *The vertebral venous plexuses: the internal veins are muscular and external veins have valves.* Clin Anat, 2012. **25**(5): p. 609-18.

100 selected scientific articles 2003-2015 citing publications by Edward Tobinick [53-78]:

- 53. Williams, M. and J.T. Coyle, Chapter 7- Historical perspectives on the discovery and development of drugs to treat neurological disorders, in Translational Neuroscience: Applications in Psychiatry, Neurology, and Neurodevelopmental Disorders, J.E. Barrett, J.T. Coyle, and M. Williams, Editors. 2012, Cambridge University Press: New York, NY. p. 129-148
- 54. Bai, L., N. Song, J. Yu, L. Tan, et al., *Elevated Plasma Levels of Soluble TNFRs and TACE Activity in Alzheimer's Disease Patients of Northern Han Chinese Descent.* Curr Alzheimer Res, 2013. **10**(1): p. 57-62.
- 55. Blaylock, R.L., *Immunology primer for neurosurgeons and neurologists part 2: Innate brain immunity.* Surg Neurol Int, 2013. **4**: p. 118.
- 56. Brambilla, L., F. Martorana, and D. Rossi, *Astrocyte signaling and neurodegeneration: New insights into CNS disorders*. Prion, 2013. 7(1): p. 28-36.
- 57. Cheong, C.U., C.P. Chang, C.M. Chao, B.C. Cheng, et al., *Etanercept attenuates traumatic brain injury in rats by reducing brain TNF- alpha contents and by stimulating newly formed neurogenesis*. Mediators Inflamm, 2013. **2013**: p. 620837.
- 58. Chio, C.C., C.H. Chang, C.U. Cheong, C.M. Chao, et al., Etanercept attentuates traumatic brain injury in rats by reducing early microglial expression of tumor necrosis factor-alpha. BMC Neuroscience, 2013. 14: p. 33.
- 59. Clark, I.A. and B. Vissel, *Treatment implications of the altered cytokine-insulin axis in neurodegenerative disease.* Biochem Pharmacol, 2013. **86**(7): p. 862-71.
- 60. Kaufman, E.L. and A. Carl, Biochemistry of Back Pain. The Open Spine Journal, 2013. 5: p. 12-18.
- 61. Petzold, A. and A. Girbes, Pain Management in Neurocritical Care. Neurocrit Care, 2013 Oct; 19(2):232-56.
- 62. Waters, R.J., G.D. Murray, G.M. Teasdale, J. Stewart, et al., *Cytokine gene polymorphisms and outcome after traumatic brain injury.* J Neurotrauma, 2013. **30**(20): p. 1710-6.
- 63. Yoshiyama, Y., V.M. Lee, and J.Q. Trojanowski, *Therapeutic strategies for tau mediated neurodegeneration*. J Neurol Neurosurg Psychiatry, 2013. **84**(7): p. 784-95.
- 64. Starke, R.M., D. Raper, D. Ding, N. Chalouhi, et al., *Tumor Necrosis Factor-alpha Modulates Cerebral Aneurysm Formation and Rupture*. Translational Stroke Research, 2014 Apr;5(2):269-77.
- 65. Allison, D.J. and D.S. Ditor, *The common inflammatory etiology of depression and cognitive impairment: a therapeutic target.* J Neuroinflammation, 2014. **11**: p. 151.
- 66. Bae, W.C. and K. Masuda, Enhancing disc repair by growth factors and other modalities, in The intervertebral disc: Molecular and structural studies of the disc in health and disease, I.M. Shapiro and M.V. Risbud, Editors. 2014, Springer-Verlag: Wein, Austria. p. 401-416.
- 67. Bastos, L.F. and M.M. Coelho, Drug repositioning: playing dirty to kill pain. CNS Drugs, 2014. 28(1): p. 45-61.
- 68. Cheng, X., Y. Shen, and R. Li, *Targeting TNF: a therapeutic strategy for Alzheimer's disease*. Drug Discov Today, 2014.
- 69. Clausen, B., M. Degn, N. Martin, Y. Couch, et al., Systemically administered anti-TNF therapy ameliorates functional outcomes after focal cerebral ischemia. J Neuroinflammation, 2014. 11(1): p. 203.
- 70. Edwards, M., V.H. Balldin, J. Hall, and S. O'Bryant, *Combining select neuropsychological assessment with blood-based biomarkers to detect mild Alzheimer's disease: a molecular neuropsychology approach.* J Alzheimers Dis, 2014. **42**(2): p. 635-40.
- 71. Faingold, C.L., Chapter 7: Network Control Mechanisms: Cellular Inputs, Neuroactive Substances, and Synaptic Changes, in Neuronal Networks in Brain Function, CNS Disorders, and Therapeutics, C.L. Faingold and H. Blumenfeld, Editors. 2014, Elsevier.
- 72. Ferreira, S.T., J.R. Clarke, T.R. Bomfim, and F.G. De Felice, *Inflammation, defective insulin signaling, and neuronal dysfunction in Alzheimer's disease*. Alzheimers Dement, 2014. **10**(1S): p. S76-S83.
- 73. Gisondi, P., F. Sala, F. Alessandrini, V. Avesani, et al., *Mild cognitive impairment in patients with moderate to severe chronic plaque psoriasis*. Dermatology, 2014. **228**(1): p. 78-85.
- 74. Yasutaka, Y., T. Watanabe, A. Nakashima, et al., *APOE-modulated Abeta-induced neuroinflammation in Alzheimer's disease: current landscape, novel data, and future perspective.* J Neurochem, epub 2015.
- 75. Grossman, J. and S.M. Chamow, *Chapter 10: Etanercept*, in *Therapeutic Fc-Fusion Proteins*, S.M. Chamow, Ryll, T., Lowman, H.B., Farson, D., Editor 2014, Wiley-Blackwell: Weinheim, Germany.
- 76. Hsiao, H.Y., F.L. Chiu, C.M. Chen, Y.R. Wu, et al., *Inhibition of soluble tumor necrosis factor is therapeutic in Huntington's disease*. Hum Mol Genet, 2014. **23**(16): p. 4328-44.
- 77. Liu, C. and J. Tang, Expression levels of tumor necrosis factor-alpha and the corresponding receptors are correlated with trauma severity. Oncol Lett, 2014. 8(6): p. 2747-2751.
- 78. Ohtori, S., G. Inoue, M. Miyagi, and K. Takahashi, *Pathomechanisms of discogenic low back pain in humans and animal models*. Spine J, 2015 June 1;15(6):1347-55.

100 selected scientific articles 2003-2015 citing publications by Edward Tobinick [79-100]:

- 79. Olmos, G. and J. Llado, *Tumor necrosis factor alpha: a link between neuroinflammation and excitotoxicity*. Mediators Inflamm, 2014:861231. doi: 10.1155/2014/861231.
- 80. Rehman, Y., N. Rehman, and R. Rehman, Peripheral cytokines as a chemical mediator for postconcussion like sickness behaviour in trauma and perioperative patients: literature review. Neurol Res Int, 2014. 2014: p. 671781.
- 81. Siniscalchi, A., L. Gallelli, G. Malferrari, D. Pirritano, et al., Cerebral stroke injury: the role of cytokines and brain inflammation. J Basic Clin Physiol Pharmacol, 2014 May 1;25(2):131-7.
- 82. Sun, Q., H. Hampel, K. Blennow, S. Lista, et al., Increased Plasma TACE Activity in Subjects with Mild Cognitive Impairment and Patients with Alzheimer's Disease. J Alzheimers Dis, 2014. 41(3): p. 877-86.
- 83. Trager, U., R. Andre, N. Lahiri, A. Magnusson-Lind, et al., *HTT-lowering reverses Huntington's disease immune dysfunction caused by NFkappaB pathway dysregulation*. Brain, 2014. **137**(Pt 3): p. 819-33.
- 84. Tuttolomondo, A., R. Pecoraro, and A. Pinto, Studies of selective TNF inhibitors in the treatment of brain injury from stroke and trauma: a review of evidence to date. Drug Design, Development and Therapy, 2014. 8: p. 2221-2239.
- 85. Varley, J., D.J. Brooks, and P. Edison, *Imaging neuroinflammation in Alzheimer's and other dementias: Recent advances and future directions*. Alzheimers Dement, 2014 Nov 15.pii: S1552-5260(14)02820-9.
- 86. Wang, K., B. Liu, and J. Ma, Research progress in traumatic brain penumbra. Chin Med J (Engl), 2014. 127(10): p. 1964-8.
- 87. Winkelstein, B.A., K.D. Allen, and L.A. Setton, *Intervertebral disc herniation: Pathophysiology and emerging therapies*, in *The intervertebral disc: Molecular and structural studies of the disc in health and disease*, I.M. Shapiro and M.V. Risbud, Editors. 2014, Springer-Verlag: Wein, Austria. p. 305-326.
- 88. Baratz, R., D. Tweedie, J.Y. Wang, V. Rubovitch, et al., *Transiently lowering tumor necrosis factor-alpha synthesis ameliorates neuronal cell loss and cognitive impairments induced by minimal traumatic brain injury in mice.* J Neuroinflammation, 2015. **12**(1): p. 237.
- 89. Butchart, J., L. Brook, V. Hopkins, J. Teeling, et al., *Etanercept in Alzheimer disease: A randomized, placebo-controlled, double-blind, phase 2 trial.* Neurology, 2015. **84**(21): p. 2161-8.
- 90. Camara, M.L., F. Corrigan, E.J. Jaehne, M.C. Jawahar, et al., *Effects of centrally administered etanercept on behavior, microglia, and astrocytes in mice following a peripheral immune challenge.*Neuropsychopharmacology, 2015. **40**(2): p. 502-12.
- 91. Clark, I.A. and B. Vissel, *A neurologist's guide to TNF biology, and to the principles behind the therapeutic removal of excess TNF in disease.* Neural Plasticity, 2015. article 358623, epub 21 May 2015.
- 92. Coelho-Santos, V., R.A. Leitao, F.L. Cardoso, I. Palmela, et al., *The TNF-alpha/NF-kappaB signaling pathway has a key role in methamphetamine-induced blood-brain barrier dysfunction.* J Cereb Blood Flow Metab, 2015.
- 93. Fasick, V., R.N. Spengler, S. Samankan, N.D. Nader, et al., *The hippocampus and TNF: Common links between chronic pain and depression*. Neurosci Biobehav Rev, 2015. **53**: p. 139-159.
- 94. Heppner, F.L., R.M. Ransohoff, and B. Becher, *Immune attack: the role of inflammation in Alzheimer disease*. Nat Rev Neurosci, 2015. **16**(6): p. 358-72.
- 95. Krauthausen, M., M.P. Kummer, J. Zimmermann, E. Reyes-Irisarri, et al., CXCR3 promotes plaque formation and behavioral deficits in an Alzheimer's disease model. J Clin Invest, 2015. 125(1): p. 365-78.
- 96. Kubra Elcioglu, H., L. Kabasakal, F. Tufan, O.H. Elcioglu, et al., *Effects of systemic Thalidomide and intracerebroventricular Etanercept and Infliximab administration in a Streptozotocin induced dementia model in rats*. Acta Histochem, 2015. **117**(2): p. 176-81.
- 97. Griessenauer, C.J., J. Raborn, P. Foreman, M.M. Shoja, M. Loukas and R. Shane Tubbs, *Venous Drainage of the Spine and Spinal Cord: A Comprehensive Review of its History, Embryology, Anatomy, Physiology, and Pathology.* Clinical Anatomy 2015 Jan; 28(1):75-87.
- 98. Rossi, D., Astrocyte physiopathology: At the crossroads of intercellular networking, inflammation and cell death. Prog Neurobiol, 2015. 130: p. 86-120.
- 99. Tai, L.M., S. Ghura, K.P. Koster, V. Liakaite, et al., APOE-modulated Abeta-induced neuroinflammation in Alzheimer's disease: current landscape, novel data, and future perspective. J Neurochem, 2015 May;133(4):465-88.
- 100. C.H.F. Camargo, F.F. Justus, G. Retzlaff, M.R.Y. Blood, M.D. Schafranski, *Action of anti-TNF-alpha drugs on the progression of Alzheimer's disease. A case report.* Dement Neuropsychol 2015. 9(2):196-200.